



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1553 – Transmural fixation of aortic endograft adjunct to endovascular aneurysm repair using helical anchors

Applicant: Medtronic Australasia

Date of MSAC consideration: MSAC 78th Meeting, 3 April 2020

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 transmural fixation of aortic endograft using helical anchors (EndoAnchors® [EA]) for the treatment of aortic aneurysms of the abdominal and thoracic region adjunct to endovascular aneurysm repair was received from Medtronic Australasia 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 did not support the public funding of transmural fixation of aortic endograft adjunct to endovascular aneurysm repair using helical anchors, due to insufficient evidence to support non-inferiority in terms of effectiveness and safety over the alternative treatment approaches. MSAC was also concerned that usage would not be limited to high-risk patients (identified as having “hostile anatomies”) but that this procedure would also be used in a wider patient population where the use of helical anchors is likely to be associated with higher costs and no, or limited, incremental benefit.

Consumer summary

Medtronic Australasia applied for public funding through the Medicare Benefits Schedule (MBS) for the use of helical anchors (EndoAnchors) when repairing aneurysms in the aorta.

Arteries carry blood away from the heart to other organs. The aorta is the main artery in the body. When an artery wall weakens, it can result in a bulge, which is called an aneurysm. If the aneurysm fills with blood and then ruptures, it bleeds inside the body. The endovascular aneurysm repair procedure involves placing a covered stent graft (a metal mesh tube with a layer of fabric) into the artery next to the aneurysm that is at risk of rupturing. This provides a route for the blood to flow, rather than pooling inside the bulge.

Consumer summary

Helical anchors are proposed for use to improve the seal between the graft and the artery and help fix the graft in the correct position.

MSAC found that there was not enough evidence to show that the use of helical anchors was any better or safer than other approaches currently used to treat aortic aneurysms. The studies that look at the effectiveness and safety of helical anchors are of low quality and only include small numbers of patients.

MSAC suggested that the Department might like to initiate discussions with the vascular surgeon craft group that supports the work of the Prosthesis List Advisory Committee and with public hospital providers of this service to help answer the question of whether there is a clinical need for a particular group of patients that has not yet been addressed.

MSAC's advice to the Commonwealth Minister of Health

MSAC did not support the public funding of this procedure, rejecting the application on the basis of poor-quality clinical evidence, particularly in relation to safety.

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

MSAC noted that this application seeks listing of transmural fixation of aortic endograft using helical anchors (EndoAnchors) for patients with aortic aneurysm adjunct to abdominal endovascular aneurysm repair (EVAR) or thoracic endovascular aneurysm repair (TEVAR).

MSAC noted that the application proposes this intervention will be used in patients with an aneurysm that has a hostile neck anatomy (population 1) and in patients with a Type Ia endoleak and/or graft migration during or after T/EVAR (population 2). Taken together, the applicant claims that these patients represent a small proportion of all aneurysm repairs (between 10% and 20% for Abdominal Aortic Aneurysms (AAA) and 2.5% and 5% for Thoracic Aortic Aneurysms (TAA)).

MSAC acknowledged that using helical anchors with an off-the-shelf tube or bifurcated graft offered the possibility of a more timely intervention for population 1 than use of a custom made fenestrated or branch graft that can take 1–2 months to manufacture. However, MSAC was concerned that helical anchors would be more widely used as adjunct to T/EVAR in uncomplicated aneurysm repairs.

MSAC noted that there are no direct comparative studies of the proposed intervention and the intervention that will be replaced. Overall, the application instead relies predominantly on single arm open studies or on single arms of randomised studies. The main evidence base for the proposed intervention is the ANCHOR registry, a prospective non-randomised study in 838 patients. The results from seven studies of the proposed intervention, 11 studies of the comparator for population 1 and 14 studies of the comparators for population 2 are used by the applicant to conduct a naïve indirect comparison (see Table 4). MSAC did not accept the applicant's arguments that this comparison was sufficiently robust to support a non-inferiority claim.

In terms of safety, MSAC noted that although the results presented by the applicant suggest the proposed intervention (EVAR + EA) has similar 30-day mortality to complex EVAR in Population 1 and to revision EVAR in population 2, with potentially lower mortality than open repair in Population 2, the data on safety were incomplete with only 3 (of 7)

EVAR+EA, 7 (of 11) complex EVAR and 7 (of 14) revision/open repair studies reporting adverse events. In addition, there was considerable variation in how these events were reported rendering a comparison between groups inappropriate.

MSAC considered whether the ANCHOR registry could provide more data in relation to safety; however, MSAC noted that there was only a small number of events and therefore it is not sufficiently large to elucidate the safety of the intervention.

In terms of effectiveness, MSAC noted there was a suggestion that there may be slightly more persistent Type 1a endoleaks with the intervention, EVAR + EA, in population 2, but again MSAC considered the overall evidence base insufficient to support a robust comparison of the intervention versus current treatment.

MSAC noted the application presented a cost-comparison of the intervention versus the comparators for Populations 1 and 2. In preparing this analysis, the application split the populations by aneurysm location (abdominal and thoracic), as follows:

- Population 1a: initial AAA repair
- Population 1b: initial TAA repair
- Population 2a: revision AAA repair
- Population 2b: revision TAA repair.

The application then further divides these populations to take account of the different comparator procedures used. Overall, the application presented eight (8) separate cost-comparisons, with the intervention claimed to be cost saving in two scenarios and to have an additional cost in 6 scenarios (see Tables 7 – 10).

The MSAC agreed with the commentary and its ESC that these cost-comparisons are associated with significant uncertainty, particularly relating to the number and type of grafts and stents used in the comparator arms. However, MSAC accepted the application's use of the cost of a fenestrated graft (**\$redacted**) in estimating the cost of FEVAR and agreed with ESC that the application had appropriately dealt with wastage of the helical anchors. MSAC also considered the cost comparison with chimney grafts was likely redundant as these grafts are rarely now used in clinical practice. Likewise the comparison with open surgery may also not be informative in this setting, as current practice is to use revision EVAR in most patients.

MSAC noted the application had not attempted to calculate a weighted average price across the different cost scenarios. The pre-MSAC response attempted to address this issue by presenting estimates of use across the populations 1a, 1b, 2a and 2b. The applicant claimed this demonstrated the proposed intervention would be associated with a cost saving of **\$redacted** on average. The MSAC noted this saving is driven primarily by the assumption that most patients will be in Population 1a and by the costs of the devices used in the comparator arms of Populations 1a and 2a, and that all of these inputs are associated with uncertainty.

MSAC reiterated its concern of the potential for use beyond Population 1 and 2 patients, as some vascular surgeons may also wish to use EVAR+EA more broadly in situations where the use of helical anchors will be associated with higher costs and no, or limited, incremental benefit.

MSAC noted the application used a hybrid market share – epidemiological approach to estimate overall usage, giving a total of 111 procedures in Year 5. However, for the reason given in the paragraph above, MSAC considered this uptake likely underestimated.

MSAC considered that further defining the patient population to identify patients who are most likely to benefit from the intervention may provide a way forward for the applicant. However, MSAC noted that such an approach would only be successful if accompanied by better quality evidence of comparative effectiveness and safety. Alternatively, the applicant may wish to pursue a listing that would allow usage in a broader population but at a lower cost. MSAC also requested the applicant provide further information to support its request for a higher price for the anchors when used in TAA versus AAA.

Other discussion

MSAC suggested that the Department might like to initiate discussions with the vascular surgeon craft group that supports the work of the Prosthesis List Advisory Committee (PLAC) to help refine the patient groups in whom the proposed intervention is likely to be used. MSAC suggested it may be useful to get data from the jurisdictions on use in public hospitals and which patient groups are receiving this treatment. This information could help answer the question of whether there is a clinical need for a patient subgroup that has not yet been addressed.

MSAC requested this matter be referred to the PLAC Secretariat in the Department.

4. Background

This is the first submission (Applicant Developed Assessment Report [ADAR]) for transmural fixation of aortic endograft adjunct to EVAR using helical anchors (EndoAnchors [EA]). MSAC has not previously considered this application.

5. Prerequisites to implementation of any funding advice

Items on the Australian Register of Therapeutic Goods (ARTG) that are relevant to this application are shown in Table 1.

Table 1 Helical anchor listed on the ARTG

ARTG no.	Product no.	Product description	Product category	Sponsor
283911	45612	The Aptus Heli-FX EndoAnchor System is comprised of an endovascular suture (the EndoAnchor) and implantation means (the Heli-FX Applier) as well as a steerable guide sheath (the Heli-FX Guide) for access and delivery within the vasculature	Medical Device Class III	Medtronic Australasia Pty Ltd
283912	45612	The Aptus Heli-FX Thoracic EndoAnchor System is comprised of an endovascular suture (the EndoAnchor) and an implantation means (the Heli-FX Applier) as well as a steerable guide sheath (the Heli-FX Guide) for access and delivery within the vasculature	Medical Device Class III	Medtronic Australasia Pty Ltd
298952	45612	The Aptus Heli-FX EndoAnchor System is comprised of an endovascular suture (the EndoAnchor) and implantation means (the Heli-FX Applier) as well as a steerable guide sheath (the Heli-FX Guide) for access and delivery within the vasculature	Medical Device Class III	Medtronic Australasia Pty Ltd
298953	45612	The Heli-FX Thoracic EndoAnchor System is comprised of an endovascular suture (the EndoAnchor) and an implantation means (the Heli-FX Applier) as well as a steerable guide sheath (the Heli-FX Guide) for access and delivery within the vasculature	Medical Device Class III	Medtronic Australasia Pty Ltd

Source: Table 8, p36 of ADAR

6. Proposal for public funding

The proposed MBS item descriptors are summarised in Table 2.

Table 2 Proposed MBS item descriptors

Category 3 – THERAPEUTIC PROCEDURES
<p><u>Proposed item descriptor:</u> ABDOMINAL AORTIC ANEURYSM, with transmural fixation of endograft to the aorta using helical anchors adjunct to endovascular aneurysm repair by tube graft in patients: With an aneurysm neck anatomy length <10mm, diameter >28 mm, angulation >60 degrees or aortic neck is conical OR Patients with a Type Ia endoleak during or following previous aneurysm repair or Patients with a device migration following previous aneurysm repair, where migration is defined as movement of the endograft greater than 10 mm or any migration of the graft which necessitates any intervention or causes endoleaks. Fee: \$1,665.41</p>
Category 3 – THERAPEUTIC PROCEDURES
<p><u>Proposed item descriptor:</u> ABDOMINAL AORTIC ANEURYSM, transmural fixation of endograft to the aorta using helical anchors adjunct to endovascular aneurysm repair by bifurcation graft to one or both iliac arteries in patients: With an aneurysm neck anatomy length <10mm, diameter >28 mm, angulation >60 degrees or aortic neck is conical OR Patients with a Type Ia endoleak during or following previous aneurysm repair, or Patients with a device migration following previous aneurysm repair, where migration is defined as movement of the endograft greater than 10 mm or any migration of the graft which necessitates any intervention or causes endoleaks. Fee: \$1850.53</p>
<p><u>Proposed item descriptor:</u> THORACIC AORTIC ANEURYSM, transmural fixation of endograft to the aorta using helical anchors adjunct to endovascular aneurysm repair in patients: With an aneurysm neck diameter ≥ 40mm, length <20 mm for TEVAR OR Patients with a Type Ia endoleak during or following previous aneurysm repair, or Patients with a device migration following previous aneurysm repair, where migration is defined as movement of the endograft greater than 10 mm or any migration of the graft which necessitates any intervention or causes endoleaks. Fee: \$2,399.05</p>

Source: Table 1, p 20 of ADAR

The proposed item descriptors in the ADAR differ to that provided in the ratified PICO¹. The ADAR justified this change on the basis that the fee for endovascular repair of aortic aneurysm differ by location (abdominal and thoracic) and by the type of graft used (tube or bifurcated graft). Consequently, three separate MBS item codes for helical anchors adjunct to thoracic endovascular aneurysm repair (T/EVAR) are proposed based on MBS items 33116, 33119 and 33103. An increase in fees is proposed to account for the additional time for insertion of the helical anchors. The applicant noted it would support alternate arrangements and structuring of the proposed MBS code/s for the proposed service should MSAC consider this appropriate.

In the pre-MSAC response, the applicant provided clarification regarding the calculations undertaken to justify the fee increase (time taken for thoracic endovascular aneurysm repair (T/EVAR) + EA compared with time taken for T/EVAR). The applicant clarified that Table 83 of the ADAR reports the additional time EA insertion added to procedure durations in the ANCHOR registry; 16% for the primary AAA population, 22% for revision AAA, 11% for primary TAA and 14% for revision TAA. As stated in the ADAR (pg. 210), a weighted average was calculated across all patients in the ANCHOR registry, resulting in an estimation

¹ Population, Intervention, Comparator and Outcomes

of EA+T/EVAR taking 17% longer than standard T/EVAR procedures, based on procedure durations of 144.8 minutes with EA insertion versus 123.6 minutes without EA insertion.

7. Summary of public consultation feedback/consumer Issues

Targeted consultation feedback was received from Australian and New Zealand Society for Vascular Surgery (ANZSVS) supporting the listing of the proposed item. In ANZSVS opinion, the benefits of transmural fixation of aortic endograft adjunct to EVAR using helical anchors include possible improved security of repair and avoidance of more complex repair. The ANZSVS was unclear on the durability of helical anchors.

8. Proposed intervention's place in clinical management

Description of Proposed Intervention

The proposed medical service is the fixation of aortic endografts using helical anchors adjunctive to aortic EVAR or T/EVAR.

Helical anchors are implanted during either an initial T/EVAR to prevent endoleak (patients with hostile anatomy), fix a Type Ia endoleak and/or graft migration detected immediately following graft placement, or during T/EVAR undertaken to fix a postoperatively detected Type Ia endoleak and/or graft migration remote from the index procedure (revision). For patients with hostile anatomy, helical anchors are used in conjunction with "standard" T/EVAR grafts, defined as tube and bifurcated grafts. The helical anchor is purported to improve the seal between the graft and the vessel, fixing the graft into the correct position. Computed tomography angiography (CTA) is performed prior to the procedure to assess the anatomy of the aorta, determine graft use and to determine eligibility.

Description of Medical Condition(s)

An aneurysm is defined as an artery that has localised dilatation more than 1.5 times greater than the usual diameter of that artery (Johnson et al. 1991). When the aneurysm occurs in the aorta it is referred to as an aortic abdominal or thoracic aneurysm dependent on its location. Most aortic aneurysms occur in the abdomen (referred to as AAA) with thoracic aortic aneurysms (TAA) occurring less frequently. Aortic aneurysms (AAs) are often asymptomatic and are often identified incidentally through imaging for symptoms unrelated to the AA. The natural history is ongoing expansion of the aneurysm, with the risk of rupture increasing with increasing size. Patients with a ruptured aneurysm have more than 50% risk of death before hospitalisation or treatment (Chaikof et al. 2018). Whilst AA is rare in people < 50 years old, the prevalence increases sharply with increasing age with more men than women affected.

The medical service is proposed for use in two patient populations:

- **Population 1:** Patients with an aortic abdominal aneurysm (AAA) or thoracic aortic aneurysm (TAA) who are undergoing initial T/EVAR and who have a hostile neck anatomy (defined as length <10mm, diameter >28 mm, angulation >60 degrees or aortic neck is conical for EVAR and diameter \geq 40mm, length <20 mm for TEVAR).
- **Population 2:** Patients with a Type Ia endoleak and/or graft migration during or after T/EVAR, where migration is defined as movement of the endograft greater than 10 mm; or, any migration of the graft which necessitates any intervention or causes endoleaks.

Use of helical anchors in patients who have experienced aneurysm rupture is outside the scope of the application.

The proposed clinical management algorithm (Figure 1) indicates that in Population 1, helical anchors are proposed to replace the use of complex T/EVAR surgery (with fenestrated, branched or chimney grafts). In Population 2, helical anchors are proposed to replace the use of additional components such as extension cuffs and ballooning. Helical anchors are also proposed to eliminate the need for open repair in some patients.

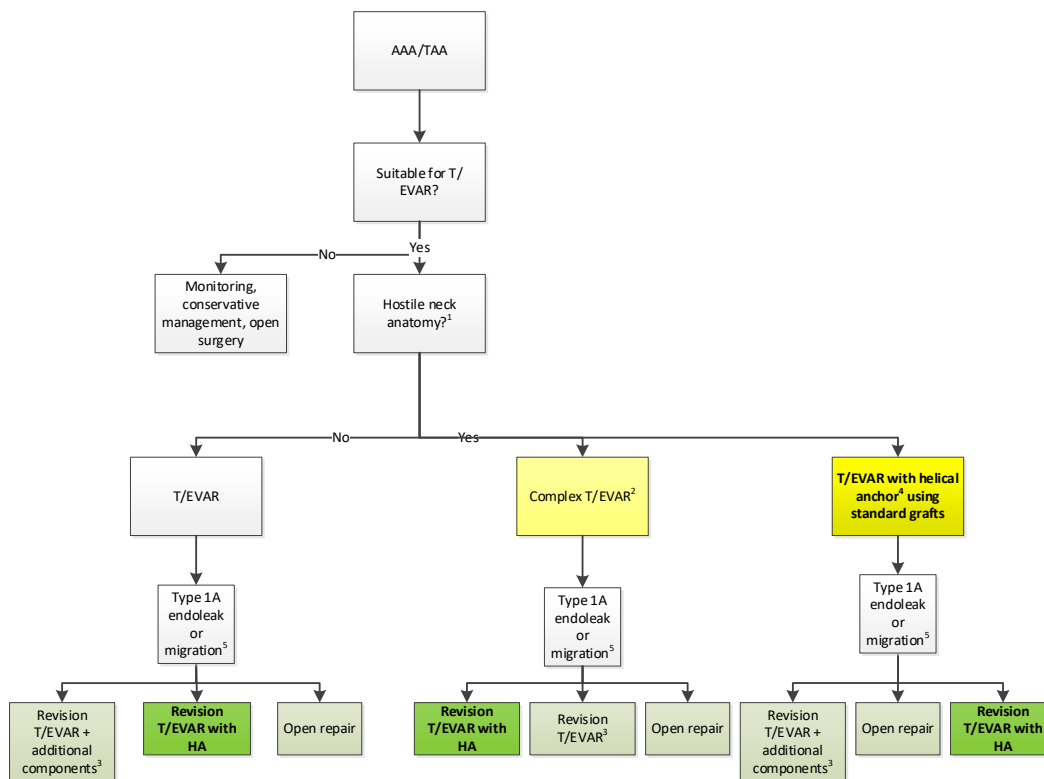


Figure 1 Proposed clinical management algorithm

Note: Population 1 is highlighted in yellow; Population 2 is highlighted in green. The proposed intervention is shown in bold. 1: Hostile neck anatomy is defined as length <10 mm, diameter >28 mm, angulation >60 degrees or aortic neck is conical. 2: Complex T/ EVAR refers to the use of fenestrated, branched or chimney grafts. 3: Additional components may include repositioning of the graft, aggressive ballooning, cuffs, extenders, converters. 4: In conjunction with simple tube or bifurcated grafts. 5: Migration defined as movement of the endograft greater than 10 mm or any migration of the graft which necessitates any intervention or causes endoleaks.

Abbreviations: AAA = abdominal aortic aneurysm, HA = helical anchors, TAA = thoracic aortic aneurysm, T/ EVAR = thoracic endovascular aneurysm repair or endovascular aneurysm repair.

Source: Figure 12, p57 of ADAR

9. Comparator

Population 1

The comparator for Population 1 is use of complex grafts defined as fenestrated, branched or chimney grafts. These grafts are used in patients with hostile anatomy where there may be insufficient healthy aorta above the graft to provide adequate sealing; therefore, standard (tube and bifurcated) grafts may not be appropriate for use.

Population 2

The comparators for Population 2 (both for Type Ia endoleak and migration) are:

- Revision T/ EVAR including addition of component pieces and/or repositioning of stent-graft, and/or aggressive ballooning i.e. angioplasty) or complex grafts
- Open repair.

The MBS item descriptors for the relevant comparators are provided in Table 3.

There are no specific MBS item numbers associated with the insertion of complex grafts (fenestrated, chimney or branched grafts); rather for a complex EVAR procedure MBS items 33116 or 33119 are claimed (despite this procedure taking longer to perform than a standard EVAR procedure) with the addition of transluminal stent insertion claimed.

There are no specific MBS item numbers limited to TEVAR procedures. Two items, 33103 and 33109 relevant to TAA repair, do not necessarily preclude treatment via endovascular means.

Table 3 Relevant MBS item for the comparators

MBS item	MBS item descriptor	Fee
Primary procedures		
33116 (tube)	INFRARENAL ABDOMINAL AORTIC ANEURYSM, replacement by tube graft using endovascular repair procedure, excluding associated radiological services	\$1,421.40
33119 (bifurcated)	INFRARENAL ABDOMINAL AORTIC ANEURYSM, replacement by bifurcation graft to one or both iliac arteries using endovascular repair procedure, excluding associated radiological services	\$1,579.40
33112	SUPRARENAL ABDOMINAL AORTIC ANEURYSM, replacement by graft including re-implantation of arteries	\$2,146.90
33115 (tube)	INFRARENAL ABDOMINAL AORTIC ANEURYSM, replacement by tube graft, not being a service associated with a service to which item 33116 applies	\$1,444.10
33118 (bifurcated)	INFRARENAL ABDOMINAL AORTIC ANEURYSM, replacement by bifurcation graft to iliac arteries (with or without excision of common iliac aneurysms) not being a service associated with a service to which item 33119 applies	\$1,604.55
33121 (bifurcation graft to 1 or both femoral arteries)	INFRARENAL ABDOMINAL AORTIC ANEURYSM, replacement by bifurcation graft to 1 or both femoral arteries (with or without excision or bypass of common iliac aneurysms)	\$1,765.05
33103	THORACIC ANEURYSM, replacement by graft	\$2,047.55
33109	Thoracoabdominal ANEURYSM, replacement by graft including re-implantation of arteries	\$2,475.50
Auxiliary medical procedures / revision procedures		
35303	TRANSLUMINAL BALLOON ANGIOPLASTY of aortic arch branches, aortic visceral branches, or more than 1 peripheral artery or vein of 1 limb, percutaneous or by open exposure	\$671.35
35309	TRANSLUMINAL STENT INSERTION, 1 or more stents, including associated balloon dilatation for visceral arteries or veins, or more than 1 peripheral artery or vein of 1 limb, percutaneous or by open exposure, excluding associated radiological services or preparation, and excluding aftercare	\$744.55
35309	TRANSLUMINAL STENT INSERTION, 1 or more stents, including associated balloon dilatation for visceral arteries or veins, or more than 1 peripheral artery or vein of 1 limb, percutaneous or by open exposure	\$762.35

AAA, abdominal aortic aneurysm; TAA, thoracic aortic aneurysm

Source: Table 14, p54 of ADAR

10. Comparative safety

Seven EVAR+EA studies were considered relevant to this submission with data available for either Population 1 and/or Population 2. The pivotal evidence is a large (N=838) prospective registry representing real-world use from >100 centres across the globe with minimal selection bias. In the context of non-comparative case series studies (NHMRC level evidence level IV), two of the seven studies had a low level of bias, and five studies were considered to have a moderate level of bias.

Eleven studies of complex EVAR in Population 1 were included in the naïve indirect comparison with EVAR+EA for Population 1. Most of the studies were conducted in countries with similar health care systems including six from the USA, two from the UK, two from multiple European countries (including France, Italy and Sweden) and one study from Japan. In the context of non-comparative case series studies (NHMRC level evidence level IV), five of the 11 studies had a low level of bias and the remaining six studies were considered to have a moderate level of bias.

Fourteen studies of revision EVAR or open conversion (OC) were included in the naïve indirect comparison with EVAR+EA for Population 2. All studies were conducted in countries with similar health care systems including the USA and Europe. In the context of non-comparative case series studies (NHMRC level evidence level IV), three of the 14 studies had a low level of bias, one had high level bias and the remaining nine studies were considered to have a moderate level of bias.

The commentary noted that the included studies were single-arm case series studies or a single arm of a comparative study (six studies), which have a high risk of bias and a low level of evidence (NHMRC level evidence level IV). Given that the studies do not have a comparator group; all comparisons are naïve indirect. The ADAR stated that the assessment of exchangeability did not identify any concerning differences between the two groups that are expected to adversely bias the results of the comparative analysis for both Population 1 and Population 2. However, the commentary noted that the assessment of exchangeability is restricted by the limited information provided by the included studies and it cannot be easily quantified to what extent the differences between studies impact the comparison of outcomes. These differences pose a high risk of bias and must be considered when interpreting the results of the naïve indirect comparisons.

A summary of study design, patient numbers (N) and included populations is provided below in Table 4.

Table 4 Selected studies

Studies	Design	N	Population
Helical anchors			
ANCHOR	Prospective, non-randomised, multicentre, registry	838	Initial aneurysm treatment, either prophylactic or to treat Type Ia endoleak (n=609); secondary procedure to arrest migration or treat Type Ia endoleaks (n=229)
De Vries 2014	Prospective, non-randomised, multicentre, registry	319	Initial EVAR procedure (n=242); and patients who had helical anchor placement remote from the initial EVAR procedure when the patients presented with Type Ia endoleak, endograft migration or both (n=77)
Ongstad 2016	Retrospective, single-arm, review	54	T/EVAR for thoracic aortic aneurysm (n=40) or thoracoabdominal aortic aneurysm with involvement of the paravisceral segment (n=14). 50% performed at the index operation and 50% reoperations
Goudekting 2019	Retrospective, observational, cohort study	51	Prophylactic helical anchor use for hostile proximal neck anatomy (N=31), with a Type Ia endoleak evident during initial endograft deployment (N=20)
Giudice 2019	Retrospective, single centre, review	17	Initial EVAR procedures to prevent proximal sealing site complications with hostile proximal aortic neck anatomy (n=9); secondary EVAR to correct postprocedural Type Ia endoleak and/or stent-graft migrations (n=8)
Reyes Valdiva 2019	Prospective, multicentre, cohort study	46	Hostile neck treated with standard EVAR and adjunctive helical anchoring to treat an intra-operative Type Ia endoleak (n=22) or to prevent a possible endoleak due to the hostile neck (n=24)
Avci 2012	Prospective, multicentre, cohort study	11	Revision of failed primary endograft due to distal migration of the main body, with or without Type Ia endoleak
Ho 2019	Retrospective, chart review, single centre	21	Prior EVAR with Type Ia endoleak (n=11); intra-operative Type Ia endoleak (n=10)
Population 1 comparator			
Barilla 2014	Retrospective, non-randomised, comparative analysis	100	Hostile neck AAAs (n=50) matched to 50 patients treated with FEVAR with similar anatomies, comorbidities and risk factors
Chisci 2009	Retrospective, non-randomised, comparative analysis	187	"Challenging" neck (wide neck:>28mm, angulated $\geq 60^\circ$; short neck: neck length <15mm; significant thrombus: $\geq 50\%$; reverse tapered neck; or neck bulge treated with either EVAR (n=74), FEVAR (n=52) or OSR (n=61)
Heneghan 2016	Retrospective, single-arm analysis	49	FEVAR for juxtarenal AAAs
Maeda 2017	Retrospective, non-randomised, comparative study	152	Juxtarenal AAAs, defined as juxtarenal aneurysm with a short proximal neck <1.0 cm treated with OSR (n=81) or complex EVAR (n=71).
Oderich 2014	Prospective, single-arm trial	67	Juxtarenal AAA (aortic aneurysm with diameter ≥ 5 cm and aortic aneurysm with a history of growth ≥ 0.5 cm per year or clinical indication for AAA repair)
O'Neill 2006	Prospective, single-arm trial	119	Short proximal necks, considered high-risk for open surgery and unacceptable for conventional endovascular repair
Saratzis 2015	Prospective, case-controlled registry trial	116	Juxtarenal AAA or short neck AAA undergoing FEVAR (n=58) or open surgery (n=58)
Scurr 2008	Single-arm, observational study	45	Juxtarenal AAA with infrarenal neck anatomy unsuitable for a standard stent-graft
Starnes 2017	Prospective, single-arm study	59	Juxtarenal AAA >5.0cm or with recent evidence of rapid growth, deemed unfit for open surgery and American Society of Anaesthesiologists class ≥ 3

Studies	Design	N	Population
Vemuri 2014	Retrospective, comparative review	99	AAA undergoing FEVAR (n=57) compared with comparative zFEN trial patients (n=42)
Wooster 2017	Retrospective, comparative review	93	Juxtarenal AAA (aneurysm dilation extending to within 4 mm of the lowest renal artery but not more proximal than the highest renal artery) treated with parallel endografting (n=54) or zFEN (n=39)
Population 2 comparator			
Nabi 2009	Retrospective, case series, single centre	12	EVAR with Type Ia endoleak
Scali 2014	Retrospective, case series, single centre	25	Type Ia endoleak who had open conversion
Azizzadeh 2005	Retrospective, case series, single centre	20	Proximal attachment failure; defined as Type Ia endoleak, Type III endoleak or inadequate seal zone <10 mm
Faries 2003	Retrospective, case series, multi centre	70	Endoleaks (Type Ia,b, II and III)
Jim 2011	Retrospective, case series, multi centre	151	Proximal fixation for treatment of pre-existing endografts with failed or failing proximal fixation or seal
Naughton 2011	Retrospective, case series, single centre	22	Endovascular intervention for Type I and III endoleaks
van Lammeren 2010	Retrospective, case series, multi centre	62	Secondary reinterventions including renewed endovascular repair or open conversion in EVAR patients with endoleaks
Katsargyris 2013	Retrospective, case series, multi centre	26	Juxtarenal AAA treated with FEVAR after failed previous EVAR
Marques de Marino 2019	Retrospective, case series, single centre	49	Type Ia endoleaks after EVAR treated with EVAR or FEVAR
Zamir 2019	Retrospective, case series, single centre	10	Type Ia endoleaks identified on CT following previous EVAR
Martin 2014	Retrospective, case series, single centre	52	Rescue for proximal neck abnormalities including endoleaks and graft migration
Montelione 2015	Retrospective, case series	24	Type I endoleaks (23 Ia and 1 Ib) in 23 pararenal AAAs and 1 TAA
Ronchey 2018	Retrospective, case series, multi centre	39	CHEVAR to treat Type Ia endoleaks
Tanius 2017	Retrospective, case series	19	CHEVAR rescue for loss of proximal fixation or seal after a previous EVAR

AAA=abdominal aortic aneurysm; EVAR=endovascular aneurysm repair; CHEVAR=chimney EVAR; FEVAR=fenestrated EVAR; T/EVAR=thoracic EVAR

Source: Table 14, p17 of the commentary

In the pre-ESC response, the applicant claimed that during the selection of studies, it ensured both sets of data enrolled patients with aneurysm characteristics overlapping with the proposed populations (population 1 – hostile neck anatomy; population 2 – Type IA endoleak at index procedure or after T/EVAR), to ensure comparability of the two sets of data. This also ensured applicability to the proposed populations. The assessment of exchangeability did not identify any concerning differences between the two groups that are expected to

adversely bias the results of the comparative analysis for Population 1 and for Population 2. The Applicant maintained that the evidence presented sufficiently support a conclusion of non-inferiority.

Population 1

The ADAR stated there were no discernible differences observed between the EVAR+EA intervention group and complex EVAR with respect to early and all-cause mortality in Population 1 suggesting non-inferiority. In terms of early 30-day mortality, the use of EVAR+EA is considered as safe as complex EVAR procedures. Overall, the early mortality rate in the EVAR+EA studies included in the naïve comparison was 1% [95% CI: 0% - 5%] and highly comparable to the mortality rate observed in the comparative complex EVAR studies (1%; [95%CI: 0% - 3%]). The moderately broader confidence interval (CI) range observed in the EVAR+EA studies is reflective of the smaller sample size. No significant heterogeneity was observed across the EVAR+EA studies.

All-cause mortality was also found to be comparable between the two groups with a mortality rate of 3% [95%CI: 1% - 5%] estimated across the EVAR+EA studies compared to 4% [95%CI: 2% - 7%] in the complex EVAR comparator.

The commentary noted that two of the helical anchors studies and seven of the complex EVAR studies reported adverse events. The data reported across the studies was limited, and there were few events reported overall. There was considerable heterogeneity in the time period in which all-cause mortality was considered (ranging from 52 days to more than 4 years).

Population 2

The ADAR stated that for Population 2, early 30-day mortality was low occurring in 2% of the revision population [95%CI: 0%, 4%] and in none of the patients treated for an intra-operative Type Ia endoleak. The early 30-day mortality rate was comparable in the revision EVAR comparator group (1% [95%CI: 0%, 3%]) but was notably higher in those undergoing OC (5%; [95%CI: 0%, 12%]). Overall, the use of EA in Population 2 was considered as safe as revision EVAR procedures and numerically favourable relative to OC. The all-cause mortality rate reported across the revision EA studies was found to be 8% [95%CI: 3%, 13%]. Similar mortality rates were observed in the subgroup of patients receiving EAs to treat intra-operative Type Ia endoleaks at the time of the index procedure of 7% [95%CI: 1%, 12%]. These all-cause mortality rates were markedly higher in the comparator groups of 12% [95%CI:3%, 31%] in the OC group and 20% [95%CI:10%, 29%] in the revision EVAR studies.

The commentary noted that three of the helical anchor studies and seven of the complex EVAR studies reported adverse events. The data reported across the studies was limited. There were few events reported overall and there was considerable variation in how these events were reported, rendering a comparison between groups inappropriate.

The commentary noted that in both populations, the main limitation of the comparative safety assessment is the lack of direct comparative evidence. The descriptive analyses of treatment harms did not identify any large differences between intervention and comparator studies, with overlapping 95% confidence intervals in most comparisons. However, the 95% confidence intervals of the point estimates were quite large due to small sample sizes in some of the studies. The evidence base appeared to be applicable to the populations of use in the Australian situation.

11. Comparative effectiveness

Population 1

The ADAR stated that the indirect naïve comparative analysis of EVAR+EA vs complex EVAR detected no discernible differences between the two groups in persistent Type Ia endoleaks, conversion to open repair, graft migration and rupture, (1% vs 0%; 0% vs 0%; 0% vs 1% and 0% vs 0%, respectively). The reintervention rate was shown to be numerically lower in the EVAR+EA studies with 5% [95%CI:1%, 12%] of patients requiring secondary procedures compared with 9% [95%CI:6%, 13%] with complex EVAR.

The proportion of patients with observed sac regression of >5mm was greater in the complex EVAR group (75% [95%CI:67%, 83%]) compared to the EVAR+EA group (47% [95%CI:31%, 62%]). Importantly, however, none of the patients in the EVAR+EA group demonstrated sac growth during the follow-up period. In contrast, two patients in the complex EVAR studies reported sac enlargements (2/106: 1.8%).

The commentary noted that the rate of persistent Type Ia endoleaks appeared to be similar between the two study groups. There was heterogeneity in follow-up periods within which reinterventions were reported, the complex EVAR study reported by Oderich (2014) in which the median follow-up period was 37 months (range 3-65) was omitted from the analysis.

Population 2

The ADAR stated no differences were observed in the rate of conversion to open repair or rupture between the revision EA and the revision EVAR groups (2% [95%CI: 0%, 4%] vs 3% [95%CI: 0%, 5%] and 0% [95%CI: 0%, 1%] vs 2% [95%CI: 0%, 3%], respectively). There were no cases of graft migration in either of the EA subgroups; graft migration occurred in one of 111 patients in the revision EVAR group (1%).

Persistent Type Ia endoleaks beyond 30 days post procedure was more frequently observed in the revision EA group (14%; [95%CI:4%, 23%]) compared with EA for intra-operative Type Ia endoleak (3% [95%CI:0%, 9%]), reflecting potential differences in the clinical presentation in these two populations. The overall rate of persistent Type Ia endoleaks was markedly lower in the revision EVAR patients (2%; [95%CI:0%, 4%]) and, as expected, no cases were observed in patients undergoing OC.

The overall incidence rate of reinterventions in the revision EVAR studies was 12% [95%CI: 5%, 19%]. While the revision EA group showed a numerically higher rate of 14% [95%CI:10%, 18%], the reintervention rate was notably lower in patients treated with EA for intra-operative Type Ia endoleak at 5% [95%CI: 0%, 10%].

A summary of the naïve comparison of EVAR+EA versus complex EVAR (Population 1) and revision EA versus revision EVAR or OC (Population 2) with respect to safety and effectiveness is provided in Table 5.

Table 5 Balance of clinical benefits and harms of using EA, relative to alternative procedures, and as measured by the critical patient-relevant outcomes in the key studies

Outcomes (units) Follow-up	Participants (studies)	Quality of evidence (GRADE)	Risk with EA	Risk with comparator % (95% CI)	Comments
Population 1					
Early (30 day) mortality	EVAR+EA, N=64, k=3 Complex EVAR, N=666; k=11	⊕⊙⊙⊙	1% (95%CI: 0% - 5%)	1% (0% - 3%)	No difference
All-cause mortality	EVAR+EA, N=219, k=3 Complex EVAR, N=546; k=9	⊕⊙⊙⊙	3% (95%CI: 1% - 5%)	4% (: 2% - 7%)	No difference
Persistent (<30 day) Type Ia Endoleak	EVAR+EA, N=201, k=4 Complex EVAR, N=452; k=7	⊕⊙⊙⊙	1% (95%CI: 0% - 3%)	0% (0% - 1%)	No difference
Reinterventions	EVAR+EA, N=263, k=4 Complex EVAR, N=477; k=7	⊕⊙⊙⊙	5% (95%CI: 1% - 12%)	9% (6% - 13%)	Numerically in favour of EVAR+EA
Rupture	EVAR+EA, N=226, k=4 Complex EVAR, N=472; k=9	⊕⊙⊙⊙	0% (95%CI: 0% - 1%)	0% (0% - 1%)	No difference
Population 2					
Early (30 day) mortality	Revision EA, N=268, k=4 Revision EVAR, N=317, k=7 OC, N=27, k=2	⊕⊙⊙⊙	2% (95%CI: 0% - 3%)	Revision EVAR: 2% (0% - 4%) OC: 5% (0% - 12%)	No difference Numerically in favour of EA compared to OC.
All-cause mortality	Revision EA, N=266, k=5 Revision EVAR, N=219, k=7 OC, N=25, k=1	⊕⊙⊙⊙	8% (95%CI: 3% - 13%)	Revision EVAR: 20% (10% - 29%) OC: 12% (3% - 31%)	Numerically in favour of EA compared to both revision EVAR and OC
Persistent (<30 day) Type Ia Endoleak	Revision EA, N=186, k=6 Revision EVAR, N=317, k=9 OC, N=12, k=1	⊕⊙⊙⊙	14% (95%CI: 4% - 23%)	Revision EVAR: 2% (0% - 4%) OC: 0% (0% - 26%)	Numerically in favour of the comparators groups OC and revision EVAR
Reinterventions	Revision EA, N=283, k=6 Revision EVAR, N=245, k=9	⊕⊙⊙⊙	14% (95%CI: 10% - 18%)	Revision EVAR: 12% (5% - 19%)	No difference
Rupture	Revision EA, N=255, k=4 Revision EVAR, N=175, k=5	⊕⊙⊙⊙	0% (95%CI: 0%, 1%)	Revision EVAR: 2% (0% - 3%)	No difference

OC=open conversion; EVAR=endovascular aneurysm repair; EA=EndoAnchor. ^a GRADE Working Group grades of evidence (Guyatt, 2013). ⊕⊕⊕⊕ **High quality:** We are very confident that the true effect lies close to that of the estimate of effect. ⊕⊕⊕⊙ **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. ⊕⊕⊙⊙ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. ⊕⊙⊙⊙ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Source: Table 2, p26 of ADAR

On the basis of the benefits and harms reported in the evidence base, the ADAR proposed that:

- In Population 1 (short/hostile proximal aortic neck anatomies), relative to complex EVAR, EVAR + helical anchors has non-inferior safety and non-inferior effectiveness.
- In Population 2 (treatment of Type Ia endoleaks and/or graft migration during or following an index procedure), relative to open conversion and revision EVAR, helical anchors has non-inferior safety and non-inferior effectiveness.

The commentary noted that for both populations, the main limitation of the comparative effectiveness assessment is the lack of direct comparative evidence. In addition, the ADAR selectively omitted some of the studies in the analyses of reintervention rates, mainly due to longer follow-up periods. This pragmatic approach may be acceptable, but it is unclear whether these decisions were made post-hoc.

The commentary noted that the GRADE evidence profile suggests that no substantial differences exist between studies of helical anchors and comparator studies. It is important to note that the last column in the table (Comments) needs cautious interpretation. The ‘differences’ were derived from naïve comparisons of independent studies.

The main issue is the inherent risk of bias and uncertainty of study comparability attached to naïve comparisons. The applicant has acknowledged this issue in multiple places throughout the ADAR; and the ADAR correctly graded the quality of the evidence as ‘very low quality’ for all the comparisons. This means there is very little confidence in the estimated effect, and there is potential the true effect could be substantially different from the estimate presented here.

In the pre-ESC and pre-MSAC response, the applicant acknowledged the lack of direct evidence as a limitation in the assessment of effectiveness and safety of EVAR+EA versus its comparators. However, the applicant argued the evidence presented represents the best level evidence available and reflects the management of TAA/AAA on a case-by-case basis with individual anatomical characteristics and comorbidities considered in determining the suitable treatment option. Further, the applicant maintains that the data presented supports a conclusion of non-inferiority.

In the pre-MSAC response, the applicant refuted the claim that the ADAR had selectively omitted some studies. The applicant confirmed one complex EVAR study was omitted from the naïve comparison of reintervention rates because of the significantly longer follow up (3 years versus 1 year for ANCHOR registry) and consequent markedly higher reintervention rate of 22%, almost double the rate of most other complex EVAR studies. The decision to omit this study from the ADAR analysis, on the basis of being an outlier, was to improve comparability and to minimise the potential from bias as a consequence of differential follow up. The applicant claimed that had this study been included, the naïve comparison would have been biased in favour of EVAR+EA, as such the approach taken may be considered conservative and appropriate in the context of reducing uncertainty.

Clinical claim

The applicant claims that T/EVAR incorporating the use of helical anchors is non-inferior to the identified comparators with respect to safety and effectiveness.

MSAC did not accept this claim (see Section 3).

12. Economic evaluation

A cost-minimisation analysis (CMA) in the form of a cost comparison was presented (Table 6). This was considered the most appropriate form of economic evaluation for T/EVAR+EA based on the clinical claims of non-inferior safety and non-inferior effectiveness.

The economic evaluation estimated the costs of T/EVAR+EA and its comparators across four populations, differentiated by prior treatments (primary and revision) and by aneurysm location (abdominal and thoracic):

- Population 1a: initial AAA repair
- Population 1b: initial TAA repair
- Population 2a: revision AAA repair
- Population 2b: revision TAA repair.

Table 6 Summary of the economic evaluation

Perspective	Healthcare
Comparator	Population 1a: Complex EVAR (FEVAR and CHEVAR) Population 1b: Complex TEVAR (CHEVAR) Population 2a: Revision EVAR and open repair Population 2b: Revision TEVAR and open repair
Type of economic evaluation	Cost comparison
Sources of evidence	Systematic review (Section B), supplemented with pragmatic literature searches to address data gaps. Additionally, cost inputs were derived from Australian data sources, i.e. Prostheses List (July 2019) and the MBS (August 2019).
Software packages used	Excel

FEVAR=fenestrated endovascular aneurysm repair; CHEVAR=chimney endovascular aneurysm repair
Source: Table 56, p190 of ADAR

Key assumptions included:

- No difference in anaesthesia costs, hospitalisation costs (length of stay), reintervention costs or adverse event costs between T/EVAR+EA and its comparators. These costs were therefore excluded from the cost comparison.
- Use of adjunct helical anchors would only impact device use associated with treating the proximal neck of aneurysms.

The commentary highlighted several limitations of the submission's model:

- The cost minimisation approach is based on the assumption that the clinical claim is upheld, that T/EVAR +EA is non-inferior to its comparators in each population. Therefore, an underlying question for this economic evaluation is whether the clinical claim is supported by the clinical evidence.
- The ADAR split the population into abdominal and thoracic treatment/repair due to the difference in complexity and time required for each operation. However, in splitting the population, the analysis failed to account for thoracoabdominal aortic aneurysms, and failed to include the cost of grafts associated with thoracoabdominal aortic aneurysms in the cost-minimisation approach to the economic analysis.
- The proposed cost of the comparator was estimated by determining the cost of fenestrated stents from the prosthesis list, costed at \$**redacted**. However, this cost appears to be at the higher end of the range of benefits for fenestrated grafts, with grafts at the lower end of the range priced at \$**redacted**. It may or may not be appropriate to use the lower price for the fenestrated graft. Likewise, the cost of

covered stents used in the economic analysis is **\$redacted**, which also significantly increases the cost of the comparators FEVAR and CHEVAR, which is favourable for EVAR+EA.

- The cost of open repair is underestimated as it does not account for hospital costs, or PBS costs (such as antibiotics), as these patients would be expected to stay in hospital for a longer period compared with EVAR+EA, due to the more invasive nature of the repair surgery. The cost of CHEVAR did not include the cost of a standard stent graft and is therefore also underestimated.
- While the analysis has assumed wastage, further advice was needed by the assessment group regarding the possibility of unused anchors from opened packs being used for other patients.
- Reintervention and adverse event costs were not included as no difference was expected based on the clinical claim of non-inferiority. Assuming this clinical claim is upheld, the assumption that there were no differences in reintervention and adverse event costs is reasonable. Anaesthesia and hospital length of stay have also not been included in the analysis, however these costs are likely to be higher in the comparator arm.

In the pre-MSAC response, the applicant stated that:

- Thoracoabdominal aortic aneurysms were not included in the cost comparison as the proposed populations were for use in abdominal and thoracic aneurysms, not thoracoabdominal. However, in response to the suggestion that EVAR+EA would also be used as a substitute for thoracoabdominal aneurysms, the application claimed that FEVAR in these patients would involve the use of the Zenith t-branch Endovascular Graft (Prostheses List price=**\$redacted**).
- The Zenith Fenestrated AAA Endovascular Graft with Flexor (costing **\$redacted**) is the only fenestrated stent graft listed on the Prostheses List. The applicant claimed other fenestrated devices listed on the Prostheses List for infrarenal aneurysms are grafts (not stent grafts). Stent grafts are placed inside the artery and used for endovascular procedures, whilst grafts are placed outside the artery and used for open surgery. As such, the applicant claimed the cost of **\$redacted** for a fenestrated stent graft applied in the ADAR is appropriate.
- The cost of CHEVAR may be underestimated as the ADAR assumed that standard stent graft (tube or bifurcated) use is the same for all primary complex endovascular grafting procedures. However, the applicant claimed the assumption of no difference in standard stent grafts used for CHEVAR compared to EA+EVAR and FEVAR was applied in the ADAR as a conservative assumption.
- The proportions of bare metal and covered stents used in FEVAR and CHEVAR is uncertain. However, the applicant claimed recent evidence suggests covered stents are more likely to be used in complex EVAR procedures. Therefore, the applicant considered the proportions applied in the cost comparison to be conservative and may underestimate the device costs associated with FEVAR and CHEVAR.

Population 1

The estimated incremental cost associated with T/EVAR+EA versus its comparators for Population 1 broken down by AAA or TAA location are shown below in Table 7 and Table 8, respectively.

For Population 1a (primary AAA), the ADAR estimated EVAR+EA to provide cost savings of **\$redacted** relative to FEVAR and cost an additional **\$redacted** relative to CHEVAR in Population 1a (primary AAA).

Table 7 Incremental cost of EVAR+EA relative to complex EVAR in the primary treatment of infrarenal aneurysms

Row	Cost item	EVAR+EA	Complex EVAR (FEVAR)	Complex EVAR (CHEVAR)	Source / calculation
A	Device costs	\$redacted	\$redacted	\$redacted	Table 72
B	Medical service costs	\$redacted	\$redacted	\$redacted	Table 77
C	Total costs	\$redacted	\$redacted	\$redacted	A+B
D	Incremental cost of EVAR+EA (relative to comparator)	-	\$redacted	\$redacted	\$redacted - C

CHEVAR=Chimney endovascular aneurysm repair; EA=EndoAnchor; EVAR=Endovascular aneurysm repair; FEVAR=Fenestrated endovascular aneurysm repair

Source: Table 79, p208 of ADAR

The commentary noted that for Population 1a, the main assumption driving this cost-minimisation approach is the cost of the fenestrated graft and questioned whether a cost of **\$redacted** is justified. Additionally, the cost of CHEVAR is underestimated as it does not account for any grafting costs.

For Population 1b (primary TAA), the ADAR estimated T/EVAR+EA to cost an additional **\$redacted** relative to CHEVAR.

Table 8 Incremental cost of EVAR+EA relative to complex EVAR in the primary treatment of thoracic aneurysms

Row	Cost item	T/EVAR +EA	Complex T/EVAR (CHEVAR)	Source / calculation
A	Device costs	\$redacted	\$redacted	Table 73
B	Medical service costs	\$redacted	\$redacted	Table 77
C	Total costs	\$redacted	\$redacted	A+B
D	Incremental cost of T/EVAR +EA (relative to comparator)	-	\$redacted	\$redacted - C

CHEVAR=Chimney endovascular aneurysm repair; EA=EndoAnchor; T/EVAR=Thoracic endovascular aneurysm repair

Source: Table 80, p208 of ADAR

The commentary noted that for Population 1b, only CHEVAR was compared with T/EVAR +EA, as the ADAR noted that there were no TGA approved devices for either FEVAR or BEVAR, while acknowledging that there is a product for thoracoabdominal aneurysms, the Zenith t-Branch Endovascular Graft. EVAR+EA would be used as a substitute for thoracoabdominal aneurysms and therefore it is appropriate to include these grafts. However, the Zenith t-Branch Endovascular Graft is priced on the prosthesis list at **\$redacted**, significantly more than helical anchors, and when combined with the appropriate medical services, are likely to be more costly than the total cost of helical anchors.

Population 2

The estimated incremental cost associated with T/EVAR+EA versus its comparators for Population 2 broken down by AAA or TAA location are shown below in Table 9 and Table 10, respectively.

For Population 2a (revision AAA), the ADAR estimated EVAR+EA to provide costs savings of **\$redacted** relative to revision FEVAR, cost an additional **\$redacted** relative to revision CHEVAR and cost an additional **\$redacted** relative to open repair.

Table 9 Incremental cost of EVAR+EA relative to complex EVAR and open repair in the revision of infrarenal aneurysms

Row	Cost item	EVAR+EA	Revision FEVAR	Revision CHEVAR	Open repair	Source / calculation
A	Device costs	\$redacted	\$redacted	\$redacted	\$redacted	Table 74 of ADAR
B	Medical service costs	\$redacted	\$redacted	\$redacted	\$redacted	Table 78 of ADAR
C	Total costs	\$redacted	\$redacted	\$redacted	\$redacted	A+B
D	Incremental cost of EVAR+EA (relative to comparator)	-	\$redacted	\$redacted	\$redacted	\$redacted – C

CHEVAR=Chimney endovascular aneurysm repair; EA=EndoAnchor; EVAR=Endovascular aneurysm repair; FEVAR=Fenestrated endovascular aneurysm repair
 Source: Table 81, p209 of ADAR

For Population 2b (revision TAA), the ADAR estimated TEVAR+EA to cost an additional **\$redacted** relative to revision CHEVAR and an additional **\$redacted** relative to open repair.

Table 10 Incremental cost of EVAR+EA relative to complex EVAR and open repair in the revision of thoracic aneurysms

Row	Cost item	T/EVAR +EA	Revision T/EVAR (CHEVAR)	Open repair	Source / calculation
A	Device costs	\$redacted	\$redacted	\$redacted	Table 75
B	Medical service costs	\$redacted	\$redacted	\$redacted	Table 78
C	Total costs	\$redacted	\$redacted	\$redacted	A+B
D	Incremental cost of T/EVAR +EA (relative to comparator)	-	\$redacted	\$redacted	\$redacted – C

CHEVAR=Chimney endovascular aneurysm repair; EA=EndoAnchor; T/EVAR=Thoracic endovascular aneurysm repair
 Source: Table 82, p209 of ADAR

The commentary noted that, the cost of open repair does not account for hospital costs, or PBS costs (such as antibiotics), as these patients would be expected to stay in hospital for a longer period compared with EVAR+EA, due to the more invasive nature of the repair surgery. The main assumptions driving this cost-minimisation approach is the cost of the fenestrated graft, and whether a cost of **\$redacted** is justified.

In the pre-MSAC response, the applicant acknowledged that hospital costs associated with open repair relative to complex endovascular procedures are likely underestimated. However, the applicant claimed there is limited evidence regarding the difference in length of stay between EA+T/EVAR and open repair for revision of T/EVAR. Therefore, the applicant claimed a conservative approach was taken in the ADAR in which hospitalisation costs were excluded from the analysis.

No sensitivity analyses were provided. The economic evaluation is a simple cost comparison including device costs and medical service costs. The key driver of comparative cost results is device use. The ADAR acknowledged the current use of comparator devices in each procedure is heterogenous and therefore uncertain. However, the applicant contends that the comparator device estimates applied in the base case of the cost comparison reflects best available evidence.

In the pre-ESC response, the applicant highlighted that the analysis assumed wastage as stipulated in Section D.4.1 of the ADAR, with the number of packs of EndoAnchors

estimated per procedure exceeding one across all populations. Should it be considered reasonable to assume no wastage, then the conducted analysis is conservative (i.e. overestimates the cost of helical anchors). The applicant stated wastage was accounted for in the analysis based on advice from clinicians that any remaining EndoAnchors in a pack will be discarded and as such will not be used for the next patient.

The applicant agreed the underlying question for the economic evaluation is whether the clinical claim is upheld and reiterated that the ADAR presented data that supports non-inferiority of EVAR+EA versus its comparators. From this, the ADAR concluded that a clinical claim of non-inferiority is reasonable, and that a cost-minimisation approach to the economic analysis is appropriate.

In the pre-MSAC response, the applicant reiterated their claim that the proportions of use across the different settings are uncertain as current MBS items do not differentiate between T/EVAR procedures (i.e. standard T/, FEVAR or CHEVAR) or treatment setting (i.e. primary or revision). The applicant attempted to estimate the proportions of used based on an estimated **redacted** complex EVAR procedures and **redacted** complex TEVAR procedures occurring in Year 1 (based on ADAR Table 95 pg. 223). Reintervention rates for primary complex T/EVAR procedures varied between 0 and 15% across EA+T/EVAR and complex T/EVAR studies included in Section B of the ADAR (ADAR Figures 23 pg. 155). Assuming a reintervention rate of 7.5%, the applicant estimated **redacted** primary and **redacted** revision complex EVAR procedures, and **redacted** primary and **redacted** revision complex TEVAR procedures will be performed in Year 1. As a result, it is estimated Population 1a accounts for 90.9% (**redacted**), Population 1b for 1.8% (**redacted**), Population 2a for 6.9% (**redacted**) and Population 2b for 0.4% (**redacted**) of all complex T/EVAR procedures. The applicant then applied this distribution to the results of the cost comparison presented in the ADAR (pg. 208-209) and claimed this results in an incremental cost savings of \$**redacted** for EA+T/EVAR versus complex T/EVAR, as presented below in Table 11.

Table 11 Weighted average cost comparison across the four populations included in the ADAR

Row	Cost item	Proportion	EVAR+EA	Complex EVAR ^a	FEVAR	CHEVAR	Source / calculation
A	Population 1a	90.9%	\$redacted	\$redacted	\$redacted	\$redacted	ADAR Table 79
B	Population 1b	1.8%	\$redacted	\$redacted	redacted	\$redacted	ADAR Table 80
C	Population 2a	6.9%	\$redacted	\$redacted	\$redacted	\$redacted	ADAR Table 81
D	Population 2b	0.4%	\$redacted	\$redacted	redacted	\$redacted	ADAR Table 82
E	Weighted average	-	\$redacted	\$redacted	redacted	redacted	
F	Incremental cost of comparator relative to T/EVAR+EA	-	-	\$redacted	redacted	redacted	\$redacted

^a Weighted average cost applying 80% FEVAR and 20% CHEVAR in Population 1a and 2a based on KoL opinion (see ADAR pg. 229), and CHEVAR only in Population 1b and 2b.
Source: Table 1, pre-MSAC response.

13. Financial/budgetary impacts

A hybrid epidemiological/market share approach was applied to estimate the utilisation and financial impact of MBS listing T/EVAR+EA across the proposed populations. A potential

market was estimated based on the historical utilisation of MBS items for unruptured aortic aneurysm replacement; 33103, 33109, 33112, 33115, 33116, 33118, 33119 and 33121.

The financial implications to the MBS resulting from the proposed listing of T/EVAR+EA summarised in the commentary are shown below in Table 12.

Table 12 Total costs to the MBS associated with T/EVAR+EA

Row	Parameter	Year 1	Year 2	Year 3	Year 4	Year 5	Source
A	Number of procedures	54	81	110	110	111	Table 40
B	Total cost of T/EVAR+EA procedures	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	Table 40
C	-cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	Table 40
D	-cost to patients	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	Table 40
E	Total cost of substituted T/EVAR procedures	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	Table 41
F	-cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	Table 41
G	-cost to patients	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	Table 41
H	Net financial impact of T/EVAR+EA listing	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	B-E
I	-cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	C-F
J	-cost to patients	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	D-G

EA=EndoAnchor; EVAR=Endovascular aneurysm repair; MBS=Medicare Benefits Schedule; T/EVAR=Thoracic endovascular aneurysm repair

Source: Table 9, pxx of the commentary

The commentary noted that the financial implications did not take into consideration the increase in utilisation if T/EVAR+EA is recommended by MSAC and listed on the MBS and do not take into account private hospital usage, and therefore utilisation and cost estimates are underestimated.

The commentary noted that the financial impact model has used small uptake rates (between **redacted**% and **redacted**% for AAA and **redacted**% and **redacted**% for TAA), which are favourable for T/EVAR+EA, and would underestimate the real net cost to the MBS (when considering higher uptake rates). However, when assessing the broader impact to the MBS, and considering the reduction in the number of transluminal stent insertion services claimed under the MBS item 35309, the savings to the MBS are also increased.

The ADAR acknowledged there is the potential for use outside of the proposed restriction, with the procedure being used in patients without hostile neck anatomy, or a Type 1a Endoleak. The potential financial implications of this additional use were estimated by applying T/EVAR+EA uptake assumptions to total T/EVAR procedures, as opposed to only complex T/EVAR procedures in the base case. The commentary considered that while this approach is acceptable, the same uptake rates were used in estimating use outside the restriction, which again could underestimate any financial implications. The incorporation of use outside the restriction into the financial impact estimates resulted in a cost to the MBS of **\$redacted** in the first year increasing to **\$redacted** in the fifth year.

The impact of substituting the uptake rates to a maximum of 100%, to obtain the upper bound estimate (without use outside the restriction) is shown below in Table 13. This analysis indicated a saving to the MBS of **\$redacted** in the first year increasing to **\$redacted** in the fifth year.

Table 13 Total to the MBS over five years with an uptake of 100% (not presented in ADAR)

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Base case cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Base case (cost to patients)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Cost of EVAR+EA services					
Total cost of EVAR+EA procedures	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to patients	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Substituted costs due to EVAR+EA listing					
Total cost of EVAR+EA procedures	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to patients	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Financial impact of EVAR+EA listing					
Net financial impact of T/EVAR+EA listing	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to patients	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Broader impact to the MBS					
Net financial impact of T/EVAR+EA listing	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to MBS (75% rebate)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
-cost to patients	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted

EA=EndoAnchor; EVAR=Endovascular aneurysm repair; MBS=Medicare Benefits Schedule; T/EVAR=Thoracic endovascular aneurysm repair

Source: Table 47, p61 of the commentary

In the pre-ESC response, the applicant stated that the market share approach estimated T/EVAR+EA use as a function of the total T/EVAR market in a private setting, i.e. based on MBS statistics as detailed in Section E.1 (pg. 217 of the ADAR). This approach specifically accounts for private hospital usage and usage in private patients treated as such in public hospitals. Further, EVAR+EA offers an alternative treatment to complex EVAR, which is currently available to all patients for which EVAR + EA. Given the high risk of rupture in this population, it is not expected that there will be a large, prevalent pool of untreated patients. The applicant therefore claimed that MBS listing of EVAR+EA is not expected to increase the proportion of endovascularly treated patients requiring complex procedures (i.e. complex EVAR and EVAR+EA).

The applicant also highlighted that the financial impact model applied uptake rates of **redacted%** in year 1 increasing to **redacted%** in year 3 in the complex infrarenal market, not **redacted%** as suggested by the commentary. The applicant argued that an uptake rate of **redacted%** is not necessarily ‘small’. The uptake rates in complex thoracic market is lower, ranging from **redacted%** in year 1 increasing to **redacted%** in year 5. The applicant acknowledged uptake rates of T/EVAR+EA are somewhat uncertain and reiterated that the impact of doubling the uptake rates in both populations were explored in sensitivity analyses (refer to Section E.6.2 of the ADAR) with results showing minimal impact on the estimated financial implications associated with MBS listing or T/EVAR+EA. The base case estimated that listing T/EVAR+EA on the MBS would result in cost savings to the MBS of between **\$redacted** in Year 1 and **\$redacted** in Year 5, whilst doubling uptake rates results in estimated MBS savings of between **\$redacted** in year 1 and **\$redacted** in year 5.

14. Key issues from ESC for MSAC

ESC key issues	ESC advice to MSAC
Very low-quality evidence	ESC considered the low confidence in the estimate of effect. The true effect may be substantially different from the estimate of effect claimed by the applicant.
Safety and effectiveness	For both populations, ESC considered that there is low confidence that T/EVAR+EA has non-inferior safety and non-inferior effectiveness relative to complex T/EVAR (FEVAR or CHEVAR) or other possible interventions.
No better-quality evidence on the horizon	ESC noted that apart from the ANCHOR registry, there are no active studies and no clinical trials currently recruiting.
Assumption T/EVAR +EA is non-inferior to its comparators in each population	AESC advised that cost-minimisation approach to the economic analysis is only appropriate if the clinical claim of non-inferiority is accepted.
The population has been split into abdominal and thoracic treatment/repair	The populations were appropriately split due to the difference in complexity and time required for each operation. However, ESC noted that the analysis failed to account for the cost of grafts associated with thoracoabdominal aortic aneurysms.
Comparator costs.	ESC queried a number of potential issues with the comparator costs included in the cost comparisons. <ul style="list-style-type: none"> • The cost for open repair may be underestimated. • The cost for FEVAR in Populations 1a and 2a may be overestimated. • The cost for CHEVAR may be underestimated. • The assumed proportions of bare metal and covered stents used in the different sub-populations may vary in clinical practice.
Cost-minimisation claim	ESC advised that a claim of cost-minimisation cannot be supported by the economic analysis presented. Based on the information included in the ADAR, the use of the intervention appears to be associated with a higher cost in some settings and to be cost-saving in others. However, as the ADAR does not include information on the proportions of use in these different settings it is not possible to conclude whether the use of the intervention will be cost-neutral overall.
Cost of device/wastage	The applicant indicates it will seek a Prostheses List benefit of \$redacted for a pack of 10 abdominal helical anchors compared with \$redacted for a pack of 10 thoracic helical anchors. If this differential pricing by indication is not accepted it has an impact on the economic analysis. ESC agreed with the pre-ESC response that the applicant's analysis has appropriately dealt with wastage, noting that whilst each pack contains multiple devices, and some patients may require more than one pack, any unused devices are discarded and not used for other patients.
Financial implications may be over or underestimated	ESC advised that the uncertainties in the cost-minimisation approach to the economic analysis flow through to the financial estimates.

EVAR = Endovascular aneurysm repair, T/EVAR = Thoracic endovascular aneurysm repair, EA = EndoAnchors, FEVAR = Fenestrated EVAR, CHEVAR = Chimney EVAR

ESC discussion

ESC noted the purpose of this application was to consider MBS listing of transmural fixation of aortic endograft using helical anchors (EndoAnchors [EA]) to treat AAA and TAA adjunct to EVAR.

ESC noted that the three MBS item descriptors in the ADAR differed from the ratified PICO. However, ESC also noted that the applicant would support alternative arrangements and structuring of the proposed MBS items. The ESC noted the rationale for an increased fee was based on the increased length of the procedure. The ESC considered this may be reasonable, but would need to be considered by Government in the context of the overall policy for setting MBS fees.

ESC noted there were some discrepancies in the calculations undertaken to justify the fee increase (time taken for thoracic endovascular aneurysm repair (T/EVAR) + EA compared with time taken for T/EVAR). In one part the ADAR states the proposed new procedure takes 17% longer, but Table 83 in the ADAR quotes 16% and 11%. ESC requested that the applicant clarifies this apparent discrepancy.

The ESC advised that these procedures appear, in the main, to require an overnight stay and to be performed under general anaesthetic or local anaesthesia with sedation. Therefore, a Type A classification appears appropriate. The ESC also considered it may be appropriate for the items to include provisions for general anaesthesia or local anaesthesia with sedation and assistance at operation, if required (noting this may have implications for the price of the procedure and the cost-minimisation approach to the economic analysis).

ESC noted the possibility of restricting claiming of the items to vascular surgeons, but considered this may not be necessary. Most surgical items are not restricted to specific specialty groups.

ESC advised that the applicant's nominated comparators appear appropriate, but noted there is uncertainty in the relative proportions of patients in Population 2 who are managed through a revision aortic EVAR or T/EVAR or through open surgery.

- The comparator for Population 1 is use of complex grafts defined as fenestrated, branched or chimney grafts.
- The comparators for Population 2 (both for Type Ia endoleak and migration) are:
 - Revision T/EVAR including addition of component pieces and/or repositioning of stent-graft, and/or aggressive ballooning i.e. angioplasty) or complex grafts,
 - Open repair.

The ESC noted the analysis failed to account for the cost of grafts associated with thoracoabdominal aortic aneurysms.

ESC noted that there are no direct comparative data in any population, so the evidence base presented by the applicant relies on naïve indirect comparisons of single-arm studies or single arms of comparative studies against other comparators.

- seven (7) studies of EVAR + EA
- eleven (11) studies of EVAR for Population 1
- fourteen (14) studies of revision EVAR or open surgery in Population 2.

The ESC noted that the assessment of exchangeability of the studies was limited by the information provided. Although acknowledging the applicant's pre-ESC response that, in its selection of studies for inclusion in the assessment, the applicant ensured both sets of data

enrolled patients with aneurysm characteristics overlapping with the proposed populations, the ESC considered concerns about the exchangeability of the trial data remain a key source of clinical uncertainty. ESC noted that the relevant Clinical Advisory Group (CAG) of the Prosthesis List Advisory Committee (PLAC) may be able to provide advice in this regard.

Thus, ESC advised MSAC that the main issue in relation to the clinical claim is the inherent risk of bias and uncertainty of study comparability associated with naïve comparisons. Although as noted by the applicant in its pre-ESC response, this is the best evidence available, this issue means it is difficult to be confident in the estimated effect, and there is potential the true effect could be substantially different from the estimate presented. However, acknowledging the limitations of the evidence presented, the available data do not indicate that helical anchors are inferior in terms of safety and effectiveness compared with the comparators. ESC also noted that there are no clinical trials on the horizon comparing the two approaches directly.

ESC noted the cost-minimisation approach to the economic analysis presented by the applicant can more properly be described as a costing study of EVAR + EA versus comparator treatments, with the comparator treatments in each Population further divided, resulting in eight (8) separate cost-comparisons (see Table 11).

The ESC noted that some of the inputs in the individual cost-comparisons may not be correct. These include

- The cost for open repair may be underestimated as it does not appear to account for the likely hospital or PBS costs that would accrue to this group.
- The cost for Fenestrated EVAR (FEVAR) in Populations 1a and 2a may be overestimated as it appears to assume all procedures will use fenestrated stent-grafts at a Prosthesis List (PL) price of \$redacted when there are other less expensive fenestrated stent-grafts (other graft prices range from \$redacted) on the PL.
- The cost for Chimney EVAR (CHEVAR) may be underestimated, as it does not appear to take account of any grafting costs.
- The cost of covered stents is significantly higher than bare stents, which increases the cost of the comparators FEVAR and CHEVAR.

The ESC also noted the Applicant's premise that listing this procedure on the MBS (and the device on the PL) will be cost-neutral overall, and hence that a cost-minimisation approach to the economic analysis is appropriate, cannot be verified on the basis of the cost comparisons presented in the application. This is because some of the cost-comparisons suggest the new procedure will be more expensive and some show it will be cost-saving, relative to the comparators. But the applicant did not provide any information on the expected proportions of patients in each of the 8 sub-populations for which a cost-comparison had been presented, so it was not possible to estimate the overall comparative costs of the proposed new procedure/device with current procedures/devices.

ESC noted the applicant's pre-ESC response in relation to the wastage issue raised in the commentary. The ESC agreed with the pre-ESC response that the applicant's analysis has appropriately dealt with wastage with the number of packs of EndoAnchors estimated per procedure exceeding one across all populations to allow for the estimated proportion of patients in whom a second pack of anchors will be used. The ESC agreed that any EndoAnchors remaining in a pack at the end of a procedure will need to be discarded and will not be available for use in another patient.

Finally, ESC noted the applicant has indicated it will seek a PL benefit of \$redacted for a pack of 10 abdominal helical anchors compared with \$redacted for a pack of 10 thoracic helical anchors. ESC noted that the absence of rationale for this differential pricing provided by the applicant. Given that the pack sizes and products are identical across the different indications ESC felt that this request for differential pricing should be brought to the attention of the PLAC.

ESC noted the uncertainties in the cost-minimisation approach to the economic analysis flow through to the financial estimates.

15. Other significant factors

Nil

16. Applicant comments on MSAC's Public Summary Document

The Applicant is disappointed with MSAC's decision to not support public funding for Transmural fixation of aortic endograft adjunct to endovascular aneurysm repair using helical anchors. The applicant acknowledges MSAC's commentary that the main limitation of the comparative safety and efficacy assessment is the lack of direct comparative evidence. The Applicant acknowledges the lack of direct evidence as a limitation, however notes that the evidence presented represents the best level evidence available for this adjunct device and reflects the management of TAA/AAA on a case by case basis with individual anatomical characteristics and comorbidities considered in determining the suitable treatment option. However, the Applicant is pleased that MSAC acknowledged that using helical anchors with an off-the-shelf tube or bifurcated graft offered the possibility of a more timely intervention for population 1 than use of a custom made fenestrated or branch graft that can take 1–2 months to manufacture. The applicant notes that MSAC considered that further defining the patient population to identify patients who are most likely to benefit from the intervention may provide a way forward for the applicant and will work with MSAC to clarify this consideration. The adoption of Heli-FX within Australia demonstrates the belief and value Vascular Surgeons see in this technology. The applicant is fully committed to supporting surgeons and patients with this important innovation with continued focus on evidence generation.

17. Further information on MSAC

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