



Australian Government

Medical Services Advisory Committee

## Public Summary Document

### ***Application No. 1652 – Transcatheter aortic valve implantation via transfemoral delivery for patients at intermediate risk for surgery***

**Applicant:** Medtronic Australasia

**Date of MSAC consideration:** MSAC 81<sup>st</sup> Meeting, 31 March – 1 April 2021

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

#### **1. Purpose of application**

An Applicant Developed Assessment Report (ADAR) requesting MBS listing of transcatheter aortic valve implantation (TAVI) via transfemoral delivery for patients with severe, symptomatic AS at intermediate risk for surgery was received from Medtronic Australasia Pty Ltd by the Department of Health.

#### **2. MSAC’s advice to the Minister**

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported Medicare Benefits Schedule (MBS) funding of transcatheter aortic valve implantation (TAVI) via transfemoral delivery for patients at intermediate risk for surgery on the grounds of acceptable safety, effectiveness and cost effectiveness compared with surgical aortic valve replacement (SAVR). Consistent with the current MBS item for TAVI (item 38495) and its November 2021 recommendation for TAVI with a balloon expandable valve in intermediate risk for surgery (Application 1603), MSAC supported an MBS item that is agnostic of the type of TAVI device.

MSAC supported the item descriptor as detailed in MSAC Application 1603 ([Public Summary Document \[PSD\] Application No. 1603](#), p5).

<b>Consumer summary</b>
Medtronic Australasia Pty Ltd applied for funding through the Medicare Benefits Schedule (MBS) for transcatheter aortic valve implantation (TAVI) in patients with symptomatic severe aortic stenosis who are at intermediate risk for surgery.
Severe aortic stenosis is a condition that stops blood from flowing easily throughout the body. Eventually this can lead to heart failure because the aortic valve in the heart develops a severe build-up of calcium, which makes it difficult for the valve to open and close.

## Consumer summary

TAVI is a procedure that helps to improve a damaged aortic valve. During a TAVI procedure, an artificial valve made of natural animal heart tissue (usually from a cow or a pig) is implanted into the heart. But instead of standard open heart surgery (where the chest cavity is opened during surgery), in TAVI, a catheter is placed in the femoral artery (in the groin) and guided into the heart.

MSAC accepted that TAVI is a safe and effective procedure, and is better value for money than surgical aortic valve replacement (open heart surgery). MSAC noted that the American College of Cardiology/American Heart Association (ACC/AHA) guidelines emphasised shared decision making on the type of procedure. These guidelines say that this decision should be made for each individual and should take into account factors such as age and other medical conditions, how long valves last before they need to be replaced, and patient preferences. This is important for patients at intermediate risk for surgery, because these people usually have a longer life expectancy than people with high risk for surgery.

MSAC also did not believe there was any overall reason to prefer one type of TAVI device (balloon expandable valve [BEV] or self-expandable valve [SEV]) over another.

### **MSAC's advice to the Commonwealth Minister for Health**

MSAC supported MBS funding for TAVI in patients at intermediate risk for surgery. MSAC considered the procedure to be safe, effective and good value for money.

## **3. Summary of consideration and rationale for MSAC's advice**

MSAC noted that TAVI is currently MBS-listed as a TAVI device agnostic item (either balloon expandable valve [BEV] or self-expandable valve [SEV]) for high-risk/inoperable surgical patients with symptomatic severe aortic stenosis (AS) under item 38495. MSAC also recalled its recent support for a MBS item agnostic of the type of TAVI device in patients with intermediate risk for surgery, noting that this advice would be re-assessed at the March 2021 MSAC meeting ([PSD Application No. 1603, p1](#)).

MSAC considered that SAVR was the appropriate comparator, and noted the clinical claim of non-inferiority.

MSAC reviewed and agreed with the ESC's evaluation of the comparative safety and clinical evidence. MSAC noted that the application was based on randomised controlled trials (RCTs) of TAVI *vs.* SAVR (SURTAVI: TAVI-SEV and PARTNER 2A: TAVI- BEV) in the intermediate risk population. Overall, TAVI is comparatively safe and effective. MSAC considered that TAVI had non-inferior safety compared with SAVR over 2–5 years. MSAC considered that TAVI had non-inferior effectiveness despite that the Kaplan-Meier plots for the primary outcome (death or disabling stroke) had converged in both key trials. MSAC noted that the conclusion of non-inferiority was consistent with its previous conclusions from its consideration of Application 1603, as it had not accepted the clinical claim of superiority of TAVI-BEV *vs.* SAVR ([PSD Application No. 1603](#), pp3-4). MSAC considered the RCT data was more a robust basis than the propensity score adjusted observational study (PARTNER 3Si) to assess the comparative effectiveness and safety of TAVI and SAVR.

MSAC considered the longer-term outcomes, particularly valve durability and paravalvular leakage with TAVI may be particularly relevant in the intermediate surgical risk population because this group may, on average, have a longer life expectancy than the higher risk and

inoperable population. MSAC noted the applicant's pre-MSAC response, which highlighted 10-year follow-up data regarding safety and durability of TAVI from registry data.

MSAC noted that the RCTs used older generation TAVI devices. MSAC noted that there is no RCT comparing the older generation of devices with the newer devices available in Australia. MSAC considered the two published meta-analyses (Tummala 2017 and Ando 2016) and an indirect comparison of the older and new TAVI devices (performed by the commentary). MSAC considered that the indirect comparison should be interpreted with caution. MSAC concluded that these suggested the newer devices (Evolut R and SAPIEN 3) were largely similar to the corresponding older devices in the RCTs (Corevalve and SAPIEN XT). The pre-MSAC response presented additional observational evidence to support its claim that the Evolut R and Evolut PRO devices had similar clinical outcomes. MSAC noted that newer TAVI devices were designed to reduce paravalvular leakage. MSAC noted the pre-MSAC response claimed that outcomes with TAVI will continue to improve due to valve development and improvements in the TAVI procedure. However, MSAC agreed with ESC and considered that there are limited data on whether outcomes are improving with newer generation TAVI devices.

MSAC noted that the cost-minimisation analysis showed that TAVI would result in cost savings to the health system when compared with SAVR. However, these savings may depend on the volume of procedures done as patients tend to have shorter hospital admissions when undergoing TAVI with operators and hospitals that performed a lot of TAVI procedures. MSAC noted that the cost-minimisation analysis depends on the health-related differences associated with faster physical recovery from TAVI than from SAVR, as this is reflected in the shorter length of hospitalisation following TAVI than following SAVR. MSAC recalled that this was a similar driver in the cost-effectiveness analyses of TAVI-BEV vs. SAVR in Application 1603.

MSAC noted the financial estimates showing cost savings to the MBS. MSAC noted that TAVI would increase costs to the MBS if it increases the total number of aortic valve replacement procedures by greater than 39%. MSAC noted that the pre-ESC response had reiterated that the projected cost savings were appropriate and that the risk of leakage into low risk populations was unlikely as patients' surgical risk would be appropriately assessed by a Heart Team. **REDACTED**. MSAC noted that the number of TAVI procedures subsidised by the MBS for the high risk and inoperable population was similar to SAVR procedures. MSAC considered TAVI use may soon exceed that of SAVR on the MBS. Therefore, MSAC concluded there is some uncertainty regarding the potential financial implications.

MSAC noted that the 2017 European Society of Cardiology and the European Association for Cardio-Thoracic Surgery Guidelines for Valvular Heart Disease considered that SAVR is generally preferred in patients under 75 years old. This is because the long-term durability of TAVI devices is unknown, with only preliminary data showing TAVI devices may last at least 5 years without any signs of early degeneration. MSAC also noted the applicant's pre-MSAC response, which highlighted recent clinical guidelines issued by the American College of Cardiology/American Heart Association (ACC/AHA), stating that in (Otto 2021)<sup>1</sup>:

- patients aged <65 years or with life expectancy >20 years: SAVR is preferred
- patients aged >80 years or with life expectancy <10 years: TAVI is preferred

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<sup>1</sup> Otto CM *et al.* 2021 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;143(5):e35-e71.

- symptomatic patients aged 65–80 years with no contraindication to transfemoral TAVI: SAVR or transfemoral TAVI is recommended after shared decision making.

MSAC noted ACC/AHA guidelines emphasised shared decision making regarding procedure choice. The ACC/AHA guidelines state that this decision must be individualised based on the specific operative risk in each patient, clinical factors such as age and comorbid conditions, valve durability, and patient preferences. Durability, safety and effectiveness may improve with newer-generation TAVI devices, however MSAC considered that this has not been demonstrated. MSAC did not consider that an age restriction would be appropriate. MSAC noted the requirement to involve the heart team before a TAVI procedure, and that these heart team discussions should help guide the patient to the appropriate choice.

MSAC noted supportive consumer feedback emphasising the importance of a less invasive procedure, fewer complications (bleeding and atrial fibrillation) faster recovery and shorter hospital stay. MSAC also noted consultation feedback from a TAVI manufacturer that was not supportive of the application and claimed that TAVI-BEV was superior to TAVI-SEV, which MSAC has not accepted.

MSAC considered that monitoring and review of utilisation is important, and that high surgical risk and intermediate surgical risk patients should have separate MBS item numbers to facilitate monitoring. MSAC reaffirmed that the item should be reviewed after 12-24 months.

MSAC concluded that this item should be device agnostic, similar to the current MBS item for TAVI (and SAVR). MSAC did not consider that there was sufficient high quality direct evidence from randomised trials comparing TAVI-BEV and TAVI-SEV to support a difference in comparative safety or effectiveness, nor to support a price advantage for one type of TAVI device over another. A device agnostic approach was supported by the TAVI Accreditation Committee.

#### **4. Background**

##### *TAVI high-risk and inoperable applications (MSAC 1361 series)*

TAVI is currently MBS listed for the treatment of symptomatic severe AS, performed via transfemoral delivery, unless transfemoral delivery is contraindicated or not feasible for patients who, as a result of a TAVI Case Conference, have been assessed as having an unacceptably high risk for surgical aortic valve replacement (SAVR) and are recommended as being suitable to receive TAVI. The current MBS item is device agnostic and does not limit subsidy to a specific TAVI device. MSAC supported the current MBS listing of TAVI at its March 2016 meeting ([MSAC Application 1361.2 Public Summary Document \[PSD\] 2016](#), p1).

##### *TAVI intermediate risk application (MSAC 1603)*

At its November 2020 meeting, MSAC considered a device-specific application ([MSAC Application 1603](#)) to fund TAVI using a balloon-expandable valve (BEV) for the intermediate risk population. This application made the clinical claim that TAVI using a TAVI-BEV system (SAPIEN 3) is superior to SAVR in intermediate risk patients ([MSAC Application Form 1603 PSD](#), p19).

MSAC supported the creation of a new MBS item for TAVI using a BEV system for patients with symptomatic severe AS at intermediate risk for surgery on the grounds of acceptable safety, effectiveness and cost effectiveness compared with SAVR. Consistent with the current MBS item for TAVI (item 38495), MSAC supported an MBS item agnostic of the type of

TAVI device, noting that this advice would be re-assessed at the March 2021 MSAC meeting consideration of the TAVI device agnostic application in intermediate risk for surgery (MSAC Application 1652).

Overall, MSAC concluded that superiority of TAVI-BEV vs. SAVR was not adequately justified over the longer-term results from propensity score analysis. MSAC considered that superiority of TAVI-BEV vs. SEV was not adequately justified.

MSAC noted that the revised modelling provided in the pre-MSAC response showed that TAVI-BEV is dominant (i.e. cheaper and more effective), even with a TAVI device cost of **\$redacted**. However, MSAC noted that the higher Prosthesis List benefit (proposed **\$redacted** for TAVI-BEV compared with the current benchmark of \$22,932 for TAVI-BEV and SEV) is not justified as the 5-year follow-up results from propensity score analysis were not a sufficient basis to conclude superiority of TAVI-BEV over SAVR. In addition, MSAC noted there is the precedent set for similar clinical performance and thus the same benefit across TAVI device options in high risk populations should be the default position in the intermediate risk population. MSAC considered there was no basis to award a higher benefit for one device when the Prostheses List had other devices at a lower benefit. MSAC noted that the pre-MSAC response indicated that the **\$redacted** includes consumables so there would be no net change to price within the private sector (previously purchased by private hospitals and/or patients).

MSAC recommended that the item should be reviewed after 12-24 months.

MSAC noted the need for consistency in MSAC's advice for applications 1652 (TAVI device agnostic application) and 1603 (TAVI-BEV). MSAC considered it would re-assess the decision to support an MBS item agnostic of the type of TAVI after its March 2021 meeting, depending on the outcome of the TAVI device agnostic application in intermediate risk for surgery (MSAC Application 1652). MSAC noted that the process allows MSAC to deal with each application on its merits while acknowledging future applications.

#### *Comparison of TAVI-related applications*

A comparison of the current ADAR (1652) with Application 1603 and Application 1361.2 in the high risk/inoperable populations is presented in Table 1.

**Table 1 Comparison of TAVI applications to MSAC**

Parameter	MSAC 1652 (current application)	MSAC1603 (November 2020)	MSAC 1361.2 (March 2016)
Intervention	TAVI-BEV-and TAVI-SEV	TAVI-BEV	TAVI-BEV-and TAVI-SEV
Patient population	Intermediate risk patients as determined by Heart Team	Intermediate risk patients as determined by Heart Team	High-risk and inoperable patients (not described)
Comparator	SAVR	SAVR and TAVI-SEV	SAVR and medical management
Clinical evidence used for economic model	Length of stay from PARTNER 2A and SURTAVI RCTs	1-year outcomes from PARTNER 3Si	5-year data from the PARTNER trial. The numerically different overall survival estimates following TAVI and SAVR were not statistically significantly
Clinical claim	Non-inferior effectiveness and safety vs. SAVR	Superior effectiveness vs. SAVR (composite outcome: death, stroke, aortic regurgitation) No claim vs. TAVI-SEV	Superior effectiveness vs. SAVR (not accepted by MSAC) and medical management. Inferior safety vs. medical management. Different safety profile vs. SAVR.
Economic evaluation	Cost-minimisation analysis	Cost-utility analysis	Cost-utility analysis
Health states	Not applicable	3 states 1) Alive, no disabling stroke 2) Alive, disabling stroke 3) Dead  The model adjusted for baseline cerebrovascular disease (9.4%) to account for the likelihood that patients have had a prior stroke.	3 states 1) Alive, standard follow-up 2) Alive, with major stroke 3) Dead  No adjustment for pre-existing complications was made.
Time horizon	Short term	10 years (base-case). 5 and 20-year time horizon presented in sensitivity analyses	5-years presented in the base-case and 10-years was presented in sensitivity analyses
Prosthesis cost	TAVI: \$22,932 SAVR: \$7,099 Included in for all patients in cost-minimisation analysis	TAVI-BEV: <b>\$redacted</b> SAVR: \$9,079 ADAR included prosthesis costs for public patients only	TAVI: \$33,348 SAVR: \$6,738 ADAR included prosthesis costs for all patients

Parameter	MSAC 1652 (current application)					MSAC1603 (November 2020)					MSAC 1361.2 (March 2016)					
Length of stay	Source	TAVI	SAVR	Diff. /Ratio		Source	TAVI	SAVR	Diff. /Ratio		Source	TAVI	SAVR	Diff./Ratio		
	Meta-analysis	Mean: 6.0 days	Mean: 10.3 days	4.2 days 1:1.7		BEV: Partner 3Si naive comparison	Median: 4 days	Median: 9 days	5 days 1: 2.25		Yong 2012	6.2 days	12 days	5.8 days 1: 2.0		
	PARTNER 2A	Mean: 6.3	Mean: 10.7	5 days 1: 2.25		SEV: SURTAVI RCT	Mean: 5.75 days ±4.85	Mean: 9.75 days ±8.03	4 days 1:1.7		PARTNER trial	8 days	12 days	4 days 1:1.5		
	SURTA VI RCT	Mean: 5.75 days ±4.85	Mean: 9.75 days ±8.03	4 days 1:1.7							MSAC accepted estimate from PARTNER trial (Smith 2011).					
Hospitalisation cost	TAVI: \$28,170 SAVR: \$47,843					TAVI: \$21,944 SAVR: \$49,375					TAVI: \$24,328 SAVR: \$48,655					
Calculation of SAVR hospital cost	Daily cost of \$4,660 (from NHCD C 2017-18) multiplied SAVR length of stay. Inflated to 2020 costs. AR-DRG codes used: F04A, F04B, F04C					<b>REDACTED.</b> AR-DRG codes used: <b>REDACTED.</b>					Calculated from NHCD C costs. AR-DRG codes used: F04A					
Calculation TAVI of hospital costs	Daily cost (\$4,660) multiplied by TAVI length of stay.					44% of SAVR cost. Based on the median length of hospital stay for TAVI-BEV (4-days) vs. SAVR patients (9-days) from PARTNER S3i					Based on TAVI/SAVR length of stay ratio from unpublished data by Yong (2012). MSAC accepted 1:1.5 from the PARTNER trial.					
Utilisation		<b>2021</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>	<b>2025</b>	<b>REDACTED</b>					Not applicable				
	Eligible (MBS)	418	425	433	440	447		<b>2021</b>	<b>2022</b>	<b>2023</b>	<b>2024</b>					<b>2025</b>
	Uptake	293	298	303	308	313	Uptake (private)	483	495	507	519					531
							Uptake (public)	310	318	326	334					342

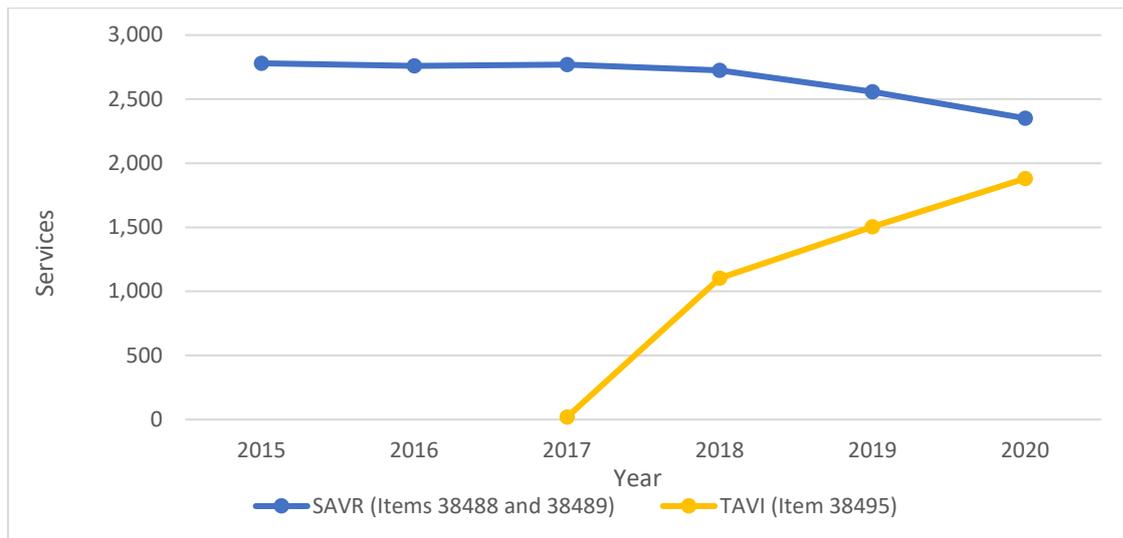
Source: Compiled during the evaluation from Application 1652 ADAR; Application 1603 PSD; Application 1603 ADAR; Application 1361 PSD and Application 1361.2 PSD.  
ADAR = Applicant Developed Assessment Report; AR-DRG = Australian refined diagnosis-related groups; BEV = balloon expandable valve; Diff = difference; NHCD C = National Hospital Cost Data Collection; PSD = Public Summary Document; RCT = randomised controlled trial; SAVR = surgical aortic valve replacement; SEV = self-expanding valve; TAVI = transcatheter aortic valve implantation

*PvA-TAVI high-risk and inoperable application*  
**REDACTED.**

**Table 2** PvA snapshot analysis of TAVI: 01 November 2017 to 31 July 2020 [Redacted]

**REDACTED.**

Figure 1 presents the MBS utilisation of SAVR items (38488 and 38489) and TAVI (item 38489).



**Figure 1** MBS utilisation of SAVR (items 38488 and 38489) and TAVI (item 38489)

Source: Medicare Item Reports, Services Australia. Extracted 15 February 2021

MBS = Medicare Benefits Schedule; SAVR = surgical aortic valve replacement; TAVI = Transcatheter Aortic Valve Implantation

## 5. Prerequisites to implementation of any funding advice

Table 3 presents the TAVI devices registered on the ARTG. There are three TAVI systems that are registered for patients at all levels of surgical risk: Medtronic's Evolut R and Evolut PRO, and Edwards Lifesciences SAPIEN 3. The aforementioned TAVI devices are registered as Class III medical devices. The Evolut R, Evolut PRO, Edwards Lifesciences SAPIEN 3, and Portico TAVI devices are listed on the Prosthesis List as at November 2020.

**Table 3 TAVI devices on the ARTG**

ARTG Number	Device name (abbreviated)	Sponsor	Intended purpose	Patient surgical risk in TGA registered indication
319850	CoreValve Evolut PRO system	Medtronic Australasia Pty Ltd	<i>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</i>	All risk levels
284003	Medtronic CoreValve Evolut R System	Medtronic Australasia Pty Ltd		All risk levels
284496	Edwards SAPIEN 3 Kit	Edwards Lifesciences Pty Ltd		All risk levels
254835	Portico Transcatheter Heart Valve	Abbott Medical Australia Pty Ltd	<i>Transcatheter delivery in patients with symptomatic severe native aortic stenosis who are considered high surgical risk</i>	High risk
326386	LOTUS Edge	Boston Scientific Pty Ltd	<i>To improve aortic valve function for symptomatic patients with severe calcific aortic stenosis (aortic valve area of &lt; 1.0 cm<sup>2</sup> or index of &lt; 0.6 cm<sup>2</sup>/m<sup>2</sup>) who are at high risk for standard surgical valve replacement.</i>	High risk

Source: Table 11, p34 of the ADAR and ARTG public summaries for ARTG entries 319850, 284003, 284496, 254835, 326386. ADAR = Applicant Developed Assessment Report; ARTG = Australian Register of Therapeutic Goods; TGA = Therapeutic Goods Administration

The key trials presented in the ADAR used older generation TAVI devices than those currently registered on the ARTG and the listed on the Prosthesis List. Table 4 presents a comparison of the TAVI devices used in the key trials and devices currently registered for use in intermediate-risk patients. The newer devices Evolut PRO and Sapien 3 have additional features designed to reduce paravalvular leakage (Classen 2020)<sup>2</sup>.

<sup>2</sup> Claessen BE, Tang GH, Kini AS, Sharma SK. Considerations for Optimal Device Selection in Transcatheter Aortic Valve Replacement: A Review. JAMA cardiology. 2020 Sep 9.

**Table 4 Comparison of older TAVI devices used in the clinical trials and newer devices registered for intermediate risk patients**

Parameter	CoreValve	Evolut R	Evolut PRO	Sapien XT	Sapien 3
Prosthesis List (Nov 2020)	No	Yes	Yes	No	Yes
Use in trials	Yes	Yes	No	Yes	No
Expansion	Self-expanding	Self-expanding	Self-expanding	Balloon expandable	Balloon expandable
Frame	Nitinol	Nitinol	Nitinol	Cobalt-chromium	Cobalt-chromium
Valve tissue	Porcine pericardial	Porcine pericardial	Porcine pericardial	Bovine pericardial	Bovine pericardial
Valve size (mm)	26, 29, 31	23, 26, 29, 34	23, 26, 29	23, 26, 29	20, 23, 26, 29
Sheath sizes	18F	14F (23-29 mm) 16F (34 mm only)	16F equivalent	16F (23 mm) 18F (26 mm) 20F (29 mm)	14F (20-26 mm) 16F (29 mm)
Positioning	Supra-annular	Supra-annular	Supra-annular	Intra-annular	Intra-annular
Repositionable	Yes	Yes	Yes	No	No
Retrievable	Yes	Yes	Yes	No	No
New features	-	-	Outer pericardial skirt to reduce paravalvular leakage	-	Outer skirt surrounding valve frame to reduce paravalvular leakage
Transvalvular gradient	May have lower gradients than intra-annular devices.			May result in higher residual gradients particularly in patients with smaller annuli (clinical significance unknown)	
Coronary access	More difficult due to higher frame height and diamond frame lattice			Easier due to lower stent frame	

Source: Compiled during the evaluation from Table 24, p61; Table 90, p159 of the ADAR; Table 1, pE3 of Classen (2020); and November 2020 Prosthesis List

ADAR = Applicant Developed Assessment Report; F = French sizing (1F = 0.33 mm); Nov = November

## 6. Proposal for public funding

The MBS item descriptor proposed in the ADAR is given in Table 5.

**Table 5 Proposed MBS item descriptor (unchanged) and proposed amendment to explanatory notes (abridged)**

Category 3 – THERAPEUTIC PROCEDURES – Surgical Operations
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. TN.8.135 Transcatheter Aortic Valve Implantation (Item 38495)
A TAVI Patient means a patient who, as a result of a TAVI Case Conference, has been assessed as having an <b>intermediate</b> <sup>a</sup> or unacceptably high risk for surgical aortic valve replacement and is recommended as being suitable to receive the service described in item 38495...”
Fee: \$1,476.95

Source: Table 12, p36 of the ADAR. **Bold** = proposed changes to the explanatory notes

ADAR = Applicant Developed Assessment Report; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality Score; TAVI = transcatheter aortic valve implantation;

<sup>a</sup> A patient is defined at intermediate risk of surgery if they meet the following criteria: No more than mild frailty; AND STS-PROM 4-8%; OR One major organ system compromise not to be improved post-operatively; OR Possible procedure-specific impediment

## 7. Summary of public consultation feedback/consumer Issues

Public consultation surveys were received from one consumer organisation, a medical device manufacturer and a specialist.

The consumer organisation (Hearts4Heart) was highly supportive of the application. The feedback highlighted that:

- patients are mobile following TAVI and can be discharged relatively quickly after the procedure. Physical recovery from SAVR is much longer. Faster discharge from hospital and faster recovery are highly valued by patients;
- there are several randomised controlled trials supporting the use of TAVI patients irrespective of surgical risk. However, TAVI is only subsidised for patients with a higher surgical risk;
- patients must be assessed by a Heart Team for TAVI. This was considered beneficial for patients, but it was noted that this is not required for SAVR;
- TAVI has similar outcomes to SAVR but patients are less likely to develop atrial fibrillation or experience life-threatening or disabling bleeding; and
- TAVI provides an alternative to SAVR that is less invasive and requires less hospital care (operating theatres, intensive care, and longer stay in hospital).

The competitor medical device manufacturer feedback considered that:

- the SAPIEN 3 TAVI-BEV device should be excluded from the current application as application 1603 for TAVI-BEV was supported by MSAC
- the SAPIEN 3 device is a comparator for SEVs and evaluating the difference between TAVI-BEV and TAVI-SEV is therefore important
- the PARTNER 2A trial is not appropriate as the SAPIEN XT valve (not marketed in Australia) was used and not the SAPIEN 3 valve. PARTNER S3i (Thourani 2016), a propensity score adjusted observational study should instead be used
- TAVI-BEV (SAPIEN 3) is clinically superior to SAVR based on Thourani 2016. TAVI-SEV using the self-expandable valves (SEV) CoreValve and Evolut R are non-inferior to SAVR based on a direct RCT (Reardon 2017)
- the clinical claim was inappropriate and uncertain as it assumed all TAVI valves are non-inferior to SAVR, reiterating the findings of Thourani 2016 and Reardon 2017. The feedback claimed non-inferiority have not been established for the Potico and

Acurate Neo SEVs. The SCOPE I trial (Lanz 2019<sup>3</sup>) reported that TAVI-SEV with ACURATE Neo being inferior compared to TAVI-BEV with SAPIEN 3. The feedback also referred to real-world observational studies Deharo (2020)<sup>4</sup> and van Belle (2019)<sup>5</sup> as supporting differences between SAPIEN 3 and Evolut R.

The specialist who has personally deployed Evolut-R valves into high risk patients, was in favour of the application and considered that the benefits to the patients would be shorter stays in hospital and less morbidity and mortality.

## **8. Proposed intervention's place in clinical management**

### **Description of Proposed Intervention**

The procedure relevant to this application consists of the transfemoral insertion of a minimally invasive prosthetic heart valve that is positioned within the native aortic annulus. Once in situ, the valve is expanded while the heart is rapidly paced. The procedure is performed under fluoroscopic and transoesophageal guidance and under general anaesthesia or sedation and local anaesthetic.

The procedure can be performed using either a self-expandable, mechanically expandable or balloon-expandable device. Once the correct position is confirmed, the heart is again rapidly paced, the balloon or valve is expanded until the device meets native annular walls, and the guide wire, catheter and balloon (if present) are removed.

### **Description of Medical Condition(s)**

Severe aortic stenosis is the abnormal narrowing of the aortic valve, which restricts the flow of blood from the left ventricle of the heart into the aorta. When the heart contracts to pump oxygenated blood from the left ventricle into the aorta, the aortic valve opens. If the aortic valve is narrowed, the heart no longer pumps blood efficiently and therefore, increases the blood pressure inside the left ventricle. In response to the extra workload, the muscle of the left ventricle thickens (concentric hypertrophy) and the chamber itself may eventually balloon out. Left untreated, congestive heart failure develops, and death is likely. This application is relevant to patients with severe, symptomatic aortic stenosis classified as being at intermediate risk for surgery. 'Intermediate risk' is historically defined by a predicted 30-day risk of surgical mortality of 4-8%, based on the Society of Thoracic Surgeons Predicted Risk of Mortality score.

### **Clinical place**

The key difference between the current and proposed clinical management pathway is the addition of TAVI as an alternative to SAVR. The ADAR's clinical management algorithm (Figure 2) differed from the Ratified PICO as it included referral to a cardiologist after presentation to a GP, included medical management as an option following referral, and removed repeat aortic valve replacement (with SAVR) following complications. The

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<sup>3</sup> Lanz J, Kim WK, Walther T, et al. Safety and efficacy of a self-expanding versus a balloon-expandable bioprosthesis for transcatheter aortic valve replacement in patients with symptomatic severe aortic stenosis: a randomised non-inferiority trial. *Lancet*. 2019;394(10209):1619-1628.

<sup>4</sup> Deharo P, Bisson A, Herbert J, et al. Impact of Sapien 3 Balloon-Expandable Versus Evolut R Self-Expandable Transcatheter Aortic Valve Implantation in Patients With Aortic Stenosis: Data From a Nationwide Analysis. *Circulation*. 2020;141(4):260-268.

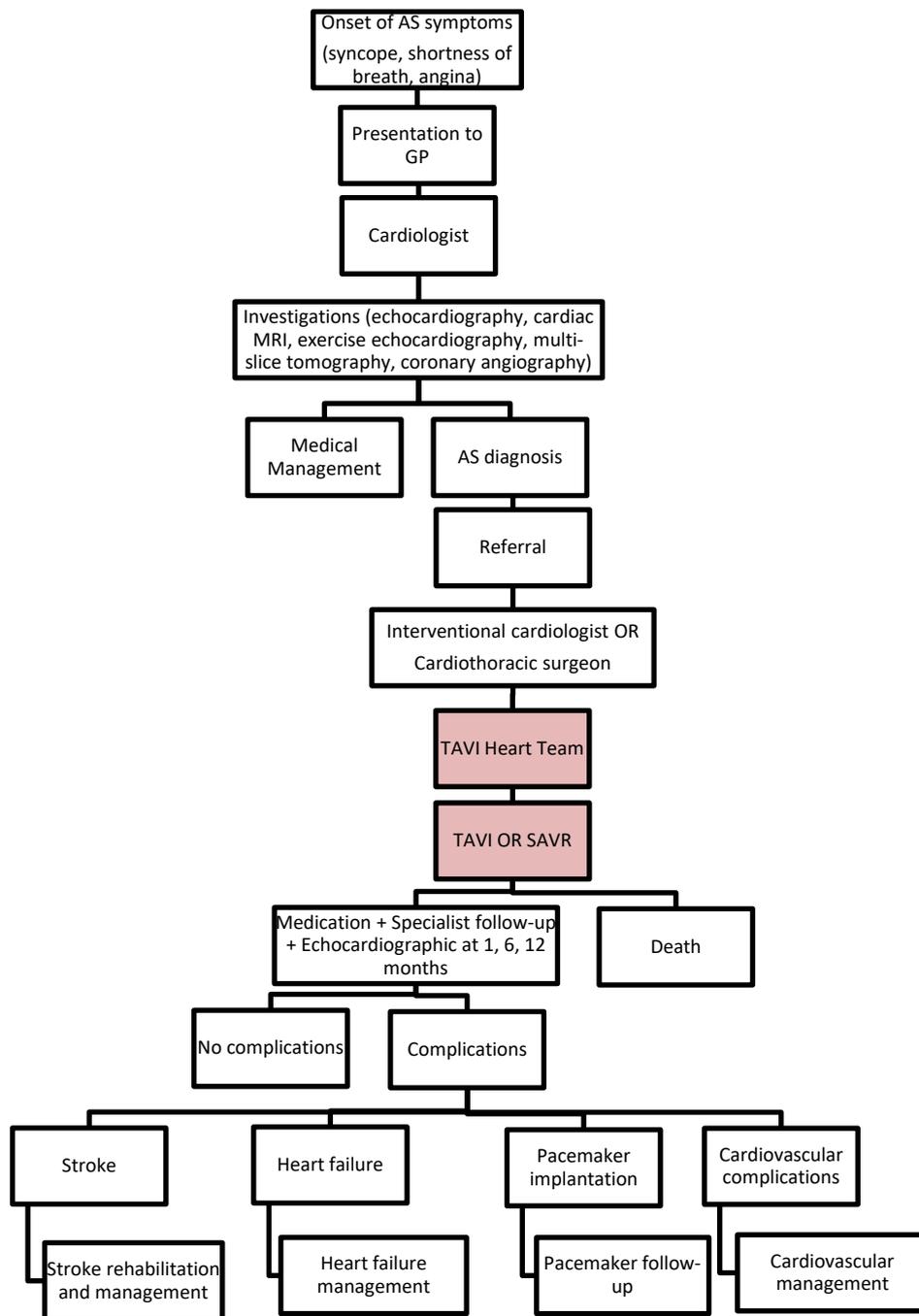
<sup>5</sup> Van Belle E, Vincent F, Labreuche J, et al. Balloon-Expandable Versus Self-Expanding Transcatheter Aortic Valve Replacement: A Propensity-Matched Comparison From the FRANCE-TAVI Registry. *Circulation*. 2020;141(4):243-259.

Commentary considered the removal of reintervention from the algorithm was not appropriate as the rates of reintervention were numerically (but not statistically significantly) higher in the TAVI arms (relative to SAVR) of the key trials. The Commentary also considered that the inclusion of medical management as a separate pathway that occurs before AS diagnosis may not be reflective of clinical practice as medical management is not a first line therapy for an operable patient.

The Commentary highlighted that the proposed algorithm did not consider the patient's age as an important factor in the choice between SAVR and TAVI-BEV. The European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Guidelines for Valvular Heart Disease, considered that SAVR is generally preferred in patients under 75 years and TAVI-BEV in patients 75 years and older. This is because the long-term durability of TAVI devices is unknown, with only preliminary data showing TAVI devices may last at least five-years without any signs of early degeneration (Baumgartner et al., 2017)<sup>6</sup>. In comparison, SAVR valves are estimated to last 10 to 15 years. The pre-MSAC response highlighted that the ESC/EACTS guidelines were developed before several studies reported on the long term durability of TAVI valves over 5-10 years follow-up.

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<sup>6</sup> Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38(36):2739-2791.



**Figure 2 Current and proposed clinical management algorithm for the TAVI in the intermediate surgical risk population**

Source: Figure 3, p42 of the ADAR noting the ADAR created this algorithm with adjustments (addition of cardiologist following presentation of GP, addition of medical management option following referral and removal of repeat aortic valve replacement following complications) from the figure in [1552 Ratified PICO](#) (p10)

ADAR = Applicant Developed Assessment Report; AS = aortic stenosis; GP = General Practitioner; MRI = magnetic resonance imaging; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation

Note: Addition of TAVI represented as orange boxes.

## 9. Comparator

The comparator for TAVI in the proposed intermediate surgical risk population is SAVR- an open-heart surgical procedure to repair or remove the narrowed aortic valve and replace it with a bioprosthesis or mechanical aortic valve. The Commentary considered that this is was appropriate and consistent with the Ratified PICO. Following the SAVR procedure, patients recover in the intensive care unit (ICU) on a ventilator with a chest drain tube and pacing wire for a few days before moving to a surgical ward.

The ADAR anticipated the following MBS items would be used in combination with the SAVR procedure (item 38488 and Item 38489): surgical assistance (item 51303), anaesthesia (items 21941 and 23118), ICU attendance (item 13870), transthoracic echocardiography (Item 55113), and Whole body perfusion for cardiac bypass (item 22060).

The ADAR considered that TAVI will replace SAVR and will provide similar clinical outcomes but reduce patient length of hospital stay (in both ICU and the surgical ward) and therefore reduces amount of hospital staff resourcing required for recovery.

## 10. Comparative safety

A systematic review of published literature was undertaken. The ADAR presented evidence from two RCTs that compared TAVI with SAVR in patients with an intermediate risk from surgery:

- PARTNER 2A<sup>7,8</sup>, a RCT with that compared TAVI (SAPIEN-XT device) with SAVR in 2,032 patients with severe AS at intermediate risk of surgery; and
- SURTAVI<sup>9</sup>, a RCT with that compared TAVI (CoreValve or Evolut R device) with SAVR in 1,660 patients with severe AS at intermediate risk of surgery.

The key RCTs presented in the ADAR are summarised in Table 6. The RCTs used predominantly older generation TAVI devices that are no longer marketed in Australia. Two observational studies (Yakubov 2020<sup>10</sup> and PARTNER 3Si<sup>11</sup>) were included in indirect comparisons (performed during evaluation) comparing the older generation devices with the corresponding newer generation device.

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<sup>7</sup> Leon MB, Smith CR, Mack MJ, et al. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med.* 2016;374(17):1609-1620.

<sup>8</sup> Makkar RR, Thourani VH, Mack MJ, et al. Five-Year Outcomes of Transcatheter or Surgical Aortic-Valve Replacement. *N Engl J Med.* 2020;382(9):799-809.

<sup>9</sup> Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med.* 2017;376(14):1321-1331.

<sup>10</sup> Yakubov SJ, Van Mieghem NM, Reardon MJ, et al. Propensity-Matched Comparison of Evolut-R Transcatheter Aortic Valve Implantation With Surgery in Intermediate-Risk Patients (from the SURTAVI Trial). *Am J Cardiol.* 2020;131:82-90.

<sup>11</sup> Thourani VH, Kodali S, Makkar RR, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. *Lancet.* 2016;387(10034):2218-2225.

**Table 6 Key features of the included evidence comparing TAVI with SAVR and comparing older and newer generation TAVI devices**

Trial/Study (device)	N	Design/duration	Risk of bias	Patient population	Key outcome(s)	Used in economic evaluation
<b>TAVI vs. SAVR</b>						
PARTNER 2A (SAPIEN-XT)	2,032	R, OL, MC 5 years	<i>Some concerns</i> <sup>a</sup>	Severe AS, intermediate risk (4.0-8.0%) <sup>a</sup>	Death, disabling stroke, bleeding, vascular, MI, AKI, AF, pacemaker implantation, paravalvular leakage, HRQoL, reintervention, length of stay	Yes (meta-analysis)
SURTAVI (CoreValve, CoreValve Evolut R)	1,746	R, OL, MC 2 years	<i>Some concerns</i> <sup>a</sup>	Severe AS, intermediate risk (3-15%) <sup>b</sup>		Yes (meta-analysis)
Meta-analysis	3,210 k=2	-	-	PARTNER 2A (TF cohort) + SURTAVI		Yes length of stay
<b>Observational studies of newer generation TAVI devices</b>						
Yakubov (2020) (CoreValve Evolut R)	570	Cohort, 1 year	Moderate	Severe AS, intermediate risk (3-15%) <sup>b</sup>	Death, disabling stroke, aortic regurgitation, reintervention	No
PARTNER 3Si (SAPIEN 3)	2,021	Cohort, 1 year	Moderate	Severe AS, intermediate risk (4.0-8.0%)	Death, disabling stroke, paravalvular regurgitation, reintervention	No

Source: Compiled during the evaluation using Section B of the ADAR; Leon (2016) and Reardon (2017)

Abbreviations: AS = aortic stenosis; HRQoL = health-related quality of life; MC=multi-centre; OL=open label (unblinded); R=randomised; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality Score; TAVI = transcatheter aortic valve implantation; TF = transfemoral

<sup>a</sup> Both trials lacked allocation concealment. More patients withdrew from the SAVR arm after randomisation but before the procedure in both trials: 6.7% vs 1.1% for SAVR and TAVI, respectively in PARTNER 2A and 5.0% vs 0.7% for SAVR and TAVI, respectively in SURTAVI.

<sup>a</sup> 30-day mortality risk as assessed by multidisciplinary Heart Team using STS-PROM. Included patients with STS-PROM < 4% if there coexisting conditions not represented in the risk model.

<sup>b</sup> 30-day mortality risk as assessed by multidisciplinary Heart Team using STS-PROM and non-traditional factors as coexisting illnesses, frailty, and disability.

Table 7 presents the key bleeding outcomes from the key trials. TAVI was associated with fewer bleeding events in the PARTNER 2A trial. This may be a more robust basis for assessment as PARTNER 2A assessing bleeding according to the Valve Academic Research (VARC-2) criteria. SURTAVI used a different definition of ‘overt bleeding’ than the standard VARC-2 definition to prevent classification of SAVR patients with procedural haemodilution as having a bleeding event without a true procedural complication and likely contributed to the SAVR arm reporting fewer bleeding events. The ADAR also presented a meta-analysis pooling bleeding outcomes from the two RCTs; however, this was considered uninformative and having poor quality of evidence due to the high statistical heterogeneity most likely due to differences in the definitions of bleeding.

**Table 7 Key bleeding outcomes from the RCTs**

Outcomes Follow-up	Participants (studies)	Quality of evidence (GRADE)	Risk with TAVI n/N (%)	Risk with SAVR n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
<b>Life-threatening or disabling bleeding – 30 days <sup>a</sup></b>						
PARTNER 2A	N = 1,550	⊕⊕⊕ Moderate	52/775 (6.7%)	320/775 (41.3%)	<b>0.16</b> (0.12, 0.21)	<b>-34.6%</b> (-38.5%, -30.7%)
SURTAVI	N = 1,660	⊕⊕⊕ Moderate	49/864 (5.7%)	47/796 (5.9%)	0.96 (0.65, 1.42)	-0.2% (-2.5%, 2.0%)
<b>Life-threatening or disabling bleeding – 2 years <sup>a</sup></b>						
PARTNER 2A	N = 1,550	⊕⊕⊕ Moderate	101/775 (13.0%)	341/775 (44.0%)	<b>0.30</b> (0.24, 0.36)	-31.0% (-35.2%, -26.8%)
SURTAVI	N = 1,660	⊕⊕⊕ Moderate	71/864 (8.2%)	65/796 (8.2%)	1.01 (0.73, 1.39)	0.05% (-2.6%, 2.7%)

Source: Table 32-33 of the ADAR and included during the evaluation; **bold** = statistically significant

ADAR = Applicant Developed Assessment Report; BARC = Bleeding Academic Research Consortium; CI = confidence interval; RCT = randomised controlled trial; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; VARC-2 = Valve Academic Research Consortium

<sup>a</sup> Both trials used the VARC-2 definition of life-threatening or disabling. SURTAVI used a modified definition of “overt bleeding” which required any of: reoperation after closure of sternotomy for the purpose of controlling bleeding (BARC Type 4); chest tube output 2 L within a 24 hour period (BARC Type 4) or 350 cc within 1st hour post operation or ≥ 250 cc. 2nd hour post operation or 150 cc 3rd hr. post operation bleeding from the vascular system outside of the access site (TAVI); bleeding from an access site that requires an intervention (TAVI); or bleeding from the vascular system outside of the surgical site (SAVR).

The meta-analysis of key safety outcomes and 5-year outcomes from PARTNER 2A are presented in Table 8. Compared with SAVR, TAVI was associated with more major vascular complications, a known risk from the delivery of TAVI through the vasculature. There were consistently more vascular complications in PARTNER 2A, however the risk difference between the TAVI and SAVR arms were consistent in both trials over 2 years.

TAVI was also associated with higher rates of aortic valve reintervention, and paravalvular regurgitation/leaks. The Commentary highlighted that at 5-years in the PARTNER 2A trial, TAVI was associated with higher rates of aortic valve reintervention due to progressive aortic-valve stenosis or regurgitation (paravalvular or combined paravalvular and transvalvular). The hazard ratio for reintervention in PARTNER 2A increased from 0.92 (0.23 to 3.67) at 2 years follow-up to 3.48 (1.30 to 9.33) at 5 years follow-up. The Commentary considered that this may suggest there was an increasing risk of aortic valve reintervention with TAVI.

The meta-analyses of permanent pacemaker implantation did not find a statistically significant difference. However, the Commentary highlighted that SURTAVI, which used the CoreValve self-expanding TAVI device, reported higher rates of permanent pacemaker implantation. The ADAR suggested that this was due to self-expanding valves exerting continuous radial force and may exert external pressure on the conduction system. Classen (2020) noted that pre-existing right bundle branch block or short membranous septal length are risk factors for permanent pacemaker implantation. Additionally, Classen (2020) highlighted that low valve implantation and increased valve oversizing are predictors for new permanent pacemaker implantation. The difference in rates of new permanent pacemaker implantation may reflect different baseline risks for conduction abnormalities, different implantation techniques and potential differences in TAVI devices. These differences may also occur in Australian clinical practice.

TAVI was associated with a lower likelihood of new onset atrial fibrillation compared with SAVR. The Commentary noted that there was substantial heterogeneity in the meta-analysis

as SURTAVI had substantially higher rates of atrial fibrillation in both arms. This made the meta-analysis difficult to interpret.

TAVI appeared to be associated with less acute kidney injury compared with SAVR. The results were statistically significant in PARTNER 2A but not in SURTAVI. The Commentary considered the meta-analysis based on relative risk may be the more reliable measure as the absolute rate of kidney injury differed in the SAVR arm of the two trials, resulting in substantial heterogeneity in the analysis of risk difference.

The Commentary considered the safety of TAVI over 2-5 years was supported by the evidence presented in the ADAR. However, the long-term safety of TAVI is unknown, particularly in terms of valve durability and paravalvular leakage.

**Table 8 Summary of key safety outcomes**

Outcomes Follow-up	Participants (studies)	Quality of evidence (GRADE)	Risk with TAVI n/N (%)	Risk with SAVR n/N (%)	Relative risk (95% CI) [I <sup>2</sup> ]	Risk difference (95% CI) [I <sup>2</sup> ]
<b>30 day outcomes</b>						
Major vascular complications (30 days)	N = 3,210 K = 2	⊕⊕⊕⊕ High	117/1639 (7.1%)	39/1571 (2.5%)	<b>3.23</b> <b>(1.38, 7.57)</b> [I <sup>2</sup> = 77%]	<b>4.7%</b> <b>(3.3%, 6.1%)</b> [I <sup>2</sup> = 0%]
Myocardial infarction (30 days)	N = 3,210 K = 2	⊕⊕⊕ Moderate	12/1,639 (0.7%)	21/1,571 (1.3%)	0.57 (0.22, 1.44) [I <sup>2</sup> = 39%]	-0.6% (-1.7%, 0.5%) [I <sup>2</sup> = 58%]
Acute kidney injury (Stage 3) (30 days)	N = 3,210 K = 2	⊕⊕⊕⊕ High	10/1,639 (0.6%)	34/1,571 (2.2%)	<b>0.30</b> <b>(0.11, 0.86)</b> [I <sup>2</sup> = 53%]	-1.5% (-3.3%, 0.3%) [I <sup>2</sup> = 79%]
Atrial fibrillation (30 days)	N = 3,210 K = 2	⊕⊕⊕⊕ High	147/1,639 (9%)	546/1,571 (34.8%)	<b>0.24</b> <b>(0.15, 0.37)</b> [I <sup>2</sup> = 82%]	<b>-25.8%</b> <b>(-34.8%, -16.9%)</b> [I <sup>2</sup> = 91%]
New permanent pacemakers (30 days)	N = 3,210 K = 2	⊕⊕ Low <sup>a</sup>	279/1,639 (17.0%)	102/1,571 (6.5%)	2.19 (0.62, 7.81) [I <sup>2</sup> = 97%]	10.0% (-8.3%, 28.4%) [I <sup>2</sup> = 99%]
Aortic valve reintervention (30 days)	N = 3,210 K = 2	⊕⊕ Low <sup>b</sup>	10/1,639 (0.6%)	1/1,571 (0.1%)	<b>6.63</b> <b>(1.20, 36.62)</b> [I <sup>2</sup> = 0%]	<b>0.5%</b> <b>(0.1%, 0.9%)</b> [I <sup>2</sup> = 0%]
<b>2-5 year outcomes</b>						
Major vascular complications (2 years)	N = 3,210 K = 2	⊕⊕⊕⊕ High	123/1,639 (7.5%)	43/1,571 (2.7%)	<b>3.21</b> <b>(1.19, 8.66)</b> [I <sup>2</sup> = 84%]	<b>4.9%</b> <b>(3.5%, 6.4%)</b> [I <sup>2</sup> = 0%]
Myocardial infarction (2 years)	N = 3,210 K = 2	⊕⊕⊕ Moderate	43/1,639 (2.6%)	45/1,571 (2.9%)	0.94 (0.54, 1.62) [I <sup>2</sup> = 41%]	-0.2% (-1.7%, 1.4%) [I <sup>2</sup> = 47%]
Acute kidney injury (Stage 3) (2 year)	N = 3,210 K = 2	⊕⊕⊕⊕ High	24/1,639 (1.5%)	56/1,571 (3.6%)	<b>0.42</b> <b>(0.26, 0.68)</b> [I <sup>2</sup> = 0%]	-2.0% (-5.3%, 1.4%) [I <sup>2</sup> = 89%]
Atrial fibrillation (2 year)	N = 3,210 K = 2	⊕⊕⊕⊕ High	238/1,639 (14.5%)	580/1,571 (36.9%)	<b>0.35</b> <b>(0.20, 0.61)</b> [I <sup>2</sup> = 92%]	<b>-22.5%</b> <b>(-27.6%, -17.4%)</b> [I <sup>2</sup> = 68%]

Outcomes Follow-up	Participants (studies)	Quality of evidence (GRADE)	Risk with TAVI n/N (%)	Risk with SAVR n/N (%)	Relative risk (95% CI) [I <sup>2</sup> ]	Risk difference (95% CI) [I <sup>2</sup> ]
New permanent pacemakers (2 years)	N = 3,210 K = 2	⊕⊕ Low <sup>a</sup>	344/1,639 (21%)	146/1,571 (9.3%)	1.96 (0.64, 6.02) [I <sup>2</sup> = 97%]	11.2% (-9.2%, 31.5%) [I <sup>2</sup> = 99%]
Aortic valve reintervention (2 years)	N = 3,210 K = 2	⊕⊕ Low <sup>b</sup>	29/1,639 (1.8%)	9/1,571 (0.6%)	<b>2.90</b> <b>(1.15, 7.32)</b> [I <sup>2</sup> = 32%]	1.1% (-0.2%, 2.4%) [I <sup>2</sup> = 68%]
Aortic valve reintervention (5 years)	N = 1,550 K = 1	⊕⊕ Low <sup>b</sup>	19/775 (2.5%)	5/775 (0.6%)	<b>3.8</b> <b>(1.43, 10.13)</b>	<b>1.9%</b> <b>(0.67, 3.13%)</b>
Paravalvular regurgitation or leaks (2 years)	N = 2,243 K = 2	⊕⊕⊕⊕ High	72/1,226 (5.9%)	4/1,017 (0.4%)	<b>14.94</b> <b>(5.54, 40.75)</b> [I <sup>2</sup> = 0%]	<b>5%</b> <b>(1%, 9%)</b> [I <sup>2</sup> = 88%]

Source: Table 33-38 and 41-47 pp77-94 of the ADAR; Table S8, pp43 of Leon (2016) Supplementary Appendix; Table S11, pp44-45 of Makkar (2020) Supplementary Appendix; Table 40, pp143-149 of the SURTAVI CSR; and calculated during the evaluation; **bold** = statistically significant

ADAR = Applicant Developed Assessment Report; CI = confidence interval; RCT = randomised controlled trial; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation

<sup>a</sup> New permanent pacemaker implantation meta-analysis reassessed as having serious limitations (-1) due to inconsistency and low quality of evidence. Quality of RCT evidence not upgraded. The Pre-ESC response agreed with the reassessment.

<sup>b</sup> Reassessed as having serious limitations (-2) in imprecision as the PARTNER 2A trial not powered to evaluate the transfemoral-access cohort separately and low number of events affecting the robustness of the results. Overall quality of evidence was reassessed as low.

## 11. Comparative effectiveness

The meta-analysis of the primary composite outcome (all-cause mortality or disabling stroke) showed no statistically significant difference between TAVI and SAVR reported at 1 year or beyond (Table 9). Non-inferiority of TAVI vs. SAVR was met in individual trials and meta-analysis of the primary end point at 2 years. The Commentary highlighted that the Kaplan-Meier plots for the primary outcome show the convergence around 3.5 years in PARTNER 2A (Figure 3) and 1.25 years for SURTAVI (Figure 4).

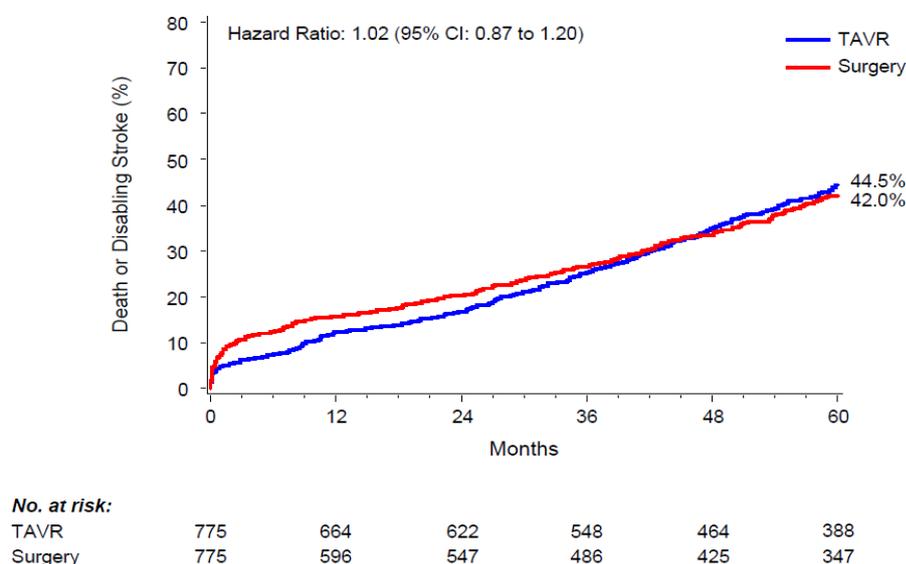
TAVI had lower rates of disabling stroke than SAVR at 30 days and at 2 years. There was no difference in mortality between TAVI and SAVR. The Commentary noted that the trials were not powered to detect differences in mortality, rather the composite of disabling stroke and mortality. PARTNER 2A consistently had higher mortality for the SAVR arms. The Commentary considered that this may be due to patients in PARTNER 2A having a slightly higher STS-PROM score (5.7-5.8 in PARTNER 2A vs. 4.4-4.5 in SURTAVI). The 30-day mortality rate with SAVR in the PARTNER 2A trial was consistent with the STS-PROM estimate of 4-8% mortality at 30 days. The transthoracic-access cohort in the PARTNER 2A trial had a higher incidence of death or disabling stroke than SAVR. The SAVR arm of SURTAVI had lower 30-day mortality than would be expected of an intermediate risk population. However, the Commentary considered these differences might be due to difficulty predicting patients' surgical mortality risk.

**Table 9 Summary of effectiveness outcomes**

Outcomes (units) Follow-up	Participants (studies)	Quality of evidence (GRADE)	Risk with TAVI n/N (%)	Risk with SAVR n/N (%)	Relative risk (95% CI)	Risk difference (95% CI)
Primary composite: all-cause mortality or disabling stroke (30 days)	N = 3,210 K = 2	⊕⊕⊕ Moderate	62/1,639 (3.8%)	89/1,571 (5.7%)	<b>0.68</b> <b>(0.49, 0.93)</b> <i>I</i> <sup>2</sup> = 0%	-1.7% (-3.4%, 7.3%) <i>I</i> <sup>2</sup> = 30%
Primary composite: all-cause mortality or disabling stroke (2 years)	N = 3,210 K = 2	⊕⊕⊕ Moderate	236/1,639 (14.4%)	246/1,571 (15.7%)	0.93 (0.78, 1.10) <i>I</i> <sup>2</sup> = 8%	-1.0% (-4.0%, 2.0%) <i>I</i> <sup>2</sup> = 32%
All-cause mortality (30 days)	N = 3,210 K = 2	⊕⊕⊕ Moderate	41/1,639 (2.5%)	44/1,571 (2.8%)	0.92 (0.55, 1.55) <i>I</i> <sup>2</sup> = 31%	0.2% (-1.7%, 1.3%) <i>I</i> <sup>2</sup> = 46%
All-cause mortality (2 years)	N = 3,210 K = 2	⊕⊕⊕ Moderate	206/1,639 (12.6%)	204/1,571 (13.0%)	0.98 (0.76, 1.26) <i>I</i> <sup>2</sup> = 48%	-0.2% (-3.6%, 3.1%) <i>I</i> <sup>2</sup> = 51%
Disabling stroke (30 days)	N = 3,210 K = 2	⊕⊕⊕ Moderate	28/1,639 (1.7%)	51/1,571 (3.2%)	<b>0.53</b> <b>(0.34, 0.84)</b> <i>I</i> <sup>2</sup> = 0%	<b>-1.4%</b> <b>(-2.4%, -0.4%)</b> <i>I</i> <sup>2</sup> = 0%
Disabling stroke (2 year)	N = 3,210 K = 2	⊕⊕⊕ Moderate	58/1,639 (3.5%)	78/1,571 (5%)	<b>0.67</b> <b>(0.47, 0.95)</b> <i>I</i> <sup>2</sup> = 0%	<b>-1.6%</b> <b>(-2.9%, -0.3%)</b> <i>I</i> <sup>2</sup> = 0%

Source: Table 49-54, pp97-102 of the ADAR

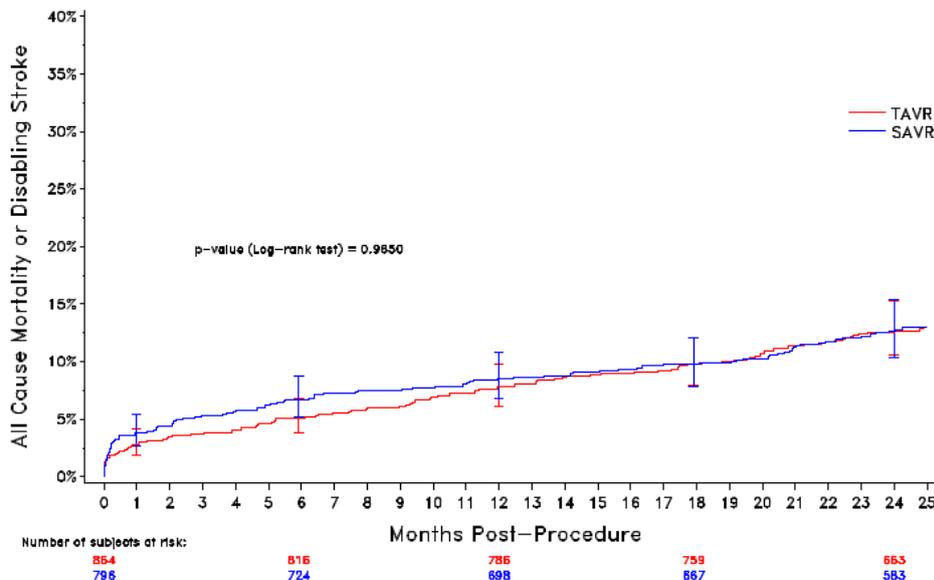
ADAR = Applicant Developed Assessment Report; CI = confidence interval; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation



**Figure 3 Kaplan Meier plot for primary outcome death or disabling stroke in PARTNER 2A (transfemoral access cohort)**

Source: Figure 41, p100 of the ADAR

ADAR = Applicant Developed Assessment Report; CI = confidence interval; TAVR = transcatheter aortic valve replacement



**Figure 4 Kaplan Meier event rate for primary outcome death or disabling stroke in SURTAVI**

Source: Figure 42, p100 of the ADAR

ADAR = Applicant Developed Assessment Report; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement

The ADAR presented changes in health-related quality of life (HRQoL), Kansas City Cardiomyopathy Questionnaire (KCCQ), EuroQoL 5-dimension 3-level (EQ-5D-3L) and 36-Item Short Form Health Survey (SF-36), noting that there was a greater improvement with TAVI at 30 days compared with SAVR. The ADAR reasonably attributed this difference was due to the differences in invasiveness and recovery between TAVI and SAVR. The ADAR considered that this was an important difference to patients at an intermediate risk as they may be younger and lead an active life. The Commentary noted that HRQoL was not different between TAVI and SAVR at 1 year or 2 years post-procedure, suggesting the incremental benefit in HRQoL was short-term.

*Indirect comparison with newer generation TAVI devices, via the common comparator SAVR*  
 The ADAR's evidence base for TAVI relied on older generation valves which are not used in current Australian practice. Two meta-analyses that compared the SAPIEN-XT valve with the SAPIEN 3 valve using observational studies were identified during the evaluation: Tummala (2017)<sup>12</sup> and Ando (2016)<sup>13</sup>. Both meta-analyses concluded that the SAPIEN 3 valve resulted in lower rates of moderate to severe paravalvular regurgitation, major vascular complications, stroke (all cerebrovascular events in Ando 2016) and serious bleeding and higher rates of permanent pacemaker implantation.

Additionally, two indirect comparisons were compiled during the evaluation to examine the applicability of results from older generation to newer generation TAVI valves in the intermediate risk population:

- SEV indirect comparison: Evolut R vs. CoreValve by comparing SURTAVI Continued Access Study (CASS, Yarkubov 2020) with the SURTAVI trial; and
- BEV indirect comparison: SAPIEN 3 vs. SAPIEN-XT by comparing the PARTNER 3Si study with the PARTNER 2A trial.

<sup>12</sup> Tummala R, Banerjee K, Sankaramangalam K, et al. Clinical and procedural outcomes with the SAPIEN 3 versus the SAPIEN XT prosthetic valves in transcatheter aortic valve replacement: A systematic review and meta-analysis. *Catheter Cardiovasc Interv.* 2018;92(3):E149-E158.

<sup>13</sup> Ando T, Briassoulis A, Holmes AA, Taub CC, Takagi H, Afonso L. Sapien 3 versus Sapien XT prosthetic valves in transcatheter aortic valve implantation: A meta-analysis. *Int J Cardiol.* 2016;220:472-478.

Overall, the Evolut R and SAPIEN 3 appeared similar to the older generation valves used in the trials. However, the Commentary considered that the indirect comparison should be interpreted with caution. The Commentary highlighted that the comparisons were not statistically independent as there was overlap of patients in the SAVR arms, affecting the estimated variance and 95% confidence intervals of the estimated relative risks. Additionally, the indirect comparison compared an observational study with a randomised trial.

The Commentary noted that no comparable studies were identified during the evaluation that reported clinical outcomes in intermediate risk patients using the Evolut PRO. Therefore the applicability of the SURTAVI results to the Evolut PRO was unclear.

### **Clinical claim**

On the basis of the benefits and harms reported in the evidence base, the ADAR proposed that, relative to SAVR, TAVI has non-inferior safety and non-inferior effectiveness. The Commentary considered that the clinical claim was supported over the 2-5 year time duration. The Commentary highlighted that the long-term effectiveness and safety of TAVI, particularly valve durability and paravalvular leakage, in the intermediate risk population is unknown. The Commentary considered that this may be more relevant in the intermediate risk population as they would be expected to have a longer life expectancy than higher risk and inoperable populations. The Commentary highlighted that the Kaplan-Meier plots of the composite outcome of all-cause mortality and disabling stroke and the point estimates for all-cause mortality shifted towards favouring SAVR but this was not statistically significant.

The Commentary considered the clinical claim was supported in the short term for the older generation TAVI devices used in the RCTs (SAPIEN-XT and CoreValve). Based on the indirect comparison conducted during the evaluation, the SAPIEN 3 and Evolut R appeared to have broadly similar outcomes at 1 year to SAPIEN-XT and CoreValve, respectively. Although the SAPIEN 3 and SAPIENT XT valves appeared broadly similar, the Commentary noted that the estimated incidence of some outcomes such as stroke, paravalvular regurgitation, permanent pacemaker implantation and major vascular complications, might be lower with SAPIEN 3. No comparable evidence was identified for the Evolut PRO.

## **12. Economic evaluation**

The ADAR presented a cost-minimisation analysis assessing the index procedure costs of TAVI and SAVR (Table 10). This was consistent with the clinical claim of non-inferiority and consistent with the cost-minimisation basis MSAC recommended for the high risk population at its March 2016 meeting. MSAC noted that this approach still favoured TAVI because this calculation assumes that the cost of hospitalisation will be evenly distributed across the length of the hospital stay, whereas it is known that the reductions in hospital stay are typically for the cheaper days (e.g. those which do not incur the costs of the procedure) ([Application 1361.2 MSAC PSD](#), p3).

The cost-minimisation analysis estimated a cost of \$53,164 with TAVI and \$58,100 with SAVR, resulting in a net saving to the health system of -\$4,936 per patient. The Commentary noted that increasing the TAVI length of hospital stay from 6.0 days to 7.1 days would result in TAVI being cost-neutral to the health system. The Commentary considered that there is potential for TAVI hospital costs to be greater than expected and increase costs to the health system. Lee (2019)<sup>14</sup> reported a length of stay of  $7.4 \pm 6.2$  days in the second year of the study, a length of stay that would increase costs to the health system.

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<sup>14</sup> Lee P, Byrnes J, Mervin M, Scuffham P. Outcomes of transcatheter aortic valve implantation for intermediate-risk patients in Australia: the SOLACE-AU trial. *J Med Econ.* 2019;22(12):1298-1306.

**Table 10 Cost-minimisation analysis**

Cost parameter	TAVI	SAVR	Difference (TAVI – SAVR)	Source
TAVI Case Conference (coordination)	\$52.50	-	\$52.50	MBS item 6080
TAVI Case Conference (attendance × 3)	\$117.45	-	\$117.45	Total fee for MBS item 6081 × 3 attendees
Prosthesis	\$22,932	\$7,099	\$15,833	TAVI: Prosthesis List benefit SAVR: average prostheses cost for cardiac valve procedure DRGs
Procedure	\$1,476.95	\$1,969.25	-\$485	TAVI: MBS item 38495 SAVR: MBS item 38488
Assistant	\$295.39	\$393.85	-\$98.46	MBS item 51303 (20% of procedure fee)
Anaesthesia	\$121.40	\$387.60	-\$267.20	TAVI: MBS item 23065 SAVR: MBS item 23119
Perfusionist	-	\$408	-\$408	MBS item 22060
Hospitalisation (per day)	\$4,660			Average daily cost for cardiac valve procedure excluding prostheses (DRG codes: F04A, F04B and F04C)
Mean length of stay (days)	6.0	10.3	-4.2 <sup>a</sup>	PARTNER 2A and SURTAVI studies (see Section B.6.2 of this ADAR)
Hospital stay	\$28,170	\$47,843	-\$19,673	Cost per day × length of stay
<b>Total cost (revised)</b>	<b>\$53,164</b>	<b>\$58,100</b>		<b>Calculated during the evaluation</b>
<b>Total cost (ADAR)</b>	<b>\$53,136</b>	<b>\$58,059</b>	<b>-\$4,924</b>	<b>Calculated by the ADAR</b>

Source: Table 42, p75 of the ADAR and revised during the evaluation to reflect updated MBS costs

ADAR = applicant-developed assessment report; DRG = diagnosis-related group; MBS = Medicare Benefits Schedule; SAVR = surgical aortic valve implantation; TAVI = transcatheter aortic valve implantation

Note: All costs are reported in 2020 Australian dollars.

### 13. Financial/budgetary impacts

The ADAR used a market-share approach to estimate the financial implications of the introduction of TAVI for the intermediate risk population. The ADAR estimated TAVI would capture market share from the proportion of SAVR use on the MBS estimated to be for the intermediate-risk population. The ADAR also estimated the size of the population with symptomatic severe AS with an intermediate surgical risk. The Commentary considered that this may have been overestimated as the prevalence estimate included both moderate and severe AS. The pre-ESC response presented revised epidemiological estimates that corrected for the inclusion of moderate AS and uptake of private health insurance. This did not affect the financial implications which were developed using a market-share approach. The financial implications are summarised in Table 11.

The ADAR estimated TAVI would be cost-saving to the MBS. The Commentary considered that this would be reasonable if TAVI does not increase the total number of aortic valve replacement procedures (TAVI and SAVR) performed on the MBS for the intermediate risk population. The Commentary estimated that if TAVI increased the number of aortic valve replacements performed on the MBS by 39% (i.e. additional TAVI procedures not replacing SAVR on the MBS), this would result in net costs to the MBS. The Commentary considered that there is potential for market growth as the estimated prevalent population eligible for TAVI, including the subset aged 75 years and older, was substantially larger than the number

of SAVR procedures performed on the MBS. The pre-MSAC response reiterated that the projected cost savings were appropriate.

The pre-MSAC response considered that it was unlikely there would be leakage into the low surgical risk population as patients surgical risk would be appropriately assessed by a Heart Team. The pre-MSAC response agreed that leakage to low risk populations would be less relevant if MSAC supports TAVI for the low risk population.

The Commentary considered that the ADAR's estimated reduction in hospital costs were likely overestimated as it double counted hospitalisation costs and operating theatre costs. Thus, the cost of operating theatre costs was not included in the Commentary's estimates. Additionally, during the MSAC's March 2016 consideration of TAVI in the high risk and operable populations, MSAC noted that that the reductions in hospital stay are typically for the cheaper days (e.g. those which do not incur the costs of the procedure, Application 1361.2 MSAC PSD, p3).

The ADAR did not calculate the net cost of prosthesis. TAVI was estimated to cost an additional \$3.9 million in Year 1, increasing to \$4.2 million in Year 5.

**Table 11 Total costs to the MBS associated with TAVI - Commentary's estimates**

Parameter	Year 1 (2021)	Year 2 (2022)	Year 3 (2023)	Year 4 (2024)	Year 5 (2025)
Severe symptomatic AS with intermediate surgical risk with private health insurance (pre-ESC response) <sup>a</sup>	3,336	3,455	3,569	3,682	3,798
≥ 75 years <sup>b</sup>	1,857	1,958	2,047	2,131	2,218
Market share estimates					
SAVR services (total)	2,648	2,693	2,738	2,784	2,831
SAVR services- intermediate risk (15.8%)	411	418	425	433	440
TAVI services (70% uptake)	293	298	303	308	313
Sub-total cost	\$324,380	\$329,897	\$335,443	\$341,057	\$346,803
Co-administered MBS services <sup>c</sup>					
Number of services	3,221	3,276	3,331	3,387	3,444
Sub-total cost	\$293,911	\$298,910	\$303,935	\$309,022	\$314,228
<b>Total cost of TAVI</b>	<b>\$618,290</b>	<b>\$628,806</b>	<b>\$639,378</b>	<b>\$650,079</b>	<b>\$661,030</b>
<b>Reduction in SAVR costs <sup>d</sup></b>	<b>-\$856,725</b>	<b>-\$871,297</b>	<b>-\$885,945</b>	<b>-\$900,773</b>	<b>-\$915,947</b>
<b>Net cost to MBS</b>	<b>-\$238,435</b>	<b>-\$242,490</b>	<b>-\$246,567</b>	<b>-\$250,694</b>	<b>-\$254,917</b>
<b>Net cost to Australian Government</b>	<b>-\$238,435</b>	<b>-\$242,490</b>	<b>-\$246,567</b>	<b>-\$250,694</b>	<b>-\$254,917</b>
<b>Net reduction in hospital costs (MBS patients excluding theatre cost <sup>e</sup>)</b>	<b>-\$5,786,343</b>	<b>-\$5,884,756</b>	<b>-\$5,983,689</b>	<b>-\$6,083,842</b>	<b>-\$6,186,328</b>
<b>Net change in prosthesis costs for private health insurance <sup>f</sup></b>	<b>\$3,936,144</b>	<b>\$4,003,090</b>	<b>\$4,070,389</b>	<b>\$4,138,517</b>	<b>\$4,208,233</b>

Source: Table 76-77, p137 of the ADAR and extracted from the Section E spreadsheet

ADAR = Applicant Developed Assessment Report; AS = aortic stenosis; ICU = intensive care unit; MBS = Medicare Benefits Scheme; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation

<sup>a</sup> Calculated from age-specific prevalence of AS multiplied by proportion that is severe (75.6%) and proportion with intermediate surgical risk (15.8%). The Pre-ESC response revised the ADAR's estimate to account for 66% of moderate to severe AS was severe AS and 44% of Australians have private health insurance.

<sup>b</sup> The Pre-ESC response estimated the number of patients aged 75 years and older were 93 in Year 1, increasing to 106 in Year 5. This could not be verified.

<sup>c</sup> TAVI case conference, surgical assistance, anaesthesia, ICU attendance, transthoracic echocardiography

<sup>d</sup> As per TAVI excluding TAVI case conference items and inclusion of perfusion (cardiac bypass) item (Item 22060)

<sup>e</sup> For reduction in 4.2 days length of stay costed at \$4,660 per day. The ADAR also estimated operating theatre costs at \$635.17 per hour from New South Wales Health Operating Theatre Cost Template which would be captured in the total hospitalisation cost for SAVR.

<sup>f</sup> Calculated during the evaluation using SAVR prosthesis costs of \$8,630.14 from AR-DRG (Round 22, 2017-18) inflated to 2020 costs.

## 14. Key issues from ESC for MSAC

ESC key issue	ESC advice to MSAC
Comparative safety	Non-inferior safety was supported in the 2–5-year duration of the key trials. However, there is uncertainty in the longer-term safety outcomes, particularly valve durability and paravalvular leakage. This may be relevant in the intermediate surgical risk population because this group may, on average, have a longer life expectancy than higher risk and inoperable populations.
Comparative effectiveness	The clinical claim of non-inferiority was supported over the 2–5-year duration of the comparative clinical evidence. However, the long-term effectiveness and safety of TAVI in the intermediate risk population is unknown.
Newer vs. older generation devices	Comparative safety and effectiveness of newer devices are dynamic issues. There are limited data on whether outcomes are improving with newer generation TAVI devices.
Clinical practice guidelines	The European Society of Cardiology and the European Association for Cardio-Thoracic Surgery Guidelines for Valvular Heart Disease considered that SAVR is generally preferred in patients under 75 years old. This is because the long-term durability of TAVI devices is unknown, with only preliminary data showing TAVI devices may last at least 5 years without any signs of early degeneration.
Utilisation and financial estimates	The projected cost savings are appropriate. Concerns that may impact the financial estimates are clinical implementation (volume of procedures) utilisation rates (substitution of SAVR and leakage to low-risk patients, which may be less relevant if TAVI is funded on the MBS for the low surgical risk population).

### ESC discussion

ESC noted that transcatheter aortic valve implantation (TAVI) is currently Medicare Benefits Schedule– (MBS) listed as a TAVI device agnostic item (either balloon expandable valve [BEV] or self-expandable valve [SEV] for high-risk/inoperable surgical patients with symptomatic severe aortic stenosis (AS) under item 38495. ESC noted that in the recent assessment of TAVI-BEV for intermediate risk for surgery (MSAC application 1603), “consistent with the current MBS item for TAVI (item 38495), MSAC supported an MBS item agnostic of the type of TAVI device, noting that this advice would be re-assessed at the March 2021 MSAC meeting consideration of the TAVI device agnostic application in intermediate risk for surgery (MSAC Application 1652 [current application])”.

ESC noted the consultation feedback, particularly from Hearts4Heart, which emphasised the benefit of patients being able to leave hospital earlier after TAVI, compared with the longer hospital stay and longer physical recovery following surgical aortic valve replacement (SAVR). The consultation feedback from Hearts4Heart also discussed the value and safety of TAVI for younger patients, particularly given the current barriers under which only sicker patients can access TAVI, when there are no such barriers for SAVR. ESC noted feedback from a medical device manufacturer claiming that TAVI-BEV devices were superior to TAVI-SEV devices. ESC also noted policy advice that the TAVI Accreditation Committee had indicated their support for device-agnostic MBS items if this service is recommended by MSAC.

ESC noted the application developed assessment report’s (ADAR’s) claim that TAVI is non-inferior to SAVR in terms of safety and effectiveness for patients with symptomatic severe

AS at intermediate risk of surgery. The two randomised controlled trials (PARTNER 2A, SURTAVI) presented in the application compared TAVI and SAVR using older-generation TAVI devices that are no longer marketed in Australia. Two observational studies were used in indirect comparisons performed by the commentary comparing the older-generation devices and the corresponding newer-generation devices (via the common comparator SAVR). ESC noted that evidence for newer-generation devices that are listed on the Australian Register of Therapeutic Goods (ARTG) is not as strong as the evidence for the older generation devices.

In terms of comparative safety, ESC noted the significantly higher bleeding rates post-procedure for SAVR compared with TAVI, as well as higher rates of acute kidney injury that were maintained at 1 year and 2 years post-procedure. Vascular complications were higher following TAVI than SAVR, and new atrial fibrillation was lower following TAVI than SAVR. ESC noted the SURTAVI trial reported a higher risk of new permanent pacemaker than the PARTNER 2A trial.

In terms of comparative effectiveness, all-cause death or disabling stroke (primary composite outcome) was lower following TAVI than SAVR at 30 days post-procedure, but the difference in all-cause death was not maintained at 1 year or 2 years post-procedure.

ESC noted that comparative safety and effectiveness of newer TAVI devices are dynamic issues given the changes in device technology and the relative differences in evidence base between older vs. newer devices. The commentary's indirect comparisons suggested that outcomes were likely similar between the older generation TAVI devices in the trials and the newer devices. ESC also noted that the indirect comparisons should be interpreted with caution as the comparisons were not statistically independent (overlap of patients in the SAVR arms of both comparisons) and compared randomised trials with observational studies. ESC considered the pre-ESC response which claimed that newer generation devices all show similar or superior efficacy and safety outcomes with the older generation devices. ESC noted:

- the SAPIEN XT and newer SAPIEN 3 BEV device were compared in two meta-analyses of observational studies (Ando 2016<sup>15</sup>, Tummala 2018<sup>16</sup>)
- the CoreValve and newer Evolut R SEV devices were compared in a meta-analysis of observational studies (Sun 2020<sup>17</sup>) and registry data
- the Evolut R and newer Evolut PRO SEV devices were compared in 3 observational studies (Hellhammer 2018<sup>18</sup>, Kalogeras 2020<sup>19</sup> and Pyada 2019<sup>20</sup>)

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<sup>15</sup> Ando T, Briasoulis A, Holmes AA, Taub CC, Takagi H, Afonso L. Sapien 3 versus Sapien XT prosthetic valves in transcatheter aortic valve implantation: A meta-analysis. *Int J Cardiol.* 2016 Oct 1;220:472-8.

<sup>16</sup> Tummala R, Banerjee K, Sankaramangalam K, Mick S, Krishnaswamy A, White J, Fares M, Mehta A, Popovic Z, Svensson LG, Kapadia SR. Clinical and procedural outcomes with the SAPIEN 3 versus the SAPIEN XT prosthetic valves in transcatheter aortic valve replacement: A systematic review and meta-analysis. *Catheter Cardiovasc Interv.* 2018 Sep 1;92(3):E149-E158.

<sup>17</sup> Sun Y, Li J, Fan R, et al. Outcomes of Evolut R Versus CoreValve After Transcatheter Aortic Valve Implantation: A Meta-Analysis. *Heart Lung Circ.* 2020;29(2):288-294.

<sup>18</sup> Hellhammer K, Piayda K, Afzal S, et al. The Latest Evolution of the Medtronic CoreValve System in the Era of Transcatheter Aortic Valve Replacement: Matched Comparison of the Evolut PRO and Evolut R. *JACC Cardiovasc Interv.* 2018;11(22):2314-2322.

<sup>19</sup> Kalogeras K, Ruparelia N, Kabir T, et al. Comparison of the self-expanding Evolut-PRO transcatheter aortic valve to its predecessor Evolut-R in the real world multicenter ATLAS registry. *Int J Cardiol.* 2020;310:120-125.

<sup>20</sup> Piayda K, Hellhammer K, Veulemans V, Afzal S, Kelm M, Zeus T. TCT-732 CoreValve Evolut PRO Versus Evolut R: A Case-Matched Comparison in Severely Calcified Anatomies. *Journal of the American College of Cardiology.* 2019 Oct 1;74(13S):B718-.

Overall, ESC considered that there are limited data on whether outcomes are improving with newer generation TAVI devices.

ESC noted that current guidelines from the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery emphasise that data on TAVI are very limited for patients under 75 years of age, and that SAVR is preferred for these patients. ESC was concerned that people under 75 years of age could be eligible for this MBS item. The durability of TAVI valves is uncertain beyond 5 years, and potential rates of replacement or reintervention should be considered for younger patients, which will affect economic and financial estimates. ESC also considered the potential for leakage of this item into the low-risk population, which creates uncertainty regarding potential future utilisation. However, this would be less relevant if TAVI is funded on the MBS for the low surgical risk population ([MSAC application 1635](#)).

ESC discussed the cost-minimisation analysis in the economic model, which resulted in an estimated saving of \$4,396 per patient based on a hospital length of stay of 6 days, compared with 10.3 days for SAVR. ESC noted that the analysis used average daily prices for hospital days, and that this approach may lead to an overestimation of savings. Overall, ESC considered that the cost-minimisation analysis was appropriate if the clinical claim of non-inferiority is accepted by MSAC.

ESC noted the financial estimates, which showed that the current application would result in net cost savings to the MBS over 5 years. Uncertainties in these estimates included that the estimated number of potentially eligible patients (severe symptomatic AS with intermediate surgical risk and aged 75 years and older) was higher than the number of SAVR procedures on the MBS. ESC noted the pre-ESC response that excluding patient with moderate AS and patients who do not have private health insurance more accurately predict the proportion of intermediate risk patients who would undergo TAVI. However, ESC remained concerned about the potential for leakage to less experienced practitioners if the volume of TAVI procedures increases.

**REDACTED.** The predicted versus actual utilisation of TAVI in the high risk/inoperable population and the change in TAVI and SAVR utilisation on the MBS are presented in Table 2 and Figure 1.

## **15. Other significant factors**

Nil.

## **16. Applicant comments on MSAC's Public Summary Document**

Medtronic is pleased that MSAC has supported MBS funding of transcatheter aortic valve implantation (TAVI) via transfemoral delivery for patients at intermediate risk for surgery based on its safety, effectiveness and cost effectiveness compared with surgical aortic valve replacement (SAVR). Medtronic is also pleased that MSAC concluded that this item should be device agnostic, allowing patients to access the most appropriate TAVI Device for each individual. We look forward to working with all stakeholders to further improve patient access to this lifechanging therapy. Medtronic's first priority is for the development of TAVI as a therapy so this decision is a great win for all stakeholders.

## **17. Further information on MSAC**

MSAC Terms of Reference and other information are available on the MSAC Website:  
[visit the MSAC website](#)