



**Australian Government**  
**Medical Services Advisory Committee**

## **Public Summary Document**

### ***Application 1640 - Transcatheter aortic valve implantation via transfemoral delivery for patients at low risk for surgery***

**Applicant: Medtronic Australasia Pty Ltd**

**Date of MSAC consideration: MSAC 82<sup>nd</sup> Meeting, 29-30 July 2021**

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

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

An application requesting Medicare Benefits Schedule (MBS) listing of transcatheter aortic valve implantation (TAVI) for patients with symptomatic severe aortic stenosis (AS) at low 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 creation of a new Medicare Benefits Schedule (MBS) item for transcatheter aortic valve implantation (TAVI) for patients with symptomatic severe aortic stenosis at low risk for surgery. MSAC advised that TAVI had acceptable safety and effectiveness compared with surgical aortic valve replacement (SAVR) that was demonstrated over a 5–10-year period. In addition, MSAC advised that TAVI has acceptable cost-effectiveness compared with SAVR. Consistent with its assessment of TAVI in all levels of surgical risk, MSAC supported an MBS item agnostic of the type of TAVI device.

MSAC supported the following item descriptor (abridged):

*TAVI, for the treatment of symptomatic severe **native calcific** 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.)*

*Notes: The Health Insurance (Section 3C General Medical Services - Transcatheter Aortic Valve Implantation) Determination 2018(Cth) (Department of Health 2018) 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*

### **Consumer summary**

Medtronic Australasia applied for public funding via the Medicare Benefits Schedule (MBS) for transcatheter aortic valve implantation (TAVI) in patients with symptomatic severe aortic stenosis who are at low 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.

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 already largely accepted that TAVI is a safe and effective procedure, and is better value for money than surgical aortic valve replacement (open heart surgery) in the short term. In the current application, MSAC considered TAVI is likely to be as safe and as effective as surgery in the longer-term. In addition, MSAC considered that there is a robust process in place for specialist Heart Teams to make the best choice for patients between TAVI and SAVR, depending on patients' needs and risk factors.

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

MSAC supported MBS funding for TAVI for patients at low risk for surgery using an item descriptor that does not specify the type of TAVI device. MSAC based its decision on the fact that it considered TAVI to be effective, safe and cost-effective compared with SAVR.

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

MSAC noted that TAVI is currently funded on the MBS for patients with symptomatic severe aortic stenosis who are at high risk for SAVR or who would otherwise be inoperable. MSAC recalled it had deferred its advice on MBS funding of TAVI via transfemoral delivery using the balloon-expandable valve system (BEV) for patients at low risk for surgery as it was concerned about valve durability over the longer term, given that the low surgical risk population is younger, has longer life expectancy and generally has good long-term outcomes with SAVR. MSAC recalled it had considered further consultation is needed to define key factors that suggest one procedure may be preferred over the other for the low surgical risk population. MSAC recalled that it had considered that the appropriate population and item descriptor for TAVI with low surgical risk would need to be further refined to ensure TAVI is used for low risk patients most likely to benefit from the procedure (Public Summary Document [PSD] [Application No. 1635](#), p1).

MSAC noted the targeted consultation feedback provided by the following organisations: the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS), the

Cardiac Society of Australia and New Zealand (CSANZ), Hearts4heart, and the Australian Society of Anaesthetists (ASA).

MSAC noted that the current application seeks to expand the current MBS item 38495 to include patients at a low surgical risk for surgery. MSAC recalled that it had previously considered that a separate MBS item should be created for TAVI in low risk population as this would assist monitoring of TAVI utilisation (PSD Application 1635, p5) and had largely accepted that TAVI is safer and more effective in the short term compared with SAVR.

MSAC noted that the TAVI Accreditation Committee had advised that the joint Australian guidance by the CSANZ and the ANZSCTS focused on accreditation rather than patient selection.

MSAC considered that surgical aortic valve replacement (SAVR) was an appropriate main comparator. MSAC noted there were three direct randomised controlled trials (RCTs) assessing TAVI vs. SAVR in the low surgical risk population: PARTNER 3, EVOLUT and NOTION. MSAC recalled that it had previously considered the PARTNER 3 and EVOLUT trials in its consideration of Application 1635 (PSD Application 1635, p3). MSAC recalled it had previously accepted the short-term evidence from the PARTNER 3 and EVOLUT trials and had considered the differences in the results in the two trials, which used two different TAVI devices, did not show differences that strongly justified a device-specific approach. MSAC noted that the current application included the NOTION trial, an all-comers trial, which predominately included patients at low-surgical risk (82%)<sup>1</sup>. MSAC noted that the NOTION trial used an older TAVI device that is no longer marketed in Australia. MSAC noted that the NOTION trial provided longer follow-up data, with 5-years data<sup>2</sup> presented in the ADAR and 8-year data<sup>3</sup> presented in the pre-MSAC response. MSAC accepted that the evidence presented supported that TAVI appeared to have non-inferior comparative effectiveness compared with SAVR.

MSAC noted, that the pre-MSAC response and consultation feedback, presented longer term TAVI valve data to address the issue of durability, especially for younger patients who may live for a long period after the procedure. There were ten long-term durability studies (including prospective cohort studies and TAVI registry studies). MSAC noted that the pre-MSAC response considered that longer term data relating to SAVR valves relate to mechanical valves rather than contemporary bioprosthetic valves which there is more limited long term durability data, and are used in almost 90% of SAVR procedures performed in Australia.

MSAC considered that the totality of the evidence, including the comparative data from the NOTION trial, demonstrated acceptable long-term outcomes, including for TAVI valve durability at 5–10 years. MSAC considered that TAVI had a different safety profile compared with SAVR. MSAC noted that patients who had TAVI were more likely to paravalvular leakage (PVL), left bundle branch block (LBBB) and need a new permanent pacemaker implanted. MSAC noted that the ANZSCTS advised that the PARTNER 3 and EVOLUT

---

<sup>1</sup> Thyregod, *et al.* (2015). "Transcatheter vs. surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the all-comers notion randomized clinical trial." *J Am Coll Cardiol* 65(20): 2184-2194.

<sup>2</sup> Thyregod *et al.* (2019). "Five-Year Clinical and Echocardiographic Outcomes from the Nordic Aortic Valve Intervention (NOTION) Randomized Clinical Trial in Lower Surgical Risk Patients". *Circulation*. 2019;10.1161

<sup>3</sup> Jørgensen TH *et al.* Eight-year outcomes for patients with aortic valve stenosis at low surgical risk randomized to transcatheter vs. surgical aortic valve replacement. *Eur Heart J*. 2021;42(30):2912-2919.

trials were conducted in highly selected populations and reported inconsistent endpoints compared with the earlier TAVI trials in higher risk populations.

MSAC noted and agreed with the ESC advice for the economic evaluation. TAVI was dominant in the base case analysis. MSAC also noted that relatively small and reasonable changes in the model inputs, such as average hospital length of stay (LOS) and cost of each day in hospital, can significantly increase the ICER. The pre-MSAC response stated there is an expectation that hospital LOS for TAVI will decrease further over time as it is a new procedure (whereas LOS for SAVR will not), and therefore TAVI will only become more cost-effective in the future. However, MSAC noted that SAVR hospital costs diminish as a patient recovers; that is, the cost is not evenly distributed over the LOS.

MSAC noted the financial estimates and agreed with ESC advice that the eligibility for TAVI was overestimated and that small changes in assumptions could result in substantial costs to Government.

MSAC maintained its preference to create a separate MBS item for TAVI in the low surgical risk population. MSAC reaffirmed its previous advice that at a future date it may be appropriate to consolidate the TAVI items based on surgical risk into a single item (PSD Application 1635, p5). As requested in the application, MSAC supported a device agnostic item descriptor. This would be consistent with the current MBS items for TAVI and thus across all levels of surgical risk.

MSAC noted that the TGA-approved indication for the TAVI valves indicated for all levels of surgical risk (see Table 4), thus encompassing the low surgical risk population, is limited to patients who have severe native calcific aortic stenosis, and that therefore the target patient population in the current item should also have severely calcified valve leaflets. MSAC noted that TAVI may be an appropriate procedure for some people with other types of aortic stenosis, however, for most, SAVR would be the preferred intervention. For that reason, the item descriptor should specify that TAVI is intended for patients with severe “native calcific” aortic stenosis. MSAC considered that this would limit use for patients with aortic stenosis due to congenital abnormalities or other causes which are more common in younger age groups than native aortic stenosis. MSAC noted that the pre-MSAC response supported this approach.

MSAC agreed with the wording in the descriptor including “performed via transfemoral delivery, unless transfemoral delivery is contraindicated or not feasible” and the explanatory note including “low risk for SAVR”. MSAC noted that this was supported by the pre-MSAC response. MSAC considered that this would be consistent with the existing item descriptor for the high-risk population and the supported item descriptors for the intermediate risk population.

MSAC considered whether the item descriptor should exclude patients aged <65 years, because 2020 American College of Cardiology and American Heart Association (ACC/AHA, Otto *et al.* 2021<sup>4</sup>) guidelines generally recommend SAVR for patients <65 years unless life expectancy is limited or other factors suggest TAVI is preferable. MSAC noted that ANZSCTS supported a preference for SAVR in patients <70 years. However, MSAC considered that being prescriptive about age is unnecessary, because the processes of Heart

---

<sup>4</sup> Otto CM *et al.* 2020 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.

Team discussions (TAVI case conference) allow for an appropriate decision to be made regarding whether a patient should have TAVI or SAVR. MSAC noted feedback from CSANZ advising that it was not supportive of a defined list of factors, noting the clinical considerations are complex and should be assessed by a Heart Team. Similarly, Hearts4heart did not support restrictions in place for heart valve patients to have access to TAVI. MSAC noted that it is difficult to be prescriptive on TAVI vs. SAVR based on age because several other factors would also affect the appropriateness of the type of procedure. MSAC also noted that patients would have to satisfy the criteria of being low risk to be eligible for this item number, regardless of their age.

MSAC noted ANZSCTS's proposal for independent surgical assessment. MSAC noted that the current MBS explanatory notes for TAVI specify that the Heart Team must consist of three or more participants where the first participant is a cardiothoracic surgeon and the second is an interventional cardiologist, where either the first or second participant is a TAVI Practitioner. MSAC noted that requirements for the composition of Heart Teams is regulated. MSAC considered that this should allow sufficient surgical input as all members of the team have to agree whether a patient is suitable for TAVI and this should also consider factors such as patient frailty and cognition. Overall, MSAC concluded that Heart Team discussions would be based on contemporary guidelines (and patient choice; see below), presenting a robust basis for clinical decision-making.

MSAC emphasised the importance of a shared decision-making process as outlined in the 2020 ACC/AHA guidelines that accounts for the patient's values and preferences and informs patients about the benefits and limitations of each approach, including the risks associated with reintervention. MSAC recalled that it had previously noted that Heart Team discussions should help guide the patient to the appropriate choice (PSD Application 1635, p4). MSAC noted that, as raised by Hearts4heart, patients may prefer TAVI as it is less invasive, and patients generally prefer the faster recovery from TAVI. However, MSAC considered that it was important that patients were informed about the limited of long-term data (beyond 10 years) available for TAVI so that patients can make informed decisions. MSAC noted that CSANZ had recommended that high quality patient information be provided explaining the progressive evolution of TAVI.

MSAC noted that repeat TAVI (valve-in-valve) procedures may become the preferred method of reintervention for TAVI patients requiring a repeat procedure. MSAC considered that repeat TAVI was likely to be less risky than repeat SAVR as repeat SAVR carries additional risks due to differences in the placement of the original SAVR and TAVI valves.

MSAC concluded that it would be appropriate to audit Heart Team documentation and decisions and considered that the process of audit would encourage compliance in the clinical community. MSAC considered that it would also be appropriate to consider audits of Heart Teams at the level of the hospital. MSAC noted that TAVI Hospitals are required to undergo an accreditation and re-accreditation process. MSAC noted that the TAVI Accreditation Committee and Cardiac Accreditation Services Limited would be involved in the auditing process.

MSAC advised that the Department should consider whether a proforma for documenting the Heart Team assessment should be developed. MSAC advised that this could also be provided to the TAVI Registry.

MSAC considered that this item should be reviewed in 2 years to assess predicted versus actual use. MSAC requested the Department include summary data from the TAVI registry,

where possible. MSAC considered that there is a risk of leakage to asymptomatic patients who are younger and at low risk for adverse clinical outcomes from aortic stenosis. This could be looked at in the TAVI registry data, and also valve durability over time. MSAC advised that the requirement for native calcific aortic stenosis in the item descriptor could be updated in the future if new evidence emerges or when MSAC considers combining the TAVI items into a single item.

MSAC noted that the TAVI registry should be able to provide data on length of stay, noting this would be for the currently subsidised high-risk population.

MSAC was concerned that consumer feedback indicated additional costs were being incurred for TAVI devices. MSAC did not consider that this additional cost to patients or hospitals was reasonable based on its assessment of cost-effectiveness. MSAC reaffirmed that its assessment of cost effectiveness and advice on the Prostheses List Benefit was based on the complete intervention which included the valve and all components of the delivery system. As presented in the revised base case of the economic model, the TAVI procedural costs included MBS costs, a hospitalisation cost of \$17,579 and a prosthesis cost of \$22,932 which should include the valve and the delivery system.

### **Other discussion**

MSAC noted that expanding the listing of TAVI would increase the number of TAVI procedures and prostheses funded by private health insurance providers. MSAC requested the Department advise private insurance providers of this recommendation.

## **4. Background**

### *TAVI low risk application 1635*

At its March-April 2021 meeting, MSAC deferred its advice on the MBS funding of TAVI via transfemoral delivery using the balloon-expandable valve system (BEV) for patients at low risk for surgery. MSAC largely accepted that TAVI-BEV is safe, effective and cost-effective compared with surgical aortic valve replacement (SAVR), but was concerned about valve durability over the longer term, given that the low surgical risk population is younger, has longer life expectancy and generally has good long-term outcomes with SAVR.

For these reasons, MSAC considered further consultation is needed to define key factors that suggest one procedure may be preferred over the other for the low surgical risk population. MSAC considered that the appropriate population and item descriptor for TAVI with low surgical risk would need to be further refined to ensure TAVI is used for low risk patients most likely to benefit from the procedure.

In addition, MSAC maintained its preference for a device-agnostic MBS item descriptor for this new item, recalling its precedent set on the basis of similar clinical performance and thus the same benefit across TAVI device options in high surgical risk and intermediate surgical risk populations. This advice would be re-assessed at the July 2021 MSAC meeting consideration of the TAVI device agnostic application for patients at low risk for surgery [MSAC Application 1640] ([Public Summary Document \[PSD\], Application No. 1635](#)).

MSAC considered that the main residual concerns in deciding whether to support the application's requested funding relate to the durability of the TAVI valves and the patient's expected longevity. MSAC considered that a patient's eligibility for TAVI should be changed from being based on the risk of adverse outcomes following SAVR to being based on the

patient’s expected longevity and comorbidities (such as frailty and cognitive function), as well as exclusion criteria due to issues such as bicuspid valve disease. MSAC noted that joint Australian guidance by the Cardiac Society of Australia and New Zealand (CSANZ) and the Australia and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) will be available in the near future.

Although MSAC largely accepted the short-term assessment of clinical evidence and the economic evaluation, it remained concerned that TAVI may be used inappropriately for patients who may be more appropriate for SAVR. For this reason, MSAC deferred its advice on public funding of TAVI in the low surgical risk population. MSAC noted the applicant’s pre-MSAC response providing longer-term data on durability of TAVI valves from registry data, but considered the long-term outcomes with TAVI and the durability of TAVI valves are yet to be demonstrated. MSAC considered that this was of greater importance for patients at low surgical risk who, on average, are younger and have a longer life expectancy than patients with intermediate or high risk of surgical mortality. In addition, MSAC noted that there is limited evidence on reintervention with TAVI (valve-in-valve procedures) and whether this procedure performs as well as an initial TAVI procedure. 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 considered that the Heart Team discussions may need to consider factors such as the limited evidence on long-term outcomes. MSAC was also concerned consumers may have a strong preference for TAVI as it is less invasive than SAVR, but may not be fully informed about the lack of long term evidence data supporting its use. In addition, patients with low surgical risk have generally have good long-term outcomes with SAVR compared with intermediate or high surgical risk patients. For these reasons, MSAC considered that the appropriate population and item descriptor for TAVI with low surgical risk would need to be further refined, such as defining key exclusion criteria, to ensure TAVI is used for low risk patients most likely to benefit from the procedure. MSAC considered further consultation is needed to define key factors that suggest one procedure may be preferred over the other.

MSAC considered that a separate MBS item should be created for TAVI in low risk population as this would assist monitoring of TAVI utilisation. MSAC anticipated its preference for a device-agnostic MBS item descriptor for this new item, and considered this would be consistent with the current MBS items for TAVI and thus across all levels of surgical risk. MSAC noted this advice would be re-assessed at the July 2021 MSAC meeting consideration of the TAVI device agnostic application for patients at low risk for surgery (MSAC Application 1640).

MSAC advised that at a future date it may be appropriate to consolidate the TAVI items based on surgical risk into a single item.

Table 1 presents comparisons of the current ADAR with Application 1635.

**Table 1 Comparison between TAVI (MSAC 1640) for low-risk patients and TAVI-BEV for low-risk patients (MSAC 1635)**

Application	MSAC 1640 (Current)	MSAC 1635 (TAVI-BEV)
Intervention	TAVI (agnostic approach)	TAVI-BEV
Patient population	Low-risk patients as determined by Heart Team STS-PROM < 4%	Low-risk patients as determined by Heart Team STS-PROM < 3%
Comparator	SAVR and TAVI-BEV	SAVR and TAVI-SEV
Clinical evidence used in the economic model	2-year outcomes from EVOLUT and PARTNER 3 for disabling stroke and mortality. 5-year data from NOTION for mortality.	redacted

Application	MSAC 1640 (Current)	MSAC 1635 (TAVI-BEV)						
Clinical claim	Superior safety and efficacy of TAVI to SAVR. TAVI-SEV and TAVI-BEV are non-inferior in terms of efficacy and safety.	Superior effectiveness vs SAVR (composite outcome: death, stroke, rehospitalisation at 1-year) No claim vs TAVI-SEV						
<b>Economic evaluation</b>								
Health states	Three health states: <ul style="list-style-type: none"> <li>• Alive, without disabling stroke</li> <li>• Alive, with disabling stroke</li> <li>• Dead</li> </ul> No adjustment at baseline for patients with previous stroke	redacted						
% private patients	No distinction was made between private and public patients	60.9%						
Time horizon	10 years (base-case). Sensitivity analysis: 5 and 20-years.	redacted years (base-case). redacted and redacted-year time horizon presented in sensitivity analyses						
Prostheses cost of TAVI-BEV	ADAR included prosthesis costs for all patients	redacted						
Prosthesis cost	TAVI BEV: \$22,932 SAVR: \$7,099	TAVI BEV: \$redacted SAVR: \$redacted						
Hospital length of stay	Mean Days	TAVI	SAVR	Diff. /Ratio	Source	TAVI	SAVR	Diff. /Ratio
	EVOLUT	2.6 ±2.1	6.2 ± 3.3	4 days 1: 2.38	TAVI-BEV: Partner 3	Median: 3 days	Median: 7 days	4 days 1: 2.33
	NOTION	8.9 ±6.2	12.9± 11.6	4 days 1: 1.45	TAVI-SEV: EVOLUT	Mean: 2.6±2.1	Mean: 6.2 ±3.3	4 days 1:2.38
	Pooled	3.6	7.3	3.6 days 1: 2.03				
Hospitalisation cost	TAVI: \$17,579 SAVR: \$35,362 SAVR-TAVI: \$17,783	TAVI: \$redacted SAVR: \$redacted SAVR-TAVI: \$redacted						
Hospital costs (use in the model)	MBS and hospital costs were applied to all patients	\$redacted						
Method for calculating hospitalisation costs for TAVI and SAVR	Input	TAVI	SAVR	redacted				
	Average hospitalisation cost per day for SAVR patients	\$4,839	\$4,839					
	Mean length of hospital stay	3.6	7.3					
	Hospital costs	\$17,579	\$35,362					
Utility values		TAVI (range)	SAVR (range)	Utility values	TAVI-BEV	SAVR		
	Alive, no disabling stroke (EVOLUT)	0.81-0.82	0.74-0.82	redacted	\$redacted	\$redacted		
	Alive, stroke (disabling)	0.470	0.470	redacted	\$redacted	\$redacted		
	Disutility major event (once off)	0	0	redacted	\$redacted	\$redacted		
Transition probabilities	Transition probabilities were calculated from trial data. For disabling stroke, treatment-specific transition probabilities were applied for 0-30 days follow-up and up to 2-years. After this, no treatment effect was assumed. Beyond the trial data, the ADAR applied the pooled rate monthly probabilities of disabling stroke from EVOLUT at 1 – 2 years. For mortality, the ADAR relied on age and sex-adjusted Australian population norms.	redacted						
<b>Results</b>								
Incremental life-years and QALYs	Life-years = 0.081 QALYs =0.095	Life-years = redacted QALYs = redacted						



Application	MSAC 1640 (Current)	MSAC 1635 (TAVI-BEV)	
Incremental cost	-\$3,569 (using corrected costs)	Revised base-case (TAVI prosthesis cost of \$22,932) = <b>\$redacted</b>  Scenario 1 using the ADAR's proposed prostheses cost of <b>\$redacted</b> =TAVI-BEV <b>\$redacted</b>	
ICER/QALY	TAVI dominant	Revised base-case (TAVI prosthesis cost of \$22,932) = TAVI-BEV dominant  Scenario 1 using the ADAR's proposed prostheses cost of <b>\$redacted</b> =TAVI-BEV Dominant	
<b>Financial estimates</b>			
Approach used	Mixed approach (market-share and epidemiological)	<b>redacted</b>	
Method for calculating SAVR procedures	Number of SAVR procedures performed in 2019 / Number of Australians aged over 18 years.	<b>redacted</b>	
		<b>redacted</b>	
Total number of eligible patients with severe AS and at low-surgical risk (2021-2025)	Mixed approach = 24,618 <sup>a</sup> Epidemiological approach = 202,981	<b>redacted</b>	
Uptake amongst eligible patients (2021-2025)	60% <sup>a</sup> (14,771)	<b>redacted</b>	
Proportion of private patients (2021-2025)	44% <sup>a</sup> (6,499)	<b>redacted</b>	
Public patients	Mixed approach = 8,271 Epidemiological approach = 80,560	<b>redacted</b>	<b>redacted</b>
Private patients	Mixed approach = 6,499 Epidemiological approach = 63,297	<b>redacted</b>	<b>redacted</b>
MBS costs for SAVR: 100%	\$3,942	<b>\$redacted</b>	
TAVI: 100%	\$2,856	<b>\$redacted</b>	
Δ	-\$1,086	<b>\$redacted</b>	
Net cost to MBS	-\$5,293,444	<b>\$redacted</b>	
Prosthesis cost			
TAVI	\$22,932	<b>\$redacted</b>	
SAVR	\$7,099	<b>\$redacted</b>	
Hospitalisation cost			
TAVI	\$17,568	<b>\$redacted</b>	
SAVR	\$35,340	<b>\$redacted</b>	
Cost to private health insurance	\$102,893,549 (prosthesis)	<b>\$redacted</b> <b>\$redacted</b>	
Cost to private hospitals	-\$12,601,016 (hospitalisations)	<b>\$redacted</b>	
Cost to public hospitals	-\$16,037,657	<b>\$redacted</b> <b>\$redacted</b>	

Abbreviations: MBS = Medicare Benefits Schedule; MSAC = Medical Services Advisory Committee; ICER = Incremental cost per QALY gained, QALY = quality-adjusted life year, SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; TAVI-BEV = transcatheter aortic valve implantation – balloon-expandable valve system; TAVI-SEV = transcatheter aortic valve implantation – self-expandable valve system.

Note:

<sup>a</sup> **Redacted**

Source: Constructed during evaluation using Section D and E of the ADAR and from Section D and E of the 1635 evaluation

Table 2 and Figure 1 compare the Markov traces for TAVI patients and Table 3 and Figure 2 compares the Markov traces for SAVR patients between MSAC applications 1640 and 1635. At 12-months follow-up, 98% of TAVI patients and 96% of SAVR patients in MSAC 1640

were alive without stroke, compared to **REDACTED** in MSAC 1635. The commentary considered that this difference was largely driven by MSAC 1640's decision to model only disabling strokes, whereas MSAC 1635 modelled any stroke (disabling and non-disabling). Additionally, the deaths rates in MSAC 1640 were **REDACTED** than in MSAC 1635. This difference was due to the trial data applied. MSAC 1640 applied trial data from EVOLUT, NOTION and PARTNER 3, whereas MSAC 1635 applied trial data from PARTNER 3. Additionally, MSAC 1640 assumed TAVI had no survival benefit after 30-days, whilst MSAC 1635 **REDACTED**.

**REDACTED**. MSAC 1640 applied treatment specific disabling stroke event rates up until 24 months based on the results on EVOLUT and PARTNER 3 that showed significant differences in the rates of disabling stroke between trial arms. Beyond the trial period, the ADAR, used the pooled rates of disabling stroke between treatment arms reported by EVOLUT at 1 and 2 years. In comparison, MSAC 1635, applied **REDACTED**.

For mortality, the ADAR applied trial data until 5-years follow-up. Mortality beyond the trial period (after 5-years) was extrapolated using Australian lifetables. However, MSAC 1635 applied **REDACTED**.

[REDACTED]

**Figure 1 Markov Traces for TAVI (MSAC 1640 – solid lines) and TAVI-BEV (MSAC 1635 – broken lines)**

Abbreviations: MSAC = Medical Services Advisory Committee; TAVI = transcatheter aortic valve implantation; TAVI-BEV = transcatheter aortic valve implantation – balloon-expandable valve system

Source: Constructed during evaluation using Section D of the ADAR and from Section D of the 1635 evaluation

**Table 2 Markov Traces – MSAC 1640 (TAVI) vs. MSAC 1635 (TAVI-BEV)**

Cycle	Alive without stroke		Alive with stroke		Dead	
	1640	1635	1640	1635	1640	1635
1	99%	REDACTED	0%	REDACTED	1%	REDACTED
12	98%	REDACTED	0%	REDACTED	2%	REDACTED
24	97%	REDACTED	1%	REDACTED	3%	REDACTED
60	80%	REDACTED	1%	REDACTED	20%	REDACTED
120	62%	REDACTED	1%	REDACTED	37%	REDACTED

Abbreviations: MSAC = Medical Services Advisory Committee; TAVI = transcatheter aortic valve implantation; TAVI-BEV = transcatheter aortic valve implantation – balloon-expandable valve system

Source: Constructed during evaluation using Section D of the ADAR and from Section D of the 1635 Evaluation.

[REDACTED]

**Figure 2 Markov Traces for SAVR (MSAC 1640 – solid lines) and SAVR (MSAC 1635 – broken lines)**

Abbreviations: MSAC = Medical Services Advisory Committee; SAVR = surgical aortic valve replacement

Source: Constructed during evaluation using Section D of the ADAR and from Section D of the 1635 evaluation

**Table 3 Markov Traces – MSAC 1640 (SAVR) vs. MSAC 1635 (SAVR)**

Cycle	Alive without stroke		Alive with stroke		Dead	
	1640	1635	1640	1635	1640	1635
1	97%	REDACTED	1%	REDACTED	2%	REDACTED
12	96%	REDACTED	1%	REDACTED	3%	REDACTED
24	95%	REDACTED	2%	REDACTED	4%	REDACTED
60	78%	REDACTED	2%	REDACTED	21%	REDACTED
120	61%	REDACTED	2%	REDACTED	38%	REDACTED

Abbreviations: MSAC = Medical Services Advisory Committee; SAVR = surgical aortic valve replacement

Source: Constructed during evaluation using Section D of the ADAR and from Section D of the 1635 evaluation

## 5. Prerequisites to implementation of any funding advice

Table 4 presents the TAVI devices included in the Australian Register of Therapeutic Goods (ARTG). Medtronic’s CoreValve Evolut R and CoreValve Evolut PRO and Edwards Lifesciences SAPIEN 3 TAVI systems have TGA approval for patients at all surgical risk levels. The Commentary noted that it is unknown whether Abbott’s Portico valve or Boston Scientific’s LOTUS Edge or ACURATE Neo is undergoing assessment for a low-risk indication by the TGA or will undergo assessment in the future.

The Evolut R, Evolut PRO, Edwards Lifesciences SAPIEN 3, and Portico TAVI devices are listed on the Prostheses List as at March 2021.

**Table 4 Details of the TAVI devices included on the ARTG**

ARTG Number	Sponsor	Device name <sup>a</sup>	Patient surgical risk in TGA registered indication
319850	Medtronic Australasia Pty Ltd	CoreValve Evolut PRO system -	All risk levels
284003	Medtronic Australasia Pty Ltd	Medtronic CoreValve Evolut R System	All risk levels
284496	Edwards Lifesciences Pty Ltd	Edwards SAPIEN 3 Kit	All risk levels
254835	Abbott Medical Australia Pty Ltd	Portico Transcatheter Heart Valve	High risk
326386 <sup>b</sup>	Boston Scientific Pty Ltd	LOTUS Edge	High risk
295813	Boston Scientific Pty Ltd	ACURATE Neo	High risk

Abbreviations: ARTG= Australian Register of Therapeutic Goods; Pty Ltd, Proprietary Limited; TGA, Therapeutic Goods Administration of Australia

<sup>a</sup> Device name abbreviated for this table, full device name can be viewed on the TGA eBS website.

<sup>b</sup> It was announced in November-2020 that Boston Scientific will discontinue to manufacture this device, see news report link

Source: Table 15, p. 32 of the ADAR.

## 6. Proposal for public funding

The MBS item descriptor proposed by the ADAR is provided in Table 5. The ADAR requested an amendment to the explanatory note for the MBS Item 38495 to remove all reference to surgical mortality risk if MSAC also supported public funding for the intermediate risk population. The ADAR considered that a single MBS item for TAVI was preferred by key opinion leaders.

**Table 5 Proposed MBS item descriptor**

<b>Category 3 – THERAPEUTIC PROCEDURES – SURGICAL OPERATIONS</b>
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. Explanatory note TN.8.135: “.A TAVI Patient means a patient who, as a result of a TAVI Case Conference, has been assessed and is recommended as being suitable to receive the service described in item 38495...”
Fee: \$1,476.95

Source: Table 12, p. 44 of the ADAR.

The PICO defined the patient population as persons with symptomatic, severe AS at low risk for surgery (STS-PROM < 4%), and with no significant frailty (as defined by the Heart Team) and no procedure-specific impediments. The commentary noted that the proposed MBS item does not specify that patients have no significant frailty (as defined by the Heart Team) and no procedure-specific impediments.

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

Public consultation survey was received from one organisation (Hearts4heart) which was supportive of the application (see [Application 1652 PSD](#), p11). Following the deferral of MSAC application 1635([Application 1635 PSD](#), p1), the MSAC commenced targeted consultation, requesting feedback from several medical and consumer organisations to help optimise the use of TAVI to treat severe, symptomatic aortic stenosis in patients with low surgical mortality risk. An item descriptor and explanatory notes for low surgical risk patients was drafted outlining (preliminary) factors that may favour TAVI or SAVR based on the 2020 ACC/AHA guidelines. Feedback was received from the following organisations:

- The Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS)
- The Cardiac Society of Australia and New Zealand (CSANZ),
- The Australian Society of Anaesthetists (ASA), and
- Hearts4heart.

### *Item descriptor*

ANZSCTS supported the subsidy of TAVI as a standalone procedure without reference to surgical risk. CSANZ supported a device agnostic TAVI item descriptor. Hearts4heart considered that the concept of low, intermediate and high risk is misleading and not patient centred. Feedback from the ASA and Hearts4heart were supportive of the subsidy of TAVI.

### *Role of the Heart Team and defining the appropriate population*

Hearts4heart did not support restrictions in place for heart valve patients to have access to TAVI. CSANZ were also not supportive of a defined list of factors favouring TAVI or SAVR. CSANZ considered that patient selection for TAVI should be made by a multidisciplinary Heart Team as the clinical considerations are complex and consider

multiple permutations of patient, anatomic and procedural factors. ANZSCTS was supportive specifying factors defining the appropriate population for TAVI. ANZSCTS considered patients aged under 70 years would be more suitable for SAVR.

ANZSCTS considered that there was considerable variation in Heart Team decision-making across Australia. This variation included appropriateness of decision-making, surgeon engagement and patients being offered TAVI. ANZSCTS considered the decision making of Heart Teams should be audited.

#### *Shared decision making*

The Hearts4heart response highlighted the importance of patient choice and patient inclusion in decision-making. CSANZ recommended that high quality patient information be provided explaining the progressive evolution of TAVI.

#### *Surgical involvement in TAVI*

ANZSCTS proposed two models with greater surgeon involvement: one where an independent surgeon would assess patients as being more appropriate for TAVI and another where there would be surgeon involvement all TAVI procedures.

#### *Procedural anaesthesia*

The ASA advised that the anaesthesia technique required for TAVI results in better patient outcomes and that anaesthesia for open heart surgery is in and of itself, a major intervention, with a higher risk to patients.

#### *Clinical evidence*

ANZSCTS was critical of the trial data and considered that patients were highly selected and reported inconsistent endpoints. The ANZSCTS feedback presented data from the 2019 Annual Report of the ANZSCTS National Cardiac Surgery Registry Data.<sup>5</sup>

The ANZSCTS response highlighted that observed 30-day mortality for isolated SAVR was 1.8% in the 10 years from 2010 to 2019 in an unselected, all-comers population. In 2019, observed 30-day mortality was lower at 1.4%. For patients undergoing elective SAVR, observed 30-day mortality was 1.1%.

#### *Long term outcomes*

ANZSCTS raised concerns relating to the need for permanent pacemaker implantation and the occurrence of left bundle branch block and paravalvular leakage.

CSANZ presented findings from cohort studies on the long-term durability of TAVI valves that reported on SVD and bioprosthetic valve failure (BVF). Hearts4heart also referred to registry data reporting on structural valve deterioration (SVD) and bioprosthetic valve failure (BVF). The results of these studies are presented in Table 6.

---

<sup>5</sup> Shardey G *et al.* The Australian and New Zealand Society of Cardiac and Thoracic Surgeons Cardiac Surgery Database Program Annual Report 2019. Monash University, Department of Epidemiology and Preventive Medicine, October 2020. Report No 12. Available from <https://anzscts.org/database/about/#reports>

**Table 6: Long term durability after TAVI presented in the consultation feedback from Costa (2019) <sup>6</sup> and other studies referred in consultation feedback**

Author	N	Age	Follow-up	Survival	SVD	BVF
Deutsch 2018 <sup>7</sup>	300	81 yrs	7.14 yrs	5 yrs: 40.2% 7 yrs: 23.2%	5 years: 13.3% 7 years: 14.9% [competing risk adjusted]	3.7%: 11 patients 4 reinterventions (TAVI)
Eltchaninoff 2018 <sup>8</sup>	378	83 yrs	3.1 yrs	5 yrs: 31.7% 8 yrs: 9.6%	8 yrs: 3.2% (95 CI: 1.4, 6.1) [competing risk adjusted]	8 yrs: 0.58% (95% CI: 0.15, 2.75) n=2 (all reoperated)
Barbanti 2018 <sup>9</sup>	288	81 yrs	6.7 yrs	8 yrs: 29.8%	8 yrs Severe: 2.4% (95% CI: 0.8%, 5.7%, n=7) Moderate: 5.9% (95% CI, 3.1%, 10.0%, n=13). [competing risk adjusted]	8yrs: 4.5% (95% CI: 2.0%, 8.8%) n=11 (4 deaths, 2 TAVI, 2 asymptomatic)
Holy 2018 <sup>10</sup>	152	81 yrs	6.3 yrs	8 yrs: 27%	NR	8 years: 4.5% [competing risk adjusted] 8 interventions 3 TAVI 1 SAVR
Antonazzo 2018 <sup>11</sup>	278	82 yrs	6.8 yrs	NR	8 yrs: 3.6% (n=3)	8 yrs: 2.5% (n=5 + 2 probable BVF)
Didier 2018 <sup>12</sup>	4,201	83 yrs	5 yrs	5 yrs: 39.2%	5 yrs: 13.3% (2.5% severe)	NR
Sathananthan 2021 <sup>13</sup>	235	82 yrs	NR	6 yrs: 28.1% 8 yrs: 13.6% 10yrs: 8.4%	SVD/BVF 6 yrs: 1.7% 8 yrs: 4.7% 10yrs: 6.5% (n=9 moderate, n=6 severe) [competing risk adjusted]	2 reinterventions (1 SAVR and death, 1 TAVI)
Durand 2019 <sup>14</sup>	1,304	83 yrs	3.9 yrs	7yrs: 18.6%	Moderate: 7.0% Severe: 4.2%	1.9% (5 reinterventions)
Vollenbroich 2019 <sup>15</sup>	257	82 yrs	7 yrs	5 yrs: 47.3% 7 yrs: 26.5%	NR	0.4% (1 reintervention)

<sup>6</sup> Costa G *et al.* Long-term Transcatheter Aortic Valve Durability. *Interv Cardiol.* 2019;14(2):62-69.

<sup>7</sup> Deutsch MA *et al.* Beyond the five-year horizon: long-term outcome of high-risk and inoperable patients undergoing TAVR with first-generation devices. *EuroIntervention.* 2018;14(1):41-49

<sup>8</sup> Eltchaninoff H *et al.* Assessment of structural valve deterioration of transcatheter aortic bioprosthetic balloon-expandable valves using the new European consensus definition. *EuroIntervention.* 2018;14(3):e264-e271.

<sup>9</sup> Barbanti M *et al.* Incidence of Long-Term Structural Valve Dysfunction and Bioprosthetic Valve Failure After Transcatheter Aortic Valve Replacement. *J Am Heart Assoc.* 2018;7(15):e008440.

<sup>10</sup> Holy EW *et al.* Long-term durability and haemodynamic performance of a self-expanding transcatheter heart valve beyond five years after implantation: a prospective observational study applying the standardised definitions of structural deterioration and valve failure. *EuroIntervention.* 2018;14(4):e390-e396.

<sup>11</sup> Panico RA *et al.* Long-term results and durability of the CoreValve transcatheter aortic bioprosthesis: outcomes beyond five years. *EuroIntervention.* 2019;14(16):1639-1647

<sup>12</sup> Didier R *et al.* Five-Year Clinical Outcome and Valve Durability After Transcatheter Aortic Valve Replacement in High-Risk Patients. *Circulation.* 2018;138(23):2597-2607.

<sup>13</sup> Sathananthan J *et al.* Ten year follow-up of high-risk patients treated during the early experience with transcatheter aortic valve replacement. *Catheter Cardiovasc Interv.* 2021;97(3):E431-E437.

<sup>14</sup> Durand E *et al.* Assessment of Long-Term Structural Deterioration of Transcatheter Aortic Bioprosthetic Valves Using the New European Definition. *Circ Cardiovasc Interv.* 2019;12(4):e007597.

<sup>15</sup> Vollenbroich R *et al.* Long-term outcomes with balloon-expandable and self-expandable prostheses in patients undergoing transfemoral transcatheter aortic valve implantation for severe aortic stenosis. *Int J Cardiol.* 2019;290:45-51.

Author	N	Age	Follow-up	Survival	SVD	BVF
Testa 2020 <sup>16</sup>	999	82 yrs	4.4 yrs	8 yrs: 26.50%	8 yrs: 3.0% (moderate) 1.6% (severe) [competing risk adjusted]	8 years: 2.5% (6 reinterventions, 1 death) [competing risk adjusted]

Source: Compiled by the Department from p3 of the CSANZ response [Table 4, p11 of Costa (2019)]; Deutsch (2018); Eltchaninoff (2018); Barbanti (2018); Holy (2018); Antonazzo (2018); Didier (2018); Sathananthan (2021); Durand (2019); Vollenbroich (2019); and Testa (2020)

Abbreviations: BVF = bioprosthetic valve failure; CI = confidence interval; N = number patients in study; n = number of patients; NR = not reported; SVD = structural valve degeneration; SAVR = surgical aortic valve replacement; TAVI = Transcatheter Aortic Valve Implantation; yr= years

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

### *Description of Proposed Intervention*

The TAVI procedure 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 TAVI 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 AS 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 AS classified as being at low risk for surgery. 'Low risk' is historically defined by a predicted 30-day risk of surgical mortality of <4%, based on the Society of Thoracic Surgeons Predicted Risk of Mortality score.

### *Clinical place*

The proposed population is patients with symptomatic (defined as NYHA functional Class II or greater and symptoms of dyspnoea, angina or syncope), severe AS (defined as severely calcified valve leaflets with reduced opening, jet velocity (Vmax)  $\geq 4$  m/s, or mean aortic valve gradient  $\geq 40$  mm Hg) and who are classified at low surgical risk by a Heart Team. Refer to Section A.4 for further details. The commentary considered that this was appropriate and was largely consistent with the definition used in the primary clinical evidence (EVOLUT, NOTION and PARTNER 3).

The commentary considered that the proposed definition of symptomatic, severe AS was consistent with the Ratified PICO for MSAC 1635 and MSAC applications 1361 and 1603

<sup>16</sup> Testa L *et al.* Long-term clinical outcome and performance of transcatheter aortic valve replacement with a self-expandable bioprosthesis. *Eur Heart J.* 2020;41(20):1876-1886.

for TAVI devices to be used in patients with symptomatic, severe AS and who are considered high and intermediate risk of surgery (p2 of the April 2015 PSD for Application 1361 and p2 of the November PSD for Application 1603).

The current and proposed clinical management algorithms as per the ADAR, is presented in Figure 3 (where orange boxes represent the addition of TAVI). The key difference between the current and proposed clinical management pathway is the addition of TAVI as a treatment alternative to SAVR for low-risk patients. Patients requiring AVR would usually have either TAVI or SAVR as per the recent 2020 ACC/AHA clinical guidelines (Otto *et al.* 2021)<sup>17</sup> as per the following recommendations:

- Among patients in whom a bioprosthesis is appropriate, decisions between SAVR and TAVI should include the presence of symptoms, patient age and anticipated life expectancy, the indication for intervention, predicted surgical risk, and anatomy or other factors referable to transfemoral TAVI feasibility (all Class 1):
  - SAVR is preferred among patients <65 years of age or with life expectancy >20 years.
  - SAVR is preferred if vascular anatomy or other factors preclude TAVI.
  - SAVR is preferred among asymptomatic patients with a Class 2a AS indication for intervention, such as an abnormal exercise test, very severe AS, rapid progression, or elevated B-type natriuretic peptide.
  - If feasible, TAVI is preferred among patients >80 years of age or with life expectancy <10 years.
  - SAVR or TAVI is recommended after shared decision making among symptomatic patients ages 65 – 80 years with no contraindication to TAVI. The commentary noted that the decision needs to take into consideration patient's longevity and valve durability.
  - After shared decision making, palliative care is recommended among symptomatic patients with predicted post-TAVI survival <12 months or for whom minimal improvement in quality of life is expected.

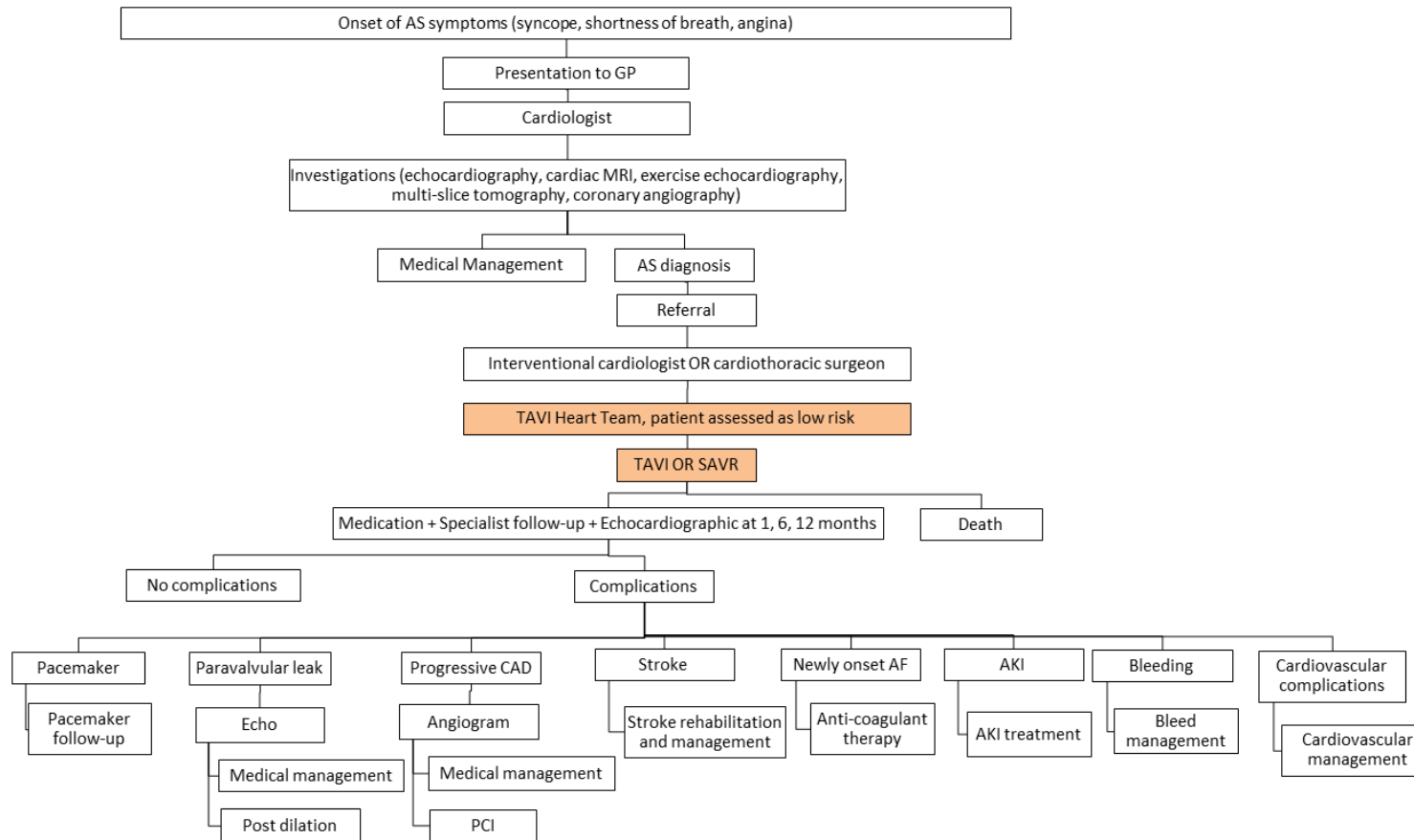
The commentary highlighted that the Ratified PICO for MSAC 1635, that the applicant (Edward Lifesciences) had been informed that the Cardiac Society of Australia and New Zealand (CSANZ) and the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) were soon to publish a consensus statement about TAVIs. They stated that they 'had 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' (p 5 of the [Ratified PICO for MSAC 1635](#)).

The commentary highlighted that some differences were identified between the proposed clinical algorithm and the one presented in the Ratified PICO for MSAC 1635. In particular, the removal of repeat AVR (a possible TAVI complication) was not considered minor and was not justified in the ADAR. The current 2020 ACC/AHA guidelines (Otto *et al.* 2021) identify this as a potential complication and state that repeat SAVR should remain the standard of care, particularly in low-risk patients. The ACC/AHA guidelines (Otto *et al.* 2021) also present an algorithm illustrating the choice of SAVR vs. TAVI when aortic valve replacement is indicated for valvular AS (Figure 4).

---

<sup>17</sup> Otto CM *et al.* 2020 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.



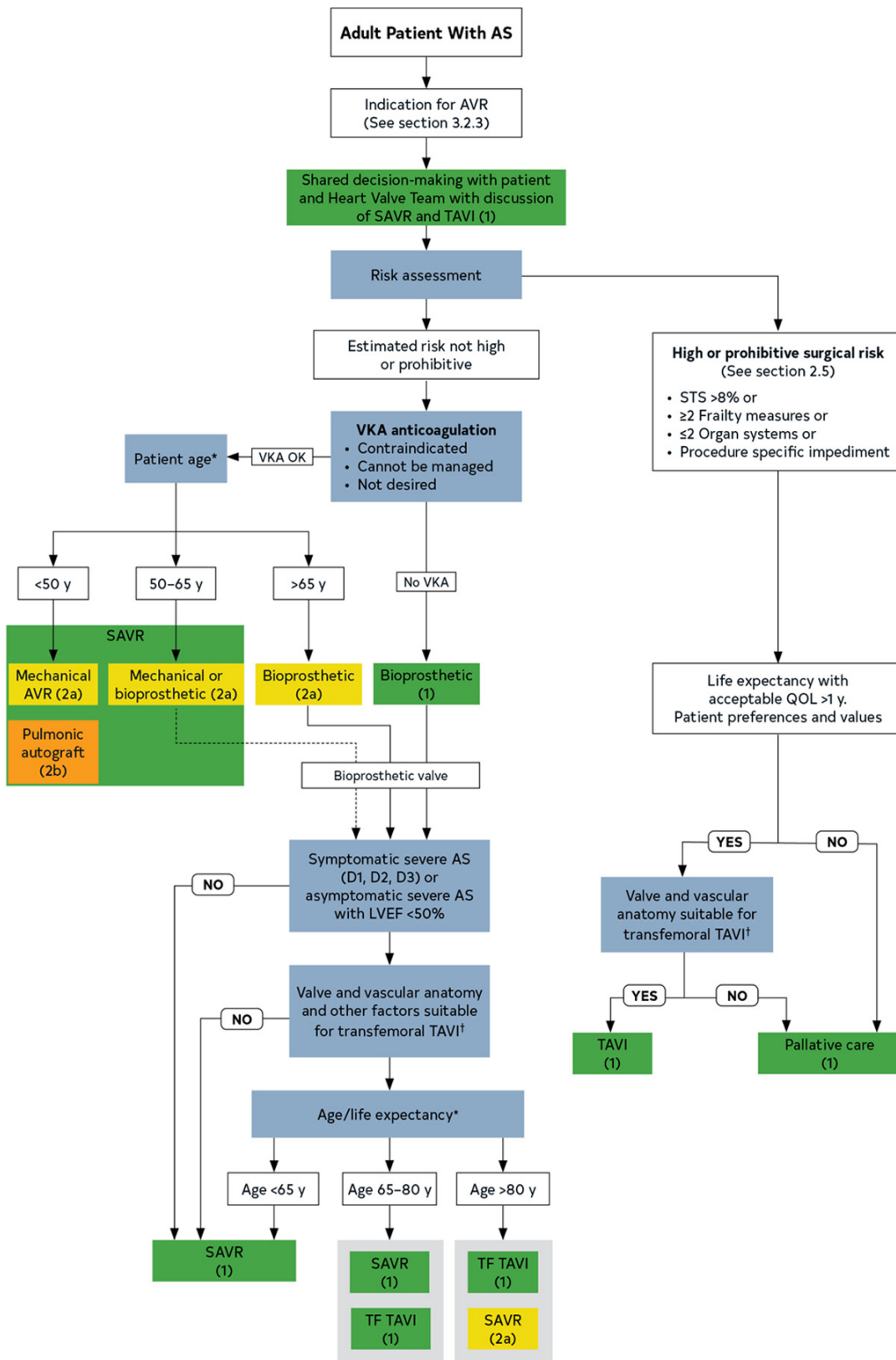


**Figure 3 Current and proposed clinical management algorithm for the proposed new intervention relative to current clinical practice**

Abbreviations: AKI, acute kidney injury; AS, aortic stenosis; CAD, coronary artery disease; GP, General Practitioner; MRI, magnetic resonance imaging; PCI, percutaneous intervention; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Source: Figure 3, p52 of the ADAR

Note: Addition of TAVI represented as orange boxes.



**Figure 4 Choice of SAVR vs. TAVI when aortic valve replacement is indicated for valvular AS**  
 Source: Figure 3 of 2020 ACC/AHA guidelines (Otto *et al.* 2021)

## 9. Comparator

The ADAR appropriately nominated SAVR as the main comparator. SAVR is an open-heart surgical procedure to repair or remove the narrowed aortic valve and replace it with a

bioprosthetic or mechanical aortic valve. The procedure requires general anaesthetic and extracorporeal circulation, with access via a sternotomy or a less invasive transthoracic approach.

The ADAR appropriately nominated TAVI-BEV as a secondary comparator. The key difference between TAVI-SEV and TAVI-BEV are the valves (self-expandable vs. balloon-expandable).

## 10. Comparative safety

The evidential basis of the ADAR consisted of three randomised trial (EVOLUT, NOTION and PARTNER 3), which directly compared TAVI to SAVR in patients with severe AS at low-surgical-risk (Table 7). The EVOLUT<sup>18</sup> and PARTNER 3<sup>19</sup> have been previously presented to MSAC in Application 1635. The NOTION<sup>20</sup> trial has not been previously assessed by MSAC. The NOTION trial was an all-comers trial, which predominately included patients at low-surgical risk (82%).

The ADAR presented a meta-analysis of the results of three randomised trials (EVOLUT, NOTION and PARTNER 3), which directly compared TAVI to SAVR in patients with severe aortic stenosis (AS) at low-surgical risk.

These same trials were also used in an indirect comparison between TAVI-SEV (EVOLUT and NOTION) and TAVI-BEV (PARTNER 3), via the common comparator, SAVR.

---

<sup>18</sup> Popma, *et al.* (2019). "Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients." *N Engl J Med* 380(18): 1706-1715.

<sup>19</sup> Mack, *et al.* (2019). "Transcatheter Aortic-Valve Replacement with a Balloon- Expandable Valve in Low-Risk Patients." *N Engl J Med* 380(18): 1695-1705.

<sup>20</sup> Thyregod, *et al.* (2015). "Transcatheter vs. surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the all-comers notion randomized clinical trial." *J Am Coll Cardiol* 65(20): 2184-2194.

Thyregod *et al.* (2019). "Five-Year Clinical and Echocardiographic Outcomes from the Nordic Aortic Valve Intervention (NOTION) Randomized Clinical Trial in Lower Surgical Risk Patients". *Circulation*. 2019;10.1161

**Table 7 Key features of the included evidence**

Trial/Study	N	Design/ duration	Risk of bias	Patient population	Key outcome	Result used in the economic model
EVOLUT (TAVI-SEV vs. SAVR)	1,403	Design: R, MC, OL NI and superiority between TAVI and SAVR Follow-up: 30-days, 1 and 2 years	<i>Low to some concerns</i>	Low-risk patients (STS-PROM < 4%) with severe aortic stenosis	All-cause mortality, disabling stroke	Yes
NOTION (TAVI-SEV vs. SAVR)	280	Design: R, MC, OL, NI and superiority between TAVI and SAVR. Follow-up: 30-days, 1, 2, and 5 years	<i>Low</i>	All comers trial. Predominately low-risk patients (81.8%) with severe AS and with anatomy suitable for TAVI or SAVR	All-cause mortality	Yes
PARTNER 3 (TAVI-BEV vs. SAVR)	946	Design: R, MC, OL, NI and superiority between and SAVR. Follow-up: 30-days, 1 and 2 years	<i>Low to some concerns</i>	Low-risk patients (STS-PROM ≤ 3%) with severe AS	All-cause mortality, disabling stroke	Yes
Meta-analysis	2,629 K = 3	EVOLUT + NOTION + PARTNER 3			All-cause mortality	Yes
Meta-analysis	N = 2,349 K = 2	EVOLUT + PARTNER 3			Disabling stroke	Yes

Abbreviations: AS= aortic stenosis; HRQoL=health-related quality of life, MC=multi-centre, NI = non-inferiority, LBBB = left bundle-branch block, OL=open label (unblinded), PPI = permanent pacemaker implanted, PVR = prosthetic valve regurgitation, R=randomised, SAVR = surgical aortic valve replacement, STS-PROM = Society of Thoracic Surgeons' Predicted Risk of Mortality, TAVI-BEV = transcatheter aortic valve implantation – balloon-expandable valve, TAVI-SEV = transcatheter aortic valve implantation – self-expandable valve  
Source: Constructed during the Evaluation.

*TAVI vs. SAVR*

A summary of the key safety outcomes of TAVI versus SAVR is provided in Table 8.

**Table 8 Summary of key safety outcomes for TAVI relative to SAVR, and as measured by randomised clinical trials: EVOLUT, NOTION, and PARTNER 3**

Timepoint	Studies	TAVI	SAVR	Risk Difference (95% CI)	Relative Risk (95% CI)	Quality of the evidence (GRADE)
<b>Bleeding events (life-threatening, disabling or major)</b>						
30-days	K = 3	81/1363 (6%)	207/1266 (16%)	-11.3% (-24.0%, 1.3%) $\chi^2 = 0.00; I^2 = 96\%$	<b>0.37 (0.15, 0.96)</b> $\chi^2 = 0.00 I^2 = 92\%$	⊕⊕⊕ Moderate <sup>a</sup>
12-months	K = 3	94/1221 (8%)	195/126 (17%)	-10.8% (-25.2%, 3.3%) $\chi^2 = 0.00; I^2 = 96\%$	<b>0.45 (0.20, 1.00)</b> $\chi^2 = 0.00 I^2 = 91\%$	⊕⊕⊕ Moderate <sup>b</sup>
24-months	K = 1 (EVOLUT)	61/725 (8%)	80/678 (12%)	<b>-3.4% (-6.5%, -0.2%)</b>	<b>0.71 (0.52, 0.98)</b>	⊕⊕⊕⊕ High
<b>Acute Kidney Injury (Stage ≥ 3, PARTNER 3 and EVOLUT)</b>						
30-days	K = 2	5/1221 (<1%)	15/1266 (1%)	-0.8% (-1.9%, 0.4%) $\chi^2 = 0.11 I^2 = 60\%$	<b>0.32 (0.11, 0.90)</b> $\chi^2 = 0.39 I^2 = 0\%$	⊕⊕⊕⊕ High
12-months	K = 1 (EVOLUT)	3/725 (<1%)	12/678 (2%)	<b>-1.4% (-2.5%, -0.3%)</b>	<b>0.23 (0.07, 0.82)</b>	⊕⊕⊕⊕ High
24-month	K = 1 (EVOLUT)	3/725 (<1%)	12/678 (2%)	<b>-1.4% (-2.5%, -0.3%)</b>	<b>0.23 (0.07, 0.82)</b>	⊕⊕⊕⊕ High

Timepoint	Studies	TAVI	SAVR	Risk Difference (95% CI)	Relative Risk (95% CI)	Quality of the evidence (GRADE)
<b>New-Onset Atrial fibrillation (PARTNER 3 and EVOLUT)</b>						
30-days	K = 2	76/1221 (6%)	382/1132 (34%)	<b>-27.5% (-30.6%, -24.4%)</b> $\chi^2 = 0.92$ $I^2 = 0\%$	<b>0.17 (0.11, 0.28)</b> $\chi^2 = 0.06$ $I^2 = 72\%$	⊕⊕⊕ Moderate
12-months	K = 2	96/1221 (8%)	404/1132 (36%)	<b>-27.8% (-30.9%, -24.6%)</b> $\chi^2 = 0.75$ $I^2 = 0\%$	<b>0.22 (0.16, 0.30)</b> $\chi^2 = 0.15$ $I^2 = 52\%$	⊕⊕⊕ Moderate <sup>b</sup>
24-month	K = 2	107/1221 (9%)	409/1132 (36%)	<b>-27.3% (-30.5%, -24.1%)</b> $\chi^2 = 0.88$ $I^2 = 0\%$	<b>0.24 (0.18, 0.32)</b> $\chi^2 = 0.15$ $I^2 = 52\%$	⊕⊕⊕⊕ High
<b>Left bundle branch block</b>						
30-days	K = 1 (PARTNER 3)	106/498 (22%)	35/454 (8%)	<b>13.7% (9.3%, 18.0%)</b>	<b>2.77 (1.93, 3.97)</b>	⊕⊕⊕⊕ High
12-months	K = 1 (PARTNER 3)	114/498 (24%)	35/454 (8%)	<b>15.3% (10.8%, 19.7%)</b>	<b>2.98 (2.09, 4.26)</b>	⊕⊕⊕⊕ High
24-month	K = 1 (PARTNER 3)	117/498 (24%)	41/454 (9%)	<b>14.6% (10.0%, 19.1%)</b>	<b>2.61 (1.87, 3.64)</b>	⊕⊕⊕⊕ High
<b>New permanent pacemaker implants</b>						
30-days	K = 3	203/1363 (15%)	60/1266 (5%)	<b>14.3% (2.2%, 26.3%)</b> $\chi^2 = 0.00$ $I^2 = 96\%$	<b>3.64 (1.44, 9.23)</b> $\chi^2 = 0.00$ $I^2 = 84\%$	⊕⊕⊕ Moderate <sup>b,c</sup>
12-months	K = 3	224/1363 (16%)	71/1266 (6%)	<b>15.4% (1.9%, 28.9%)</b> $\chi^2 = 0.00$ $I^2 = 97\%$	<b>3.43 (1.32, 8.90)</b> $\chi^2 = 0.00$ $I^2 = 89\%$	⊕⊕⊕ Moderate <sup>b,c</sup>
24-month	K = 3	243/1363 (18%)	77/1266 (6%)	<b>16.4% (2.4%, 30.3%)</b> $\chi^2 = 0.00$ $I^2 = 97\%$	<b>3.27 (1.35, 7.89)</b> $\chi^2 = 0.00$ $I^2 = 89\%$	⊕⊕⊕ Moderate <sup>b,c</sup>
5-years	K = 1 (NOTION)	58/142 (41%)	10/134 (7%)	<b>33.4% (24.2%, 42.6%)</b>	<b>5.47 (2.92, 10.26)</b>	⊕⊕⊕ Moderate <sup>c</sup>
<b>Aortic valve reintervention</b>						
30-days	K = 3	2/1363 (0%)	2/1266 (0%)	-0.01% (-0.3%, 0.3%) $\chi^2 = 1.00$ $I^2 = 0\%$	0.94 (0.13, 6.62) $\chi^2 = 0.95$ $I^2 = 0\%$	⊕⊕⊕ Moderate <sup>c</sup>
12-months	K = 2	7/1221 (1%)	5/1132 (0%)	0.1% (-0.4%, 0.7%) $\chi^2 = 0.93$ $I^2 = 0\%$	1.30 (0.41, 4.08) $\chi^2 = 0.94$ $I^2 = 0\%$	⊕⊕⊕⊕ High
24-month	K = 3	8/1221 (1%)	8/1132 (1%)	-0.1% (-0.7%, 0.6%) $\chi^2 = 0.96$ $I^2 = 0\%$	0.93 (0.35, 2.46) $\chi^2 = 0.98$ $I^2 = 0\%$	⊕⊕⊕⊕ High
5-years	K = 1 (NOTION)	3/142 (2%)	1/134 (1%)	1.4% (-1.4%, 4.1%)	2.83 (0.30, 26.88)	⊕⊕⊕ Moderate <sup>c</sup>
<b>Moderate/severe paravalvular leaks</b>						
30-days	K = 2	28/1190 (2%)	2/1029 (0%)	1.9% (-0.8%, 4.6%) $\chi^2 = 0.00$ $I^2 = 90\%$	<b>9.81 (2.70, 35.65)</b> $\chi^2 = 0.86$ $I^2 = 0\%$	⊕⊕⊕ Moderate <sup>d</sup>
12-months	K = 2	19/877 (2%)	4/708 (1%)	1.6% (-1.5%, 4.7%) $\chi^2 = 0.01$ $I^2 = 86\%$	3.35 (0.92, 12.18) $\chi^2 = 0.25$ $I^2 = 26\%$	⊕⊕⊕ Moderate <sup>d</sup>
24-month	K = 2	6/501 (1%)	0/415 (0%)	2.6% (-4.4%, 9.6%) $\chi^2 = 0.02$ $I^2 = 81\%$	5.76 (0.71, 46.92) $\chi^2 = 0.76$ $I^2 = 0\%$	⊕⊕⊕⊕ High
5-years	K = 1 (NOTION)	6/85 (7%)	0/84 (0%)	<b>7.1% (1.2%, 12.9%)</b>	12.85 (0.74, 224.53)	⊕⊕⊕ Moderate <sup>c</sup>
<b>Myocardial Infarction</b>						
30-days	K = 2	15/1363 (1%)	22/1266 (2%)	-0.4% (-1.2%, 0.4%) $\chi^2 = 0.47$ $I^2 = 0\%$	0.64 (0.33, 1.22) $\chi^2 = 0.83$ $I^2 = 0\%$	⊕⊕⊕ Moderate
12-months	K = 2	22/1363 (2%)	24/1266 (2%)	-0.4% (-1.4%, 0.6%) $\chi^2 = 0.43$ $I^2 = 0\%$	0.73 (0.42, 1.28) $\chi^2 = 0.58$ $I^2 = 0\%$	⊕⊕⊕ Moderate

Timepoint	Studies	TAVI	SAVR	Risk Difference (95% CI)	Relative Risk (95% CI)	Quality of the evidence (GRADE)
24-month	K = 2	28/1363 (2%)	30/1266 (2%)	-0.2% (-1.2%, 0.9%) $\chi^2 = 0.63$ $I^2 = 0\%$	0.87 (0.52, 1.45) $\chi^2 = 0.72$ $I^2 = 0\%$	⊕⊕⊕ Moderate
5-years	K = 1 (NOTION)	11/142 (8%)	11/134 (8%)	-0.5% (-6.9%, 5.9%)	0.94 (0.42, 2.10)	⊕⊕⊕ Moderate <sup>c</sup>
<b>Valve Endocarditis</b>						
30-days	K = 2	2/1363 (0%)	2/1266 (0%)	-0.1% (-0.5%, 0.3%) $\chi^2 = 0.32$ $I^2 = 13\%$	0.82 (0.13, 5.06) $\chi^2 = 0.36$ $I^2 = 1\%$	⊕⊕⊕ Moderate <sup>e</sup>
12-months	K = 2	6/1363 (0%)	6/1266 (0%)	-0.2% (-0.6%, 0.2%) $\chi^2 = 0.56$ $I^2 = 0\%$	0.94 (0.28, 3.10) $\chi^2 = 0.51$ $I^2 = 0\%$	⊕⊕⊕ Moderate <sup>e</sup>
24-month	K = 2	2/1221 (0%)	9/1132 (1%)	-0.3% (-0.8%, 0.2%) $\chi^2 = 0.29$ $I^2 = 11\%$	0.32 (0.06, 1.59) $\chi^2 = 0.67$ $I^2 = 0\%$	⊕⊕⊕⊕ Moderate <sup>a,e</sup>
5-years	K = 1 (NOTION)	9/142 (6%)	6/135 (4%)	1.9% (-3.4%, 7.2%)	1.43 (0.52, 3.90)	⊕⊕⊕ Moderate <sup>c,e</sup>
<b>Major Vascular Complications</b>						
30-days	K = 3	46/1363 (3%)	30/1266 (2%)	1.0% (-0.4%, 2.4%) $\chi^2 = 0.31$ $I^2 = 14\%$	1.39 (0.88, 2.20) $\chi^2 = 0.38$ $I^2 = 0\%$	⊕⊕⊕ Moderate <sup>c</sup>
12-months	K = 2	31/1221 (3%)	19/1266 (2%)	0.9 (-0.4%, 2.2%) $\chi^2 = 0.54$ $I^2 = 0\%$	1.30 (0.81, 2.09) $\chi^2 = 0.39$ $I^2 = 0\%$	⊕⊕⊕⊕ High
24-months	K = 1 (EVOLUT)	27/725 (4%)	22/678 (3%)	0.5% (-1.4%, 2.4%)	1.15 (0.66, 2.00)	⊕⊕⊕⊕ High

Abbreviation: CI = confidence interval, NE = not estimable, TAVI = transcatheter aortic valve implantation, SAVR = surgical aortic valve replacement.

<sup>a</sup> Overall quality of evidence (GRADE) was not upgraded for this outcome for large/very large magnitude of effect since outcome had serious limitations in at least one other domain.

<sup>b</sup> Heterogeneity is considered considerable since  $I^2 > 75\%$ ,  $p < 0.05$  and confidence intervals of one trial do not overlap with confidence intervals of other trials

<sup>c</sup> The NOTION study was not powered to demonstrate a potential significant difference between the treatment arms (140 subjects in each arm as reported in Thyregod 2013; Thyregod 2015)

<sup>d</sup> EVOLUT only reported statistically significant difference, not PARTNER 3.

<sup>e</sup> Event numbers were considered low hence variations may lead to changes in the direction of the point estimate or become non statistically significant.

**Bold text** = statistically significant at  $p$ -value  $< 0.05$

Source: Table 31- 40, pp61-69 of the commentary.

### TAVI-SEV vs. TAVI-BEV

The results of the indirect comparison of TAVI-BEV vs. TAVI-SEV for comparative safety (and effectiveness) is presented in Section 10 Comparative effectiveness (see Table 10).

## 11. Comparative effectiveness

### TAVI vs. SAVR

The pooled results of two clinical trials: EVOLUT and PARTNER 3 demonstrated that patients treated with TAVI had significantly lower rates of disabling stroke at both 30-days, 12-months and 2-years follow-up. However, as follow-up was limited to 2-years, the commentary considered that it was uncertain whether TAVI patients continue to have lower rates of disabling stroke after this period (2-years).

TAVI patients also had statistically significantly lower rates of mortality at 30 days post-surgery compared to SAVR patients based on the meta-analysis of the three clinical trials: EVOLUT, NOTION and PARTNER 3. However, the commentary highlighted that at 30-days follow-up, there were no statistically significant differences between treatment arms for

any of the trials or pooled estimates. The commentary noted that visual inspection of the curves for death or disabling stroke from the trials (see Figure 6 [EVOLUT], Figure 7 [PARTNER 3], p71 of the commentary) showed that the treatment effect could be attenuated over time. The 5-year results for NOTION showed no difference in mortality rates, with both TAVI and SAVR arms, reporting a mortality rate of 28%. The commentary considered that this suggested that TAVI was non-inferior to SAVR in the long-term (up to 5-years) with regards to mortality.

TAVI patients also had lower rates of rehospitalisation at 30-days, 12-months and 2-years follow-up, had a shorter hospital stay and spent less time in the ICU compared to patients treated with SAVR.

A summary of the key efficacy outcomes is provided in Table 9.

**Table 9 Summary of key efficacy outcomes for TAVI relative to SAVR, and as measured by randomised clinical trials: EVOLUT, NOTION, and PARTNER 3**

Timepoint	Studies	TAVI	SAVR	Risk Difference (95% CI)	Relative Risk (95% CI)	Quality of the evidence (GRADE)
<b>Mortality</b>						
30-days	K = 3	8/1363 (1%)	18/1266 (1%)	<b>-0.8% (-1.5%, -0.1%)</b> $\chi^2 = 0.89; I^2 = 0\%$	<b>0.42 (0.18, 0.96)</b> $\chi^2 = 0.87; I^2 = 0\%$	⊕⊕⊕ Moderate <sup>a</sup>
12-months	K = 3	26/1363 (2%)	38/1266 (3%)	<b>-1.0% (-2.1%, 0.1%)</b> $\chi^2 = 0.67; I^2 = 0\%$	0.64 (0.39, 1.06) $\chi^2 = 0.63; I^2 = 0\%$	⊕⊕⊕ Moderate <sup>a</sup>
24-months	K = 3	34/1363 (2%)	43/1266 (3%)	<b>-0.9% (-2.1%, 0.3%)</b> $\chi^2 = 0.63; I^2 = 0\%$	0.75 (0.48, 1.17) $\chi^2 = 0.47; I^2 = 0\%$	⊕⊕⊕ Moderate <sup>a</sup>
5-years	K = 1 (NOTION)	39/142 (28%)	37/134 (28%)	<b>-0.2% (-10.7%, 10.4%)</b>	0.99 (0.68, 1.46)	⊕⊕⊕ Moderate <sup>a</sup>
<b>Disabling stroke (PARTNER 3 and EVOLUT only)</b>						
30-days	K = 2	3/1363 (<1%)	13/1266 (1%)	<b>-0.8% (-1.6%, 0.1%)</b> $\chi^2 = 0.18; I^2 = 45\%$	<b>0.24 (0.08, 0.78)</b> $\chi^2 = 0.84; I^2 = 0\%$	⊕⊕⊕ Moderate <sup>a</sup>
12-months	K = 2	6/1363 (<1%)	18/1266 (1%)	<b>-0.9% (-1.7%, -0.1%)</b> $\chi^2 = 0.33; I^2 = 0\%$	<b>0.31 (0.12, 0.78)</b> $\chi^2 = 0.76; I^2 = 0\%$	⊕⊕⊕ Moderate <sup>a</sup>
24-months	K = 1 (EVOLUT)	6/725 (1%)	16/678 (2%)	<b>-1.5% (-2.9%, -0.2%)</b>	<b>0.35 (0.14, 0.89)</b>	⊕⊕⊕ Moderate <sup>a</sup>
<b>Stroke (disabling and non-disabling)</b>						
30-days	K = 3	29/1363 (2%)	37/1266 (3%)	<b>-1.1% (-2.4%, 0.3%)</b> $\chi^2 = 0.26; I^2 = 25\%$	0.58 (0.22, 1.49) $\chi^2 = 0.11; I^2 = 54\%$	⊕⊕⊕ Moderate
12-months	K = 3	29/1363 (2%)	37/1266 (3%)	<b>-1.1% (-2.4%, 0.2%)</b> $\chi^2 = 0.42; I^2 = 0\%$	0.71 (0.40, 1.25) $\chi^2 = 0.24; I^2 = 29\%$	⊕⊕⊕ Moderate
24-months	K = 3	47/1363 (3%)	52/1266 (4%)	<b>-0.7% (-2.2%, 0.7%)</b> $\chi^2 = 0.75; I^2 = 0\%$	0.84 (0.57, 1.24) $\chi^2 = 0.69; I^2 = 0\%$	⊕⊕⊕ Moderate
5-years	K = 1 (NOTION)	13/142 (9%)	10/134 (8%)	<b>1.7% (-4.8%, 8.2%)</b>	1.23 (0.56, 2.70)	⊕⊕⊕ Moderate
<b>Composite of death and disabling stroke (PARTNER 2 and EVOLUT, primary endpoint for EVOLUT)</b>						
30-days	K = 2	7/1221 (1%)	23/1132 (2%)	<b>-1.3% (-2.2%, -0.4%)</b> $\chi^2 = 0.30; I^2 = 7\%$	<b>0.28 (0.12, 0.66)</b> $\chi^2 = 0.91; I^2 = 0\%$	⊕⊕⊕⊕ High
12-months	K = 2	23/1221 (2%)	40/1132 (4%)	<b>-1.8% (-3.0%, -0.5%)</b> $\chi^2 = 0.39; I^2 = 0\%$	<b>0.52 (0.31, 0.87)</b> $\chi^2 = 0.39; I^2 = 0\%$	⊕⊕⊕⊕ High
24-months	K = 2	37/1221 (3%)	47/1132 (4%)	<b>-1.1% (-2.6%, 0.4%)</b> $\chi^2 = 0.67; I^2 = 0\%$	0.73 (0.48, 1.12) $\chi^2 = 0.71; I^2 = 0\%$	⊕⊕⊕⊕ High

Timepoint	Studies	TAVI	SAVR	Risk Difference (95% CI)	Relative Risk (95% CI)	Quality of the evidence (GRADE)
<b>Composite of death, stroke and rehospitalisation (primary endpoint for PARTNER 3)</b>						
30-days	K = 1 (PARTNER 3)	21/496 (4%)	42/454 (9%)	<b>-5.0% (-8.2%, -1.8%)</b>	<b>0.46 (0.28, 0.76)</b>	⊕⊕⊕⊕ High
12-months	K = 1 (PARTNER 3)	42/496 (9%)	68/454 (15%)	<b>-6.5% (-10.6%, -2.4%)</b>	<b>0.57 (0.39, 0.81)</b>	⊕⊕⊕⊕ High
24-months	K = 1 (PARTNER 3)	57/496 (12%)	79/454 (17%)	<b>-5.9% (-10.4%, -1.4%)</b>	<b>0.66 (0.48, 0.91)</b>	⊕⊕⊕⊕ High
<b>Re-hospitalisations (PARTNER 2 and EVOLUT)</b>						
30-days	K = 2	25/1363 (2%)	45/1266 (4%)	<b>-1.8% (-3.5%, -0.1%)</b> $\chi^2 = 0.22; I^2 = 33%$	<b>0.51 (0.32, 0.83)</b> $\chi^2 = 0.79; I^2 = 0%$	⊕⊕⊕ Moderate <sup>b</sup>
12-months	K = 2	56/1363 (4%)	87/1266 (7%)	<b>-3.0% (-4.8%, -1.2%)</b> $\chi^2 = 0.73; I^2 = 0%$	<b>0.60 (0.43, 0.83)</b> $\chi^2 = 0.36; I^2 = 0%$	⊕⊕⊕ Moderate <sup>b</sup>
24-months	K = 2	67/1363 (5%)	96/1266 (8%)	<b>-2.7% (-4.7%, -0.8%)</b> $\chi^2 = 0.40; I^2 = 0%$	<b>0.65 (0.48, 0.87)</b> $\chi^2 = 0.71; I^2 = 0%$	⊕⊕⊕ Moderate <sup>b</sup>
<b>Health-related quality of life (EQ-5D, mean change from baseline)</b>						
30-days	K = 1 (EVOLUT)	<b>0.11 (0.23)</b>	<b>0.01 (0.24)</b>	<b>&lt;0.00001</b>	-	-
12-months	K = 1 (EVOLUT)	0.09 (0.24)	0.08 (0.24)	0.57	-	-
<b>Median ICU stay</b>						
Procedure	K = 1 (PARTNER 3)	2	3	<b>-1.0 (p&lt;0.001)</b>	-	Not assessed
<b>Mean length of hospital stay for the index procedure (days, EVOLUT and NOTION)</b>						
Procedure	K = 2	3.6	7.3	<b>-3.6 (-3.9, -3.3)</b> $\chi^2 = 0.73; I^2 = 0%$	-	⊕⊕⊕ Moderate

Abbreviation: CI = confidence interval, NE = not estimable, TAVI = transcatheter aortic valve implantation, SAVR = surgical aortic valve replacement.

Note:

<sup>a</sup> Overall quality of evidence (GRADE) was not upgraded for this outcome for large/very large magnitude of effect since outcome had serious limitations in at least one other domain. Event numbers were considered low hence variations may lead to changes in the direction of the point estimate or become not statistically significant.

<sup>b</sup> Outcome definition was slightly different between EVOLUT LR and PARTNER 3 (see Section B.5)

**Bold text** = statistically significant at p-value < 0.05

Source: Tables 41-48, pp71-79 of the commentary

### The impact of including or excluding NOTION in the meta-analysis

The ADAR also presented a sensitivity analysis, in which the NOTION trial was removed from the meta-analysis, as 18% of the patients enrolled in the NOTION trial were classified as moderate surgical risk (Thyregod *et al.* 2015) (Table 49 of the commentary). The commentary considered that the pooled estimates for comparative safety and efficacy were largely consistent with and without the inclusion of the NOTION trial. However, the likelihood of TAVI patients requiring a permanent pacemaker implant was significantly reduced by the removal of the NOTION trial. The commentary considered that this may be explained due to the use of newer generation devices in EVOLUT and PARTNER 3 trials. The commentary noted that all three devices (i.e., CoreValve, EVOLUT R, and EVOLUT PRO) are TGA included and available and could be used in clinical practice in Australia. Therefore, the longer-term efficacy data from the NOTION trial was considered informative and applicable to Australian patients.



*TAVI-SEV vs. TAVI-BEV*

Table 10 presents the results of the indirect treatment comparison between TAVI-BEV (PARTNER 3) and TAVI-SEV (EVOLUT and NOTION), via the common comparator, SAVR. Results were presented including and excluding the NOTION trial.

The results of the indirect comparison presented by the ADAR found there were no significant differences in terms of key efficacy outcomes: death, disabling stroke or any strokes (disabling and non-disabling).

However, the commentary highlighted that patients treated with TAVI-SEV were significantly more likely to require a permanent pacemaker, experience bleeding events and develop moderate to severe paravalvular leaks at 30 days and 12-months follow-up, but not at 24 months follow-up. Importantly this did not result in any significant differences in the rates of aortic valve reintervention between the two devices. The rates of bleeding events at 30 days in the TAVI arms of the key trials were relatively similar (4% in PARTNER 3, 7% in EVOLUT and 11% in NOTION) but varied substantially across the SAVR arms of the trials (24% in PARTNER 3, 10% in EVOLUT and 21% in NOTION).

**Table 10 Indirect comparison TAVI-SEV versus TAVI-BEV, via the common comparator SAVR**

Outcome	TAVI-BEV (PARTNER 3) versus TAVI-SEV (EVOLUT and NOTION)			TAVI-BEV (PARTNER 3) versus TAVI-SEV (EVOLUT)		
	TAVI-BEV	TAVI-SEV	Indirect Comparison RD (95% CI)	TAVI-BEV	TAVI-SEV	Indirect Comparison RD (95% CI)
<b>30-days</b>						
All-cause mortality or disabling stroke	NA	NA	NA	-0.9% (-2.1%, 0.3%)	<b>-1.8% (-3.1%, -0.5%)</b>	0.9% (-0.9%, 2.7%)
All-cause mortality	-0.7% (-1.8%, 0.4%)	-0.9% (-1.9%, 0.1%)	0.2% (-1.3%, 1.7%)	-0.7% (-1.8%, 0.4%)	-0.8% (-1.7%, 0.2%)	0.1% (-1.4%, 1.5%)
Disabling stroke	NA	NA	NA	-0.4% (-1.0%, 0.2%)	<b>-1.2% (-2.3%, -0.1%)</b>	0.8% (-0.5%, 2.0%)
Any Stroke	<b>-1.8% (-3.4%, -0.2%)</b>	-0.2% (-1.9%, 1.5%)	-1.6% (-3.9%, 0.7%)	<b>-1.8% (-3.4%, -0.2%)</b>	0.1% (-1.8%, 1.9%)	-1.9% (-4.3%, 0.6%)
Bleeding events <sup>a</sup>	<b>-20.8% (-25.1%, -16.5%)</b>	<b>-4.6% (-7.4%, -1.7%)</b>	<b>-16.3% (-21.4%, -11.1%)</b>	<b>-20.8% (-25.1%, -16.5%)</b>	<b>-3.5% (-6.4%, -0.7%)</b>	<b>-17.3% (-22.4%, -12.1%)</b>
New onset atrial fibrillation	NA	NA	NA	<b>-27.7% (-32.3%, -23.1%)</b>	<b>-27.4% (-31.4%, -23.3%)</b>	-0.3% (-6.5%, 5.8%)
New permanent pacemaker	2.5% (-0.3%, 5.3%)	14.6% (11.5%, 17.6%)	<b>-12.1% (-16.2%, -7.9%)</b>	2.5% (-0.3%, 5.3%)	11.3% (8.1%, 14.6%)	<b>-8.9% (-13.2%, -4.5%)</b>
Aortic valve reintervention	0.0% (0.0%, 0.0%)	0.0% (-0.5%, 0.5%)	0.0% (-0.5%, 0.5%)	0.0% (0.0%, 0.0%)	0.0% (-0.6%, 0.5%)	0.0% (-0.5%, 0.6%)
Paravalvular leakage (moderate/severe)	NA	NA	NA	<b>0.8% (0.0%, 1.6%)</b>	<b>3.1% (1.7%, 4.5%)</b>	<b>-2.3% (-3.9%, -0.6%)</b>
<b>12 months</b>						
All-cause mortality or disabling stroke	NA	NA	NA	<b>-1.9% (-3.6%, -0.1%)</b>	-1.6% (-3.5%, 0.2%)	-0.2% (-2.8%, 2.3%)
All-cause mortality	-1.4% (-3.1%, 0.3%)	-0.9% (-2.5%, 0.7%)	-0.5% (-2.8%, 1.8%)	-1.4% (-3.1%, 0.3%)	-0.6% (-2.1%, 1.0%)	-0.8% (-3.1%, 1.4%)
Disabling stroke	NA	NA	NA	-0.7% (-1.6%, 0.3%)	<b>-1.4% (-2.6%, -0.1%)</b>	0.7% (-0.9%, 2.2%)
Any Stroke	-1.9% (-3.7%, 0.0%)	-0.4% (-2.2%, 1.5%)	-1.5% (-4.1%, 1.1%)	-1.9% (-3.7%, 0.0%)	-0.1% (-2.2%, 1.9%)	-1.8% (-4.5%, 1.0%)
Bleeding events	NA	NA	NA	<b>-18.1% (-22.8%, -13.5%)</b>	<b>-3.8% (-6.9%, -0.7%)</b>	<b>-14.3% (-19.9%, -8.7%)</b>
New onset atrial fibrillation	NA	NA	NA	-27.2% (-32.0%, -22.4%)	-28.2% (-32.4%, -24.0%)	1.0% (-5.4%, 7.4%)
New permanent pacemaker	2.0% (-1.1%, 5.0%)	<b>15.9% (12.7%, 19.1%)</b>	<b>-13.9% (-18.3%, -9.5%)</b>	2.0% (-1.1%, 5.0%)	<b>12.4% (9.0%, 15.8%)</b>	<b>-10.4% (-15.0%, -5.9%)</b>
Aortic valve reintervention	NA	NA	NA	0.2% (-0.8%, 1.1%)	0.1% (-0.6%, 0.8%)	0.1% (-1.1%, 1.2%)
Paravalvular leakage (moderate/severe)	NA	NA	NA	0.3% (-0.8%, 1.4%)	3.1% (1.1%, 5.1%)	<b>-2.7% (-5.0%, -0.4%)</b>
<b>24 months</b>						

Outcome	TAVI-BEV (PARTNER 3) versus TAVI-SEV (EVOLUT and NOTION)			TAVI-BEV (PARTNER 3) versus TAVI-SEV (EVOLUT)		
	TAVI-BEV	TAVI-SEV	Indirect Comparison RD (95% CI)	TAVI-BEV	TAVI-SEV	Indirect Comparison RD (95% CI)
All-cause mortality or disabling stroke	NA	NA	NA	-0.7% (-3.0%, 1.6%)	-1.4% (-3.4%, 0.6%)	0.7% (-2.4%, 3.7%)
All-cause mortality	-1.4% (-3.1%, 0.3%)	-0.6% (-2.4%, 1.2%)	-0.8% (-3.3%, 1.6%)	-1.4% (-3.1%, 0.3%)	-0.3% (-2.0%, 1.4%)	-1.1% (-3.5%, 1.3%)
Disabling stroke	NA	NA	NA	NA	NA	NA
Any Stroke	-1.1% (-3.3%, 1.1%)	-0.4% (-2.3%, 1.5%)	-0.7% (-3.6%, 2.2%)	-1.1% (-3.3%, 1.1%)	-0.1% (-2.2%, 2.0%)	-1.0% (-4.0%, 2.1%)
Bleeding events	NA	NA	NA	NA	NA	NA
New onset atrial fibrillation	NA	NA	NA	<b>-27.0% (-31.9%, -22.2%)</b>	<b>-27.6% (-31.8%, -23.3%)</b>	0.5% (-6.0%, 7.0%)
New permanent pacemaker	2.3% (-1.0%, 5.6%)	17.1% (13.9%, 20.4%)	-14.8% (-19.5%, -10.2%)	2.3% (-1.0%, 5.6%)	<b>13.6% (10.2%, 17.1%)</b>	<b>-11.3% (-16.1%, -6.6%)</b>
Aortic valve reintervention	NA	NA	NA	-0.1% (-1.2%, 1.1%)	0.0% (-0.8%, 0.8%)	0.0% (-1.4%, 1.4%)
Paravalvular leakage (moderate/severe)	NA	NA	NA	0.5% (-0.2%, 1.1%)	5.7% (0.3%, 11.2%)	-5.3% (-10.7%, 0.2%)

Abbreviations: BEV= balloon expandable valve; NA= not available; TAVI= transcatheter aortic valve implantation; RD= risk difference; SAVR= surgical aortic valve replacement; SEV= self-expandable valve.

Notes:

<sup>a</sup> TAVI patients in NOTION received dual therapy with aspirin and clopidogrel, whilst TAVI patients in PARTNER 3 received low-dose aspirin. TAVI patients in EVOLUT did not appear to receive any antiplatelet therapy before treatment. This may have contributed to differences in the rates of disabling and major bleeding between trial arms.

Source: Table 51, pp83-84 of the commentary

The ADAR further reiterated that the results of the indirect comparison closely aligned with a published indirect comparison (Elgendy *et al.* 2020<sup>21</sup>), who concluded there were no significant differences between TAVI-BEV and TAVI-SEV based on the rates of all-cause mortality and stroke, based on the results of EVOLUT, NOTION and PARTNER 3. Further, the commentary highlighted that a published perspective by Tang *et al.* (2019)<sup>22</sup>, concluded that “both trials [PARTNER 3 and EVOLUT] showed that TAVR was superior to SAVR for [short-term] clinical outcomes, with remarkable concordance between the 2 trials”.

### *Clinical claim*

#### TAVI vs. SAVR

The clinical claim is that TAVI for the treatment of symptomatic severe AS is superior in terms of effectiveness and safety compared to SAVR for patients at low risk of surgery.

The commentary considered the clinical claim of superior efficacy was reasonable up to 2-years post-procedure where TAVI patients had significantly lower rates of disabling stroke and perioperative mortality. The pooled results of two clinical trials: EVOLUT and PARTNER 3 demonstrated that patients treated with TAVI had significantly lower rates of disabling stroke at both 30-days, 12-months and 2-years follow-up. However, there was no survival benefit after 30-days post-surgery. Further, TAVI patients also reduced length of hospital stay and fewer rehospitalisations than SAVR patients. The commentary suggested the following clinical claim: TAVI for the treatment of symptomatic severe AS is superior in terms of efficacy compared to SAVR in the short term (for up to 2 years) and non-inferior thereafter. The commentary noted that the durability of TAVI is unknown beyond 5 years.

The clinical claim of superior safety was considered reasonable by the commentary for the outcomes: (1) major or life-threatening or disabling bleeding, (2) stage  $\geq 3$  acute kidney and (3) atrial fibrillation. However, patients treated with TAVI were significantly more likely to (1) require a permanent pacemaker implant, (2) had higher rates of moderate to severe paravalvular leaks and (3) rates of new left bundle branch block. The commentary considered these procedural complications suggested that TAVI has a different safety profile relative to SAVR.

#### TAVI-SEV vs. TAVI-BEV

For the supplementary comparator, TAVI-BEV, the ADAR claimed that TAVI-SEV had non-inferior safety and efficacy to TAVI-BEV. The commentary considered that this was reasonable and was supported by the results of the indirect comparison between TAVI-SEV and TAVI-BEV, via the common comparator SAVR.

## **12. Economic evaluation**

### *Translation Issues*

The ADAR presented a modelled economic evaluation, which utilised trial data from EVOLUT, NOTION and PARTNER 3. Consistent with MSAC Applications 1603 and 1361.2, the ADAR’s economic model was a Markov cohort of consisted of three health states: (1) alive without disabling stroke, (2) alive with disabling stroke and (3) death. This

---

<sup>21</sup> Elgendy, I, Gad, M, Mahmoud, A, *et al.* 2020. “Meta-analysis comparing outcomes of self-expanding versus balloon-expandable valves for transcatheter aortic valve implantation” *Am J Cardiol* 128: 202–209

<sup>22</sup> Tang, Verma, *et al.* (2019). "Transcatheter aortic valve replacement in low-risk patients: A new era in the treatment of aortic stenosis." *Circulation* 140(10): 801-803.

differed from Application 1635 which considered all strokes rather than disabling strokes (PSD Application 1635, p24).

The ADAR applied treatment specific disabling stroke event rates up until 24 months based on the results on EVOLUT and PARTNER 3 that showed significant differences in the rates of disabling stroke between trial arms. Beyond the trial period, the ADAR using the pooled rates of disabling stroke between treatment arms reported by EVOLUT at 1 and 2 years. The commentary considered that this was reasonable.

For mortality, treatment-specific rates were applied during the perioperative period (cycle 0). From 30-days to 5-years (cycle 1-59) pooled mortality rates from trial data were applied, as the trial data showed no significant difference in survival between arms between treatment arms. Mortality beyond the trial period (after 5-years) was extrapolated using Australian lifetables. Overall, the commentary considered the methods used by the ADAR were appropriate and were able to be verified by the Evaluation.

The utility values applied to patients in the 'Alive, without disabling stroke' state, were derived from the EVOLUT trial. As the evidence presented in Section B (see Table 9) showed that TAVI patients had significantly improved health-related quality of life compared to SAVR patients in the perioperative period, treatment-specific values were applied in the first cycle (TAVI = 0.82 vs. SAVR = 0.74). After this, the ADAR applied the trial average utility values as there were no significant differences between treatment arms. The commentary considered that this was reasonable.

For patients in the Alive with disabling stroke state, the ADAR applied the same utilities (of 0.47) that were applied (Zhou *et al.* 2021<sup>23</sup>). These utility values were derived from (Sturm *et al.* 2004<sup>24</sup>), which was an Australian cohort study of the health-related quality of life in stroke survivors. The commentary considered that was reasonable.

The economic evaluation is summarised in Table 11.

---

<sup>23</sup> Zhou *et al.* (2021). "Cost-effectiveness of transcatheter vs. surgical aortic valve replacement in low-risk patients with severe aortic stenosis." *Heart Lung Circ* 30(4): 547-554.

<sup>24</sup> Sturm *et al.* (2004). "Quality of life after stroke: The north east melbourne stroke incidence study (nemesis)." *Stroke* 35(10): 2340-2345.

**Table 11 Summary of the economic evaluation**

Perspective	Health care payer
Comparator	SAVR
Type of economic evaluation	Cost-utility analysis
Sources of evidence	Trial data from EVOLUT, NOTION and PARTNER 3
Time horizon	10 years
Outcomes	QALYs
Methods used to generate results	Markov model with a hypothetical cohort of patients aged 74 years (mean age in EVOLUT and PARTNER 3).
Health states	Following the TAVI or SAVR procedure, the health states are: 1. Alive, without disabling stroke 2. Alive with disabling stroke 3. Dead
Cycle length	Monthly
Discount rate	5%
Software packages used	Microsoft Excel 2016

Abbreviations: QALY = quality adjusted life year; RCT = randomised controlled trial; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation

Source: Table 83, p 159 of the ADAR

The commentary highlighted the following key issues with the ADAR’s economic evaluation for the TAVI vs. SAVR comparison:

- The ADAR estimated the hospitalisation cost of treatment with TAVI and SAVR based on the average length of hospital stay reported in EVOLUT and NOTION (TAVI = 3.6 days and SAVR = 7.3 days), multiplied by the weighted average cost for a day stay in hospital for SAVR patients <sup>25</sup> (\$4,836, revised to \$4,839 in the commentary). However, this approach assumes that hospitalisation costs for SAVR are “evenly distributed across the length of the [patient’s] hospital stay, whereas it is known that the reductions in hospital stay are typically for the cheaper days” (PSD MSAC 1361.2, p3). MSAC previously agreed that this assumption favours TAVI as the reductions in hospital stay are typically for the cheaper days and not evenly distributed (PSD MSAC 1603, p6).
- The economic model did not include the cost of treating adverse events and their associated disutilities (except for the cost of treating patients with permanent pacemakers in a sensitivity analysis). The direction of bias resulting from the ADAR’s decision to exclude adverse events is unknown, given that relative to SAVR, TAVI is inferior in terms of new permanent pacemakers, vascular complication, aortic valve reintervention and paravalvular leaks and superior in terms of atrial fibrillation, acute kidney injury, myocardial infarction and disabling or life-threatening bleeding.
- The ADAR’s economic model did not consider the loss in utility and increased rates of mortality and other associated complications for patients requiring aortic reintervention. The pre-ESC response estimated the impact of the costs and disutility associated that were different between TAVI and SAVR. This included bleeding, acute kidney injury, atrial fibrillation, LBBB and new PPI (see Table 14).

Compared to the SAVR group, the TAVI- patients lived longer and spent more years in the ‘Alive, without disabling stroke’ state, which resulted in an incremental QALY gain of 0.095. As the costs of treatment with TAVI were also less expensive (cost-savings of \$3,569), this resulted in TAVI being the dominant treatment (see Table 12).

<sup>25</sup> SAVR DRGs: F04A, F04B and F04C (cardiac valve procedures without invasive cardiac investigations)

**Table 12 Stepped economic evaluation (5% discounting applied)**

Step and component	TAVI <sup>a b c</sup>	SAVR <sup>a b c</sup>	Increment
<b>Step 1: trial-based economic evaluation (5 years)</b>			
Cost	\$42,616	\$45,856	-\$3,240
LYs	4.22	4.17	0.045
QALYs	3.41	3.35	0.057
Incremental cost per LY gained			TAVI dominates
Incremental cost per QALY gained			TAVI dominates
<b>Step 2: trial-based economic evaluation (5 years), plus include costs of stroke</b>			
Cost	\$42,813	\$46,307	-\$3,495
LYs	4.22	4.17	0.045
QALYs	3.41	3.35	0.057
Incremental cost per LY gained			TAVI dominates
Incremental cost per QALY gained			TAVI dominates
<b>Step 3: modelled economic evaluation extrapolated to 10 years</b>			
Cost	\$42,981	\$46,550	-\$3,569 <sup>d</sup>
LYs	6.80	6.72	0.081
QALYs	5.49	5.40	0.095
Incremental cost per LY gained			TAVI dominates
Incremental cost per QALY gained			TAVI dominates

Abbreviation: LY = life year; QALY= quality-adjusted life year; SAVR = surgical aortic valve implantation; TAVI= transcatheter aortic valve implantation

Note:

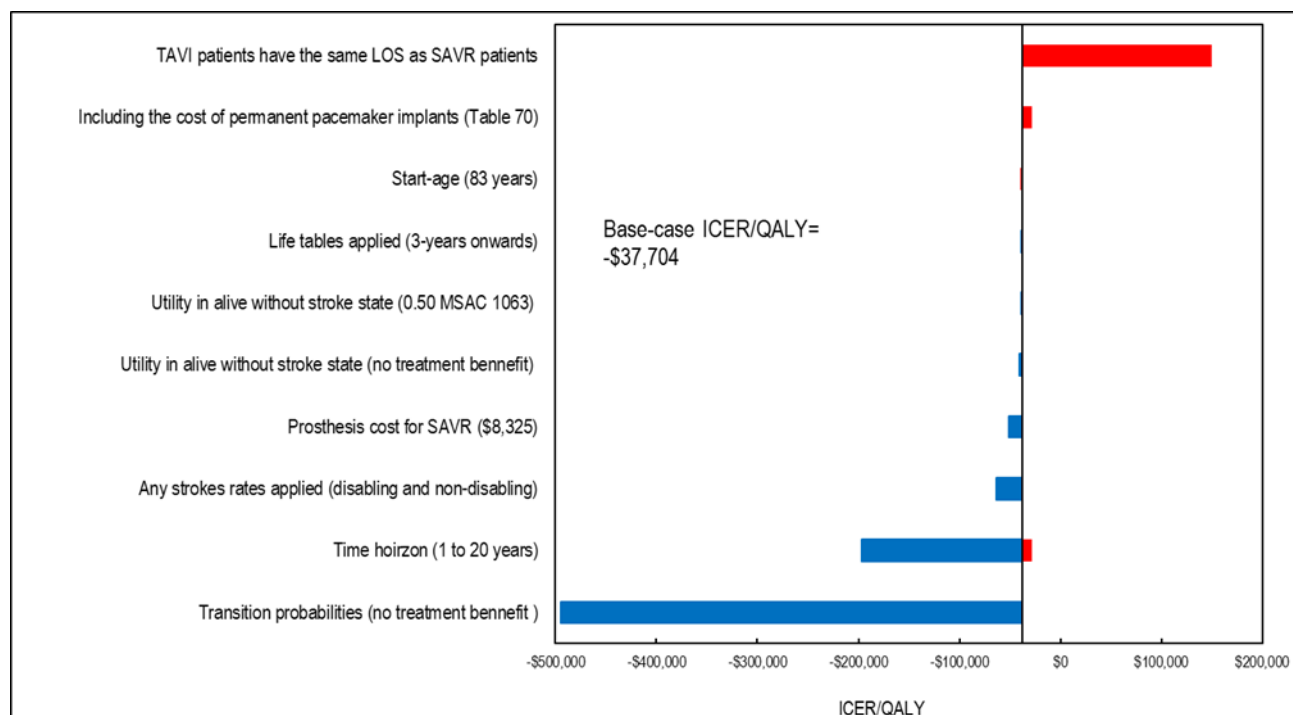
<sup>a</sup> The ADAR model did not include the cost of whole body perfusion in the MBS estimates. <sup>b</sup> Hospital costs were updated to Round 23

<sup>c</sup> During the Evaluation it was found that cells 'Inputs and Results'!D47:E47 were not capturing all the associated treatment costs. This was corrected during the Evaluation.

<sup>d</sup> The ADAR estimated the incremental cost savings of SAVR were \$1,955. However, due to the corrections made above to the ADAR the Evaluation estimated TAVI resulted in cost savings of \$3,569

Source: Table 96, p 176 of the ADAR

Overall, the sensitivity analyses conducted by the ADAR and the commentary found that treatment with TAVI was the dominant treatment option in most scenarios (Figure 5).



**Figure 5 Tornado Diagram**

Abbreviations: ICER = incremental cost-effectiveness ratio; LOS = length of stay, QALY = quality-adjusted life year; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation

Source: Constructed during the evaluation

This included changes in utility values, prosthesis cost of SAVR and TAVI, the inclusion of both, non-disabling and disabling strokes, assuming no treatment benefit between TAVI and SAVR, including the cost of permanent pacemaker implants and the start-age of patients in the model. The exception was when the hospitalisation costs for treatment with TAVI were adjusted based on the length of hospital stay for TAVI vs. SAVR patients. TAVI was no longer the dominant treatment option in the corrected economic model once the assumed average length of hospital stay increases from 3.6 days to approximately 4.37 days.

The pre-ESC response noted that MSAC have previously stated that “reductions in hospital stay are typically for the cheaper days that do not incur the costs of the procedure”. Thus, the applicant removed the cost of the operating room component of the DRGs costs (direct costs and overheads) reducing the cost per hospital bed day from \$4,839 (the cost calculated by the evaluators using the most recent Round 23 public sector sample cost weights) to \$3,862. Applying this lower daily cost in the ADAR model generates an ICER of approximately \$10,350 per QALY gained using the ADAR’s economic model (\$211/QALY using the revised model). The pre-ESC response claimed that TAVI still appears cost-effective when this lower bed day cost is applied to the incremental LOS.

The pre-ESC response also highlighted that the Australian sub-study of EVOLUT reported that TAVI patients were managed in the cardiac care unit (mean stay 2.1 day) and all SAVR patients were managed in the ICU (mean stay 3.0 days). Therefore, the applicant considered that the economic model conservatively excluded cost savings associated with shorter and with less intensive patient management, post-procedure with TAVI compared with SAVR. However other data presented in the pre-ESC response reported no patients treated with SAVR were admitted to the ICU (Table 13).

**Table 13 Length of hospital stay data from the Australian substudy of the EVOLUT LR trial**

<b>Outcome</b>	<b>TAVI (N=16)</b>	<b>SAVR (N=12)</b>
<b>Length of hospitalisation</b>		
Mean (SD)	2.75 days (1.29)	6.92 days (1.56)
Median (range)	3 days (1, 5)	7 days (4,9)
Interquartile range	1.5 to 3 days	6 to 8 days
<b>Length of stay by setting</b>		
Cardiac care unit	15 (94%)	10 (83%)
Intensive care unit	0 (0%)	0 (0%)
Mean (SD)	51.07 hours (34.54)	70.60 hours (66.79)
Median (range)	48 hours (0, 125)	36.5 hours (10, 216)
Interquartile range	24 to 72 hours	24 to 120 hours

Source: Table 2 – Table 3, p6 of the pre-ESC Response.

SAVR = surgical aortic valve replacement; SD = standard deviation; TAVI = Transcatheter Aortic Valve Implantation

The pre-ESC response also calculated the average costs and disutilities for these adverse events based on the published economic evaluation by Zhou (2020). The pre-ESC response concluded that including the cost and disutility from adverse events did not impact the conclusions that TAVI dominates SAVR and is cost-effective.



**Table 14 Costs and disutilities associated with significant differences in adverse event rates at 24 months**

Adverse event	Event rate at 24 months <sup>a</sup>			Event costs <sup>b</sup>				Event disutilities <sup>b</sup>			
	TAVI	SAVR	Inc.	Cost	TAVI	SAVR	Inc.	Value	TAVI	SAVR	Inc.
Bleeding <sup>c</sup>	8%	12%	-3%	\$6,596	\$555	\$778	-\$223	0.041	0.003	0.005	-0.001
AKI (stage 3+)	0%	2%	-1%	\$8,447	\$35	\$150	-\$115	0.094	0.000	0.002	-0.001
New-onset AF	9%	36%	-27%	\$3,379	\$296	\$1,221	-\$925	0.038	0.003	0.014	-0.010
LBBB	23%	9%	14%	\$7,756	\$1,822	\$700	\$1,122	0.003	0.001	0.000	0.000
New PPI	18%	6%	12%	\$7,756	\$1,383	\$472	\$911	0.003	0.001	0.000	0.000
<b>Total</b>	-	-	-	-	<b>\$4,091</b>	<b>\$3,321</b>	<b>\$770</b>	-	<b>0.008</b>	<b>0.021</b>	<b>-0.012</b>

Abbreviations: AF = atrial fibrillation; AKI = acute kidney injury; Inc = incremental; LBBB = left bundle branch block; PPI = permanent pacemaker implants

<sup>a</sup> 'TAVI via transfemoral delivery for patients at low risk for surgery', Final Evaluation Report, Table 4

<sup>b</sup> One-off cost and disutility from Zhou 2020 (Table A2 and Table A1, respectively)

<sup>c</sup> Life-threatening, disabling, major

Source: Table 5, Pre-ESC Response

### 13. Financial/budgetary impacts

The ADAR used a mixed market-share and epidemiological approach to estimate the financial implications of the listing of TAVI in patients with symptomatic, severe AS and at low surgical risk. The ADAR did not consider the cost of treating public patients. Therefore, the commentary adjusted the ADAR's patient numbers to account for both public and private patients. The commentary also included the cost of treating public patients using the same cost of prostheses and hospitalisation costs using as described in Section D.4 of the evaluation and included the cost of the prosthesis for private patients (as the ADAR only considered hospitalisation costs). Over the next five years (2021-2025), the ADAR estimated that MBS-listing TAVI for low-risk patients would result in approximately \$21.3 million in cost-savings to the Australian government (Table 15).

**Table 15 Net financial implications to the MBS and State and Territory Government Health Budgets and private hospitals due to the MBS-listing of TAVI**

Parameter	2021	2022	2023	2024	2025	Total
<b>Cost to the MBS</b>						
Private patients (44%)	1,257	1,278	1,299	1,321	1,343	6,498
Cost to the MBS due to listing TAVI (75% fee) <sup>a</sup>	\$2,691,684	\$2,737,604	\$2,782,588	\$2,829,714	\$2,876,840	\$13,918,430
Cost-savings to the MBS due to listing TAVI (75% fee)	-\$3,714,842	-\$3,778,023	-\$3,841,539	-\$3,905,837	-\$3,971,633	-\$19,211,874
<b>Net-cost to the MBS</b>	<b>-\$1,023,158</b>	<b>-\$1,040,420</b>	<b>-\$1,058,951</b>	<b>-\$1,076,123</b>	<b>-\$1,094,793</b>	<b>-\$5,293,444</b>
<b>Cost to the state and territory government health budgets<sup>a b c</sup></b>						
Public patients (66%)	1,599	1,627	1,654	1,682	1,710	8,272
Cost of treatment with TAVI	\$64,769,666	\$65,871,257	\$66,978,669	\$68,099,729	\$69,246,916	\$334,966,238
Cost-savings due to TAVI (reduction in SAVR)	\$67,870,736	\$69,025,070	\$70,185,502	\$71,360,237	\$72,562,350	\$351,003,895
<b>Net cost to state and territory governments</b>	<b>-\$3,101,070</b>	<b>-\$3,153,812</b>	<b>-\$3,206,833</b>	<b>-\$3,260,508</b>	<b>-\$3,315,434</b>	<b>-\$16,037,657</b>
<b>Cost to the Australian government</b>						
Net-cost to the Australian government	-\$4,124,228	-\$4,194,232	-\$4,265,784	-\$4,336,631	-\$4,410,226	-\$21,331,101
<b>Cost to private health insurance<sup>d</sup></b>						
Net prosthesis costs due to listing TAVI	\$19,895,679	\$20,234,062	\$20,574,232	\$20,918,594	\$21,270,983	\$102,893,549
<b>Cost to private hospitals<sup>c d</sup></b>						
Net private hospital cost-savings due to listing TAVI	-\$22,332,234	-\$22,712,057	-\$23,093,886	-\$23,480,422	-\$23,875,966	-\$115,494,566
Net cost to private health insurance	-\$2,436,555	-\$2,477,995	-\$2,519,655	-\$2,561,828	-\$2,604,983	-\$12,601,016

Abbreviations: ADAR = applicant developed assessment report; MBS = Medical Benefits Scheme; PHI = private health insurance; TAVI = transcatheter aortic valve implantation; SAVR = surgical aortic valve replacement

Note:

<sup>a</sup> The ADAR did not consider the cost of treating public patients. Therefore, the commentary adjusted the ADAR's patient numbers to account for both public and private patients.

<sup>b</sup> The evaluation included prostheses costs and hospital stay costs for public patients

<sup>c</sup> Hospital costs were updated to Round 23

<sup>d</sup> The commentary included the cost of the prosthesis for private patients

Source: Table 85, Table 88, Table 89 and Table 90 of Section E of the commentary

The commentary considered the cost of listing of TAVI is uncertain for the following reasons:

- The ADAR considered that all patients currently treated with SAVR would be eligible for treatment with TAVI if it was available. However, some SAVR patients have AS due to congenital bicuspid aortic valves (which increases the risk of aortic stenosis among young adults) and rheumatic fever. As TAVI devices are only TGA approved for patients with severe native calcific aortic stenosis, the ADAR may have overestimated the number of eligible patients. This would result in reduced cost-savings to the Australian government;
- The ADAR assumed that 60% of eligible patients that are currently treated with SAVR would switch to TAVI if listed. Although the current 2020 ACC/AHA guideline recommends either SAVR or TAVI in patients aged 65-85 years, it states that the decision needs to take into consideration the patient's longevity and valve durability (Otto *et al.* 2021). In particular, SAVR is preferred for patients with a longer life expectancy. This would result in reduced cost-savings to the Australian government;
- The ADAR estimated the hospitalisation cost of treatment with TAVI and SAVR based on the average length of hospital stay for patients EVOLUT and NOTION (TAVI = 3.6 days vs. SAVR = 7.3-days), multiplied by the average cost per day stay in hospital of \$4,660. However, this approach assumes that hospitalisation costs for

SAVR are evenly distributed over the length of the patient’s hospital stay when it is known that the bulk of the patient’s treatment cost occurs in the first few days of the patient’s hospital stay. Hence, there is considerable uncertainty in the reduction in hospital costs that would be achieved with treatment with TAVI.

The pre-ESC response advised that the financial implications in the ADAR should be considered an upper estimate. This was because some patients undergoing SAVR have AS due to causes other than severe native calcific AS. Additionally, the estimated that 20% of valve replacement procedures claimed under MBS item 38488 would be to replace other heart valves based on procedure data from the National Hospital Morbidity database.<sup>26</sup>

#### 14. Key Issues from ESC for MSAC

ESC key issue	ESC advice to MSAC
Long term outcomes	<p>The ADAR included the NOTION trial, a new trial, which provides 5-year data comparing TAVI and SAVR in a predominantly low risk population. Longer-term data are required to assess the clinical implications of paravalvular leaks, left bundle-branch block and uncertain valve durability. These issues are particularly pertinent to young and low-risk patients who have longer life expectancies and generally have good long-term outcomes with SAVR.</p> <p>ESC noted that following the deferral of TAVI using a balloon-expandable valve system for low surgical risk (Application 1635) due to potential concerns about long term outcomes and valve durability, that targeted consultation data for these matters, and related to the appropriate population and item descriptor for TAVI may be provided to the MSAC July 2021 meeting.</p>
Item descriptor	<p>It may be reasonable for the item descriptor to:</p> <ul style="list-style-type: none"> <li>Specify that TAVI is intended for patients with native calcific aortic stenosis (AS) as this would align with the registered indications for the TAVI valves, and</li> <li>have consistent wording with respect to frailty and procedure-specific impediments across surgical risk levels.</li> </ul> <p>MSAC may wish to consider whether the item descriptor should:</p> <ul style="list-style-type: none"> <li>be limited to transfemoral TAVI and whether this should apply across the different surgical risk populations, and</li> <li>exclude patients aged &lt;65 years as clinical guidelines recommend SAVR for patients &lt;65 years unless life expectancy is limited.</li> </ul>
ICER sensitivity	Relatively small and reasonable changes in the model inputs such as average length of hospital stays and cost of hospital day can significantly increase the ICER.
Financial implications (savings) may be overestimated	Eligible patient population may be smaller than that eligible for SAVR as not all patients undergoing SAVR would be appropriate for TAVI. TAVI uptake may be lower due to possible preference for SAVR by patients with longer life expectancy. Small changes to the assumptions relating to the cost of hospitalisation could result in substantial costs to Government.

#### ESC discussion

ESC noted that TAVI is currently MBS-listed as a TAVI device agnostic item (either self-expandable valve [SEV] or balloon expandable valve [BEV]) for high-risk/inoperable surgical patients with symptomatic severe aortic stenosis (AS) under item 38495. ESC also noted that the MSAC supported a new MBS item agnostic of the type of TAVI device for

<sup>26</sup> [Procedures data cube under Australian Classification of Health Interventions \(ACHI\) Edition 10](#), 2018-19, National Hospital Morbidity Database

intermediate surgical risk ([Public Summary Document \[PSD\], Application No. 1652, 2021](#)). The Applicant Developed Assessment Report (ADAR) sought to expand the MBS funding of TAVI to include patients at a low surgical risk for surgery.

ESC noted that Application 1635 (TAVI low surgical risk, with a BEV) was deferred at the March 2021 MSAC meeting and will be re-assessed at the July 2021 MSAC meeting ([PSD, Application No. 1603, 2020](#); [PSD, Application No. 1635, 2021](#)). ESC noted the following matters from MSAC's consideration of Application 1635 that may be applicable to the current application:

- Concerns for valve durability over the longer term, given that the low surgical risk population is younger, has longer life expectancy and generally has good long-term outcomes with SAVR;
- The appropriate population and item descriptor for TAVI with low surgical risk would need to be further refined to ensure TAVI is used for low-risk patients most likely to benefit from the procedure. Further consultation is being undertaken to define key factors that suggest one procedure may be preferred over the other for the low surgical risk population;
- MSAC considered that a separate MBS item should be created for TAVI in low risk population as this would assist monitoring of TAVI utilisation. MSAC advised that at a future date it may be appropriate to consolidate the TAVI items based on surgical risk into a single item; and
- MSAC maintained its preference for a device-agnostic MBS item descriptor.

ESC noted the Department's advice that the consultation data may be provided to the MSAC July 2021 meeting.

ESC also noted the Department's policy advice that TAVI for the intermediate and low-risk (if supported by the MSAC) populations would be implemented as stand-alone MBS items for the purposes of specific risk cohort data and monitoring for leakage, and compliance with the item descriptor. ESC advised that this approach was appropriate.

ESC noted that the descriptor should be amended so that it is consistent with other TAVI items. Currently the item does not specify that patients have no significant frailty (as defined by the Heart Team) and no procedure-specific impediments, despite best practice involving a multidisciplinary Heart Team assessing patients on an individual basis. ESC noted that the target patient population should have severely calcified valve leaflets, as this aligns with the Therapeutic Goods Administration– (TGA-) approved indication for TAVI devices. ESC also noted that two of the key trials (PARTNER 3 and EVOLUT) excluded patients in whom transfemoral access could not be achieved and advised that it may be reasonable to restrict to transfemoral access only. ESC considered that it may be reasonable to have consistent descriptors in terms of patient frailty, calcific aortic stenosis and transfemoral access, for the high, intermediate, and low risk (if supported by the MSAC) populations.

ESC also considered that the MSAC should consider whether the item descriptor should exclude patients aged <65 years, noting this would likely affect a small proportion of the eligible population as few patients aged <65 years have calcific aortic stenosis and many have bicuspid or unicuspid aortic valves. ESC noted that clinical guidelines for TAVI have evolved as new evidence has supported use in patients with lower surgical mortality risk. ESC noted that the 2017 European Society of Cardiology (ESC) and the European

Association for Cardio-Thoracic Surgery (EACTS) Guidelines (Baumgartner *et al.* 2017)<sup>27</sup> considered SAVR was preferred in patients aged < 75 years. However, the 2020 American College of Cardiology (ACC) and American Heart Association (AHA) Guidelines (Otto *et al.* 2020)<sup>28</sup> recommends SAVR for adults <65 years of age unless life expectancy is limited. ESC highlighted that the 2020 ACC/AHA guidelines also states:

The availability of TAVI for treatment of symptomatic severe aortic stenosis across the surgical risk spectrum emphasizes the need to have discussions about younger age at implantation, valve durability, and the potential need for permanent pacemaker implantation. For young patients (eg, <65 years of age) who opt for a surgical bioprosthesis, strategies for sequential procedures over a longer follow-up period (ie, valve-in-valve [ViV] TAVI versus reoperation) must be addressed.

ESC advised that the MSAC could should consider whether the paradigm to assess patient eligibility for TAVI should evolve from one based on risk of adverse outcomes post-SAVR to one based on a holistic assessment of the patient, taking into consideration expected survival, comorbidities (cognitive function, frailty), and patient preferences.

From a consumer perspective, ESC noted that patients undergoing TAVI on the MBS can experience high out-of-pocket costs, and that these costs were higher than those for comparable cardiac procedures.

ESC highlighted that the ADAR included the NOTION trial which has not been previously considered by MSAC. Compared with the PARTNER 3 and EVOLUT trials previously considered by MSAC, the NOTION trial provided longer follow-up data (5-years) but was a smaller trial (N=280) and used an older TAVI device.

ESC considered that TAVI has a different, not superior, safety profile to SAVR. TAVI patients have significantly reduced rates of major or life-threatening or disabling bleeding, stage  $\geq 3$  acute kidney injury and atrial fibrillation. However, TAVI patients were significantly more likely to require a permanent pacemaker implant (PPI), have higher rates of moderate to severe paravalvular leaks (PVLs), and have higher rates of new left bundle branch block (LBBB).

The pre-ESC response addressed some of the safety outcomes with TAVI however, ESC considered that the applicant's advice needed further context:

- The applicant agreed that TAVI was inferior to SAVR for new LBBB and new PPIs. However, the applicant considered that these two outcomes (LBBB and PPIs) should not be considered individually, given that they are not mutually exclusive (i.e. a common treatment for significant LBBB is implantation of a specialised type of pacemaker [Melbourne Heart Rhythm 2014]). ESC noted that the main reason for PPI after TAVI was due to bradycardia and atrioventricular block, rather than isolated LBBB.<sup>29</sup> ESC highlighted that LBBB is not benign as it can reduce cardiac function over time and needs ongoing monitoring.

---

<sup>27</sup> Baumgartner H *et al.* 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38(36):2739-2791.

<sup>28</sup> Otto CM *et al.* 2020 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.

<sup>29</sup> Lilly SM *et al.* 2020 ACC Expert Consensus Decision Pathway on Management of Conduction Disturbances in Patients Undergoing Transcatheter Aortic Valve Replacement: A Report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol.* 2020;76(20):2391-2411.

- PPI rates are expected to decrease with TAVI using a new implantation technique currently being rolled out for Medtronic devices, called “cusp overlap technique”.
- The applicant claimed that the meta-analyses presented in the ADAR showed that TAVI is non-inferior to SAVR in terms of moderate/severe PVLs given that there was no statistically significant difference in moderate/severe PVL at 1 year, 2 years and 5 years in terms of relative risk. ESC noted that TAVI was associated with higher rates of moderate/severe PVL at 30-day (based on the meta-analysis of relative risk) and at 1-year (EVOLUT trial) and 5-years (NOTION trial).

ESC noted that longer-term data are required to assess the clinical implications of PVLs, LBBB, and uncertain valve durability. These issues are particularly pertinent to younger and low-risk patients, with longer life expectancy, who generally have good long-term outcomes with SAVR. ESC considered that the incidence of PPI following TAVI may decrease if future improvements in TAVI valve design reduce its impact on the atrioventricular (AV) node.

ESC noted that the ADAR claimed that TAVI had superior efficacy to SAVR. The pooled results of two clinical trials, EVOLUT and PARTNER 3, demonstrated that patients treated with TAVI had significantly lower rates of disabling stroke at 30 days, 12 months and 24 months follow-up. However, as follow-up was limited to 2 years, it was uncertain whether TAVI patients continue to have lower rates of disabling stroke after this period.

ESC noted that TAVI patients also had statistically significantly lower rates of mortality at 30 days post-surgery compared to SAVR patients based on the meta-analysis of the three clinical trials, EVOLUT, NOTION and PARTNER 3. However, after 30 days follow-up, there were no statistically significant differences between treatment arms for any of the trials or pooled estimates. The 5-year results for NOTION showed no difference in mortality rates, with both TAVI and SAVR arms, reporting a mortality rate of 28%. This suggested TAVI was non-inferior to SAVR in the long-term (up to 5 years) with regards to mortality.

ESC noted that the ADAR had presented indirect comparisons comparing TAVI-SEV and TAVI-BEV both with and without the NOTION trial which used an older TAVI-SEV. ESC noted the results and considered the new evidence supported MSAC’s previous conclusion that clinical evidence did not show differences between TAVI-BEV and TAVI-SEV that strongly justified a device-specific approach ([PSD Application 1635](#), p3).

ESC noted that TAVI patients also had lower rates of rehospitalisation at 30 days, 12 months and 24 months follow-up, had a shorter hospital stay and spent less time in the intensive care unit compared to patients treated with SAVR.

ESC noted that three health states were used in the economic model and that this is reasonable. While there are two currently accepted model approaches (one to model disabling stroke and one to model any stroke), the model used in the current application was consistent with Application 1603 (TAVI for patients with intermediate surgical risk, using a BEV; [PSD, Application No. 1603](#), p7). ESC noted that the economic model did not apply half-cycle correction but considered that this may be reasonable as the cycle length was short.

ESC noted that the commentary updated costs used in the model and that these may be reasonable. ESC considered that the reduction in hospitalisation costs were contentious. ESC noted that the main driver of the economic model and financial analysis were the hospitalisation costs in patients treated with TAVI compared to SAVR. TAVI is no longer dominant once the assumed average length of TAVI hospital stay increases from 3.6 days to

4.37 days. The ADAR estimated the hospitalisation cost of treatment with TAVI and SAVR based on the average length of hospital stay reported in EVOLUT and NOTION (TAVI = 3.6 days and SAVR = 7.3 days), multiplied by the weighted average cost for a day stay in hospital for SAVR patients (\$4,839 as revised by the commentary). However, this approach assumes that hospitalisation costs for SAVR are “evenly distributed across the length of the [patient’s] hospital stay, whereas it is known that the reductions in hospital stay are typically for the cheaper days”. ESC noted that for Application 1361.2, MSAC agreed that this assumption favours TAVI as the reductions in hospital stay are typically for the cheaper days and not evenly distributed ([PSD Application No. 1361.2](#), p3). ESC noted that the daily cost of post-procedure hospital care could be accurately addressed in a micro-costing study. ESC noted that the daily cost of hospitalisation has been revised in the pre-ESC response to remove operating theatre costs. ESC considered that the resulting ICER, in which TAVI no longer dominates SAVR, may provide for a more appropriate base case.

ESC noted that the cost of hospitalisation was calculated differently between the current ADAR and Application 1635. ESC noted the ADAR multiplied the daily cost of hospitalisation for SAVR (excluding prosthesis) and multiplied this by the lengths of hospital stay (TAVI = 3.6 days and SAVR = 7.3 days) to estimate hospital costs. ESC noted that Application 1635 had estimated the hospitalisation cost of treatment with TAVI-BEV based on the ratio of hospital stay for patients in PARTNER 3 (TAVI-BEV = 3-days vs. SAVR = 7-days). The weighted average length of stay for the SAVR diagnosis related group (DRG) codes was 11 days ([PSD Application No. 1635](#), p24). As a result of these differences, the ADAR estimated a smaller difference between the cost of TAVI and SAVR procedure than Application 1635 (refer to Table 1).

ESC noted that the base case used in the economic model did not include the cost of treating adverse events and their associated disutilities. The direction of bias resulting from this assumption is unknown, given that relative to SAVR, TAVI is inferior in terms of new permanent pacemakers, vascular complication, aortic valve reintervention and PVLs and superior in terms of atrial fibrillation, acute kidney injury, myocardial infarction and disabling or life-threatening bleeding. The pre-ESC response presented an analysis calculating the costs and disutility from the adverse events that differed between TAVI and SAVR using published values from Zhou (2020)<sup>30</sup>. The resulting difference in costs (\$770) and utility (-0.012) was small. ESC noted that the most appropriate base case should be determined.

Overall, the sensitivity analyses conducted by the ADAR and the commentary found that treatment with TAVI was dominant in most scenarios. The exception was when the hospitalisation costs for treatment with TAVI were adjusted based on the length of hospital stay for TAVI versus SAVR patients. TAVI was no longer the dominant treatment option once the assumed average length of hospital stay increases from 3.6 days to 4.37 days, using the commentary’s updated model. Reducing the daily cost of hospitalisation by 25% (from \$4,839 to \$3,629 using revised costs) changed the ICER from TAVI been the dominant treatment to TAVI having an incremental cost-effectiveness ratio (ICER) of \$9,261 per quality-adjusted life year (QALY) in the commentary’s updated model. On the basis of a two-way sensitivity analysis, ESC noted that if reductions in the average length of hospital stay, and the daily cost of hospitalisation, were to be smaller than in the base case, this could

---

<sup>30</sup> Zhou JY *et al.* Cost-Effectiveness of Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients With Severe Aortic Stenosis. *Heart Lung Circ.* 2021;30(4):547-554.

result in a considerably higher ICER per QALY gained than what is suggested by the base case.

ESC noted that the ADAR compared the baseline demographics of patients enrolled in EVOLUT, NOTION and PARTNER 3 to two observational cohort studies of Australian patients who underwent treatment with TAVI devices and enrolled low-risk patients (Quine et al. 2020, Rashid et al. 2017). Overall, patients in the randomised controlled trials (RCTs) were significantly younger than patients in the two Australian cohort studies (74–79 years vs 82–84 years) and were at lower surgical risk (mean STS-PROM score of 1.9–3.1% vs 3.8%). The latter suggests that the trial populations were generally not comparable to the Australian cohort studies. This is likely because the use of TAVI devices in low-risk patients and those under 75 years (i.e. longer life expectancy) has only recently been supported by the most current American College of Cardiology/American Heart Association 2020 clinical guideline. Further, TAVI devices are currently not MBS funded for use in low-risk patients.

ESC noted that the ADAR's financial estimates assumed that all patients eligible for SAVR would be eligible for TAVI, and that this may overestimate eligibility and, in turn, cost-savings. ESC considered that small changes to the assumptions, such as the length and cost of hospitalisation, could result in substantial costs to Government. ESC noted the pre-ESC response acknowledged that the ADAR estimates were an upper estimate.

ESC noted that, as a result of Application 1635, the Department has commenced consultations with the Cardiac Society of Australia and New Zealand and the Australian and New Zealand Society of Cardiac and Thoracic Surgeons, to look at outcome registries for SAVR and TAVI. ESC queried whether Australian registry data are available looking at the groups of low-risk patients who are having SAVR and whether there are any subgroups to analyse.

## **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 Low 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. Medtronic looks forward to working with all stakeholders to ensure patients have access to the lifechanging TAVI therapy as soon as possible.

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

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