



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

## **Public Summary Document**

### ***Application 1656 – Vertebral body tethering for adolescent idiopathic scoliosis***

**Applicant:** Zimmer Biomet Pty Ltd

**Date of MSAC consideration:** 83<sup>rd</sup> MSAC Meeting, 25-26 November 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 vertebral body tethering (VBT) for the management of adolescent idiopathic scoliosis (AIS) was received from Zimmer Biomet 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 did not support public funding of VBT for the treatment of AIS. MSAC accepted that there was a clinical need for VBT but considered that the evidence for comparative safety, effectiveness and cost-effectiveness for VBT compared with posterior spinal fusion (PSF) was uncertain. For these reasons, MSAC advised that the MBS items currently being used to claim VBT need to be reviewed to exclude this use.

#### **Consumer summary**

This application was from Zimmer Biomet to confirm that vertebral body tethering (VBT) for adolescent idiopathic scoliosis (AIS) should be claimed on the Medicare Benefits Schedule (MBS). Surgeons in Australia are already claiming the procedure under MBS item numbers for posterior spinal fusion (PSF).

Adolescent scoliosis, or 'curvature of the spine', happens when the spine does not develop straight during childhood growth. Mild scoliosis may not cause a person any problems, or problems that can be managed without surgery, but more severe scoliosis may result in impaired lung function, pain, emotional and self-image distress, which can affect day-to-day activities and may need surgery.

There are two surgical options available in Australia: VBT and PSF. PSF is when two or more bones in the spine (vertebra) are re-aligned and fused together with screws and rods so that the spine grows in a straight line. VBT is when screws are placed along one side of

## **Consumer summary**

the spine (the shortened ‘convex’ side), then a tensioning cord (i.e. tether) is placed in the screws and pulled tight so that the growth continues on the opposite side (the long ‘concave’ side), thus straightening the spine.

MSAC noted that there are some benefits of VBT compared to PSF: it does not inhibit bone growth after surgery, it has a shorter surgery time, less blood loss and shorter recovery time, it results in less scarring and may allow more movement after surgery. However, MSAC was concerned about some of the disadvantages of VBT: it is crucial that as the patients selected for the procedure were not yet skeletally mature (still had capacity for bone growth) before surgery, it can result in overcorrection (that is, the spine ends up curving the other way), the screws and tethers can break, resulting in the need for repeat tether or PSF anyway, and that there were no long-term data for safety and effectiveness. MSAC also noted that the Spinal Society of Australia did not routinely recommend VBT, and that it was not used in the United Kingdom. MSAC considered that the safety, effectiveness and cost-effectiveness of VBT compared to PSF were all uncertain and more data were needed.

MSAC noted that about 60 VBT procedures are performed each year, but that this number would likely increase if separate MBS item numbers were created for its use. Since correct patient selection was crucial for the success of VBT, MSAC was concerned about this potential increase in usage.

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

MSAC did not recommend making separate MBS item numbers for VBT, because the effectiveness, safety and cost-effectiveness were all uncertain. MSAC considered that the current MBS item numbers used to claim VBT should no longer be available to use for this purpose. MSAC could reconsider the application after a trial comparing VBT with PSF in Finland is completed.

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

MSAC noted that this application, from Zimmer Biomet, was for the MBS listing of VBT for the management of AIS.

MSAC noted this was the first time this service was being considered, but that spine surgeons are already using existing MBS item numbers (about 60 per year), which are for PSF, to claim this procedure:

- one of item numbers 51020–51026 (depending on the number of vertebral bodies being fused)

AND

- 51165 (anterior exposure of thoracic/lumbar spine).

MSAC noted that in its pre-MSAC response, the applicant was requesting confirmation that the existing MBS item numbers could be used to claim for VBT; or whether new MBS item numbers for VBT were more appropriate, which may be useful to better define the patient population and so the use of VBT and its outcomes could be tracked.

MSAC noted that correct patient selection is critical for VBT, and the most important criterion is determining skeletal immaturity of the patient.<sup>1</sup> Other important selection criteria include Cobb angle, spinal flexibility, type and rotation of curve and patient age. MSAC noted that different methods of assessing skeletal maturity are available, such as Risser staging (ilium x-ray) and Sanders classification (hand x-ray). MSAC considered the Sanders classification to be the best determinant of VBT eligibility and predictor of curve progression. MSAC noted that Risser staging overestimates skeletal maturity, resulting in about 1 in 5 (21.5%) patients who appear nearly skeletally mature (i.e. considered at low risk of curve progression so not offered surgery), actually have very significant remaining growth (by Sanders classification). Also, about 1 in 10 (11.5%) assumed nearly mature were still in their most rapid phase of growth and, overall, 1 in 4 risk misclassification/mistreatment if Risser is used<sup>2</sup>.

MSAC noted the commentary's amended MBS item for the index procedure, which was largely agreed to by the applicant in the pre-ESC response (see Table 2), and a proposed modified item for the revision procedure (see Table 3). MSAC noted the Cobb angle range of 30° - 70°. The lower threshold was inconsistent with the majority of the published evidence and the definition of severe AIS as captured in the clinical management algorithm. However, the upper threshold was broadly consistent with published evidence.

Both PSF and VBT require the procedure to be performed by suitably trained orthopaedic surgeons under general anaesthesia. MSAC noted that the potential advantages of VBT compared to spinal fusion are that it allows more spinal movement and growth, the surgery time is shorter, recovery time is shorter, it is less invasive, there is less scarring, and it requires less hardware. These advantages were delineated by parents/carers in the consumer feedback, which was supportive of the application, and highlighted in the pre-MSAC response. MSAC also noted the consumer feedback highlighted that some families were paying for the procedure overseas.

MSAC noted the clinical management algorithm, and disagreed with the initial patient selection, as not all patients present with back pain. MSAC also noted that the proposed criteria for VBT are unclear for degree of curvature and severity, age and skeletal maturity.

MSAC noted the PICO for the application, and noted that range of motion, lumbar bending flexibility, trunk endurance and motor strength of trunk muscles were not explicitly included as effectiveness outcomes in the PICO but accepted they could be expected to favour VBT over PSF given the latter makes the spine rigid.

MSAC noted that the tether required for VBT is not currently listed on the Prostheses List (PL) resulting in high potential out-of-pocket costs. The applicant-developed assessment report (ADAR) noted that the screws and anchors are funded via existing items on the PL. In the pre-MSAC response the applicant indicated they would apply to list the prosthesis on the PL if this MSAC application was successful.

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<sup>1</sup> Alanay A et al. Thoracoscopic vertebral body tethering for adolescent idiopathic scoliosis: follow-up curve behavior according to Sanders skeletal maturity staging. *Spine* (Phila Pa 1976). 2020; 45(22):E1483–E1492

<sup>2</sup> Minkara A, et al. High risk of mismatch between Sanders and Risser staging in adolescent idiopathic scoliosis: are we guiding treatment using the wrong classification? *J Pediatr Orthop* 2018; 40:60–64.

MSAC noted that the ADARs literature review identified three matched cohort studies: Pehlivanoglu 2021<sup>3</sup>, Newton 2020<sup>4</sup>, and a conference abstract by Mathew 2020<sup>5</sup>. MSAC noted the ADAR also supplemented this with two single-arm studies providing health-related quality of life (HRQoL) data using the disease specific Scoliosis Research Society 22-item. MSAC noted the commentary included a single-arm meta-analysis (Shin 2021<sup>6</sup>) published after the ADAR was submitted.

MSAC noted the claim of non-inferior safety was uncertain due to:

- patient selection (possible underreporting of adverse events in PSF studies)
- no available longer-term data
- more pulmonary complications with VBT (atelectasis with pulmonary oedema and pleural effusion [thoracentesis])
- more revisions with VBT and that a proportion of patients progress to PSF.

MSAC noted the high degree of heterogeneity in the VBT studies, making comparison difficult. MSAC noted the meta-analysis showed that the most common complications for VBT were tether breaks (7.5%), overcorrection (7.5%) and lung complications (4.8%). The most common complications for PSF were neurologic complications (0.5%), screws loosening or falling out (0.5%) and infection (0.5%). MSAC concluded that overall, adverse events (AEs) were more common with VBT (26%) compared to PSF (2.0%), and that device-related AEs were more common in VBT (18%) than PSF (6.0%). MSAC noted there were no differences in neurologic complications or infection, but there was a difference in lung complications favouring PSF (odds ratio = 33.4 [95% confidence interval (CI): 4.8-1442.7]).

MSAC noted the effectiveness claim of superiority was highly uncertain, and there were between-group differences for many outcomes:

- There was no statistically significant difference in major thoracic curve difference before and after surgery between VBT and PSF (4.0°, 95% CI -3.8°, 11.8°), although noting analyses were not adjusted for differences in baseline Cobb angles. However, the proportional change in major thoracic (MT) Cobb angle and clinical success (as defined by study) favoured PSF
- There was no statistically significant difference in the ADARs meta-analysis of post-operative SRS-22 (see Table 8) but the commentary's additional meta-analysis (inclusive of Shin 2021) showed some domains (total scores and mental health) favoured VBT (see Figure 2; however as these were post-operative scores only no assessment could be made against the minimal clinically important difference (MCID))
- The functional outcomes reported in Pehlivanoglu 2021 favoured VBT.
- The shorter surgery time and less blood loss favoured VBT.

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<sup>3</sup> Pehlivanoglu T, et al. Comparison of clinical and functional outcomes of vertebral body tethering to posterior spinal fusion in patients with adolescent idiopathic scoliosis and evaluation of quality of life: preliminary results. *Spine Deformity* 2021; 9(4):1175–1182.

<sup>4</sup> Newton P. Anterior spinal growth modulation in skeletally immature patients with idiopathic scoliosis: a comparison with posterior spinal fusion at 2 to 5 years post-operatively. *J Bone and Joint Surgery* 2020; 102(9):769–777.

<sup>5</sup> Mathew S et al. AVBT vs. posterior spinal fusion for idiopathic scoliosis: results from a single tertiary care center. *Spine Deformity* 2020; 8:1413–1414.

<sup>6</sup> Shin M et al. Complications, reoperations, and mid-term outcomes following anterior vertebral body tethering versus posterior spinal fusion: a meta-analysis. *JB JS Open Access* 2021; 6(2).

In addition, MSAC noted that VBT does allow continued growth, which may improve lung function; however, PSF also improves lung function by making the spine rigid.

Overall, MSAC considered the HRQoL evidence to be very low certainty as some of the comparisons were naïve, there was substantial heterogeneity among studies in meta-analyses and that clinically important outcomes could not be demonstrated. Overall, MSAC considered the claim of superior effectiveness was not supported, but agreed that VBT did offer some advantages over PSF. However, MSAC noted the long-term effects of VBT are unknown due to the short follow-up time of studies.

MSAC noted the pre-ESC and pre-MSAC response acknowledged the shortcomings of the comparative matched cohort studies.

In addition, MSAC noted the issues raised in consultation feedback by the Spine Society of Australia (SSA), which considered the clinical place of VBT was not defined due to the low certainty evidence. The SSA also suggested a temporary item number which could limit availability to high volume surgeons (see Section 7). MSAC also noted the issues raised at ESC that other international jurisdictions restrict or do not use VBT.

MSAC noted the economic evaluation was a cost-utility analysis. The clinical inputs were all based on Newton 2020, utility values were based on meta-analysis SRS-22 data from Newton 2020 and Pehlivanoglu 2021. MSAC agreed with ESC and considered that the mapping algorithm to convert SRS-22 data used was appropriate; however, there was high uncertainty assuming that HRQoL improvements will continue to improve over time.

In addition, MSAC noted the model incorrectly assumed significantly lower cost for revisions, as it assumed no prostheses costs for revisions and assumed a similar hospital stay for VBT vs. PSF. MSAC noted the base case incremental cost-effectiveness ratio (ICER) was sensitive to plausible variation in these inputs in one-way sensitivity analysis. MSAC also noted the multivariate analysis developed by ESC using utilities from a Food and Drug Administration (US) registration study<sup>7</sup> and Aghdasi 2020<sup>8</sup>, which resulted in ICERs of up to \$122,517 depending on the utility value used, and VBT revision hospital stay length (see Table 10). MSAC agreed with ESC and considered the base case ICER to be very uncertain.

MSAC noted the applicant's claim in its pre-MSAC response that VBT would not increase costs to the MBS as it was already being claimed, but MSAC considered the patient demand impact is understated. MSAC noted that, depending on the percentage of PSF substitutions, the costs to the MBS could increase from \$25,535 to \$309,348 in Year 1 and from \$26,693 to \$364,797 in Year 5 (see Table 12).

MSAC noted the ESC advice that there is an upcoming randomised controlled trial (RCT) in a population similar to the proposed MBS population, and that it may provide more data in the future. MSAC advised that the applicant could resubmit the application when these data become available; however, larger studies and longer-term follow-up is also needed. MSAC also noted that the Medical Research Futures Fund (MRFF) could be approached to fund an RCT comparing VBT and PSF.

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<sup>7</sup> US Food and Drug Administration, Summary of safety and probable benefit (SSPB) vertebral body tethering system, 2019.

<sup>8</sup> Aghdasi B. Patient-reported outcomes following surgical intervention for adolescent idiopathic scoliosis. *Clin Spine Surg* 2020 Feb;33(1):24–34.

Overall, MSAC did not support public funding of VBT for the treatment of AIS. Although MSAC acknowledged a clinical need for VBT, it considered the evidence for the comparative safety, effectiveness and cost-effectiveness for VBT compared with PSF was too uncertain. MSAC advised that the MBS items currently being used to claim VBT need to be reviewed to exclude this use. MSAC noted this may have implications for existing items on the PL. MSAC noted that PLAC would need to be advised of its decision to not support public funding of VBT.

### Other discussion

MSAC considered the use of MBS item numbers 51020–51026 and 51165 for VBT to be a compliance issue, and the Department may need to consider the wording for these item numbers to exclude use of VBT through these items. If the Department required more information, MSAC noted it could approach the MSAC Executive for this.

## 4. Background

This is the first submission (Applicant Developed Assessment Report [ADAR]) for VBT for the treatment of AIS.

The ADAR stated that currently, the VBT procedure is performed in private hospitals in Australia with almost all procedures using the system called Reflect (Globus Medical). Funding for the VBT procedure is currently coming from existing MBS items for the medical service. The implants are funded largely by private health insurers with the screws and anchor funded via existing rebate codes on the PL. The cord component is either funded by ‘ex gratia’ payments by the private health insurer or is provided at no charge by the company.

## 5. Prerequisites to implementation of any funding advice

The proposed technology includes a therapeutic good that requires Therapeutic Goods Administration (TGA) approval. All implantable components of the VBT system (that is, the cord, anchor and screws) are included under ARTG 111775 (Table 1).

**Table 1** Details of VBT devices listed on the ARTG

ARTG no.	Product no. (GMDN)	Product description	Intended purpose	Product category	Sponsor
111775	37272 Fixation device, internal, spine, construct	Zimmer Spine - Fixation device, internal, spine, construct	Implants used to stabilize, support or correct alignment of spinal vertebrae	Medical Device Class IIb	Zimmer Biomet Pty Ltd

ARTG, Australian Register of Therapeutic Goods; GMDN, Global Medical Device Nomenclature; VBT, vertebral body tethering  
Source: Therapeutic Goods Administration, accessed 24 March 2021 [Link to TGA.gov.au](https://www.tga.gov.au)

## 6. Proposal for public funding

The ADAR proposed new MBS item for the VBT index procedure is summarised in Table 2. The commentary amendments to the index procedure are marked up below (in red text and strikethrough).

**Table 2 Proposed MBS item descriptor- index procedure; *commentary amendments marked up***

Category 3 – Therapeutic Procedures – Surgical Operations
<b>Proposed item descriptor:</b> SCOLIOSIS, in a skeletally <i>immature</i> child or adolescent aged 10-18 years with a Cobb angle of $\geq 40^\circ$ , <i>who has failed standard care including external bracing</i> , anterior correction of, with vertebral body tethering. <i>Skeletal maturity is to be assessed using the Sanders classification.</i>
<b>Note:</b> <del>Skeletal maturity is to be assessed using a validated bone age assessment tool</del>
Multiple Operation Rule (Anaes.) (Assist)
<b>Proposed fee:</b> \$3,534.05

*Note, typographical error corrected ('immature' rather than 'mature') to align with description of patient population*  
Source: Commentary p.xiv, Table 2.

The commentary considered there were several issues with the proposed descriptor and fees for the index procedure:

- The ADAR did not appropriately justify the proposed MBS fee (based on MBS item 50608), including advising on time and complexity as raised by PASC. In regard to surgical time, it was noted surgical time was significantly longer in patients undergoing PSF compared with VBT
- Standard of care was not included (nor defined) in the MBS item as requested by PASC. This was added in during evaluation (see above)
- The upper age limit (18 years) is not supported by the literature, nor by the consultation feedback, which suggested an upper age limit of 16 years of age. In regard to the lower age limit (10 years), there is some evidence in the literature of the use of the procedure provided to a child aged 9 years. In addition, the suitability and need of the proposed aged criteria is questioned, given the inclusion of skeletal immaturity assessment.
- While the descriptor recommends assessment of bone age, it does not specify which measure. While this gives flexibility, it should be noted there is level II evidence in the literature that suggests the Sanders classification should be used to guide treatment options in patients with AIS due to the limited sensitivity of Risser staging during peak growth velocity (Minkara 2020<sup>9</sup>); although this evidence has not been formally adopted into a clinical guideline. For these reasons, the commentary considered skeletal maturity should be assessed with the Sanders classification (see above).

The pre-ESC response largely agreed with the amendments proposed by the commentary. In addition, the applicant agreed with:

- amending the qualifying Cobb angle range to  $30^\circ - 70^\circ$  and the upper age limit to 16 years, noting, however, that an explicit upper age limit may not be necessary when including the phrase “skeletally immature child or adolescent” in the descriptor
- setting the MBS item fee(s) for VBT to the existing fees for ‘fixation of motion segment with vertebral body screw, pedicle screw or hook instrumentation including sublaminar tapes or wires’ (MBS items 51021-51025).

The pre-ESC response also advised that based on previous correspondence with spinal surgeons in Australia, it is strongly believed that several existing MBS items are currently used to claim VBT procedures, including:

<sup>9</sup> Minkara, A., et al., High Risk of Mismatch Between Sanders and Risser Staging in Adolescent Idiopathic Scoliosis: Are We Guiding Treatment Using the Wrong Classification? J Pediatr Orthop, 2020. 40(2): p. 60-64.

- MBS Items 51021-51025.
- MBS items 50624 or 50628 (‘scoliosis, in a child or adolescent, anterior correction of, with fusion and segmental fixation’; ‘not more than 4 levels’ or ‘more than 4 levels’, respectively).
- These MBS items are typically claimed alongside MBS item 51165 (‘anterior exposure of thoracic or lumbar spine, more than one motion segment’) or 38418 (‘thoracotomy, exploratory, with or without biopsy’).

The surgeons also advised that these existing MBS items understate the complexity of the VBT procedure.

The ADAR considered that the existing MBS item 50616 already covers revisions to the index VBT procedure. However, a proposed item descriptor (a modification of MBS item 50616 as shown by the strikethrough but with the same fee) has been provided below if required.

**Table 3 Proposed modified MBS item 50616 – revision procedure**

Category 3 – Therapeutic Procedures – Surgical Operations
<b>Proposed item descriptor:</b> SCOLIOSIS, in a child or adolescent, re-exploration for adjustment or removal of <del>segmental instrumentation</del> <i>vertebral body tethering instrumentation</i> used for correction of spine deformity
<b>Proposed fee:</b> \$638.70

Source: ADAR p.24, Table A3.2

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

The department received targeted consultation responses from one specialist organisation: the Spine Society of Australia (SSA).

The SSA generally supported the application with the following clarifications:

- SSA suggested a temporary MBS item number for use by clinicians with sufficient volume performance threshold in this field. Patient related outcomes could then be followed for 2-5 years until the patients are skeletally mature, with a review of the MBS items at 5 years
- SSA noted that VBT is technically demanding and specific training requirements and a volume performance threshold should be considered
- SSA queried whether the current evidence would support the claim that VBT is superior to PSF; it indicated that its exact role is not defined, and higher quality evidence is needed
- SSA queried the proposed fee and referred to MBS items. In the paediatric spinal portion of the MBS schedule, the closest numbers are 50624 and 50628, but both of these procedures are not direct comparators. In the general spine portion of the MBS 51011-51171 there are appropriate direct comparator numbers: 51023 or 51024 for fixation of 3-6 motion segments; and 51165 for anterior approach to 2 or more motion segments which can be used by either the primary or approach surgeon.

An individual from a health organisation also supported the application and suggested that the MBS item descriptor should include a requirement to limit the intervention to a paediatric population under 16 years of age, in a growing spine.

Post PASC, consultation feedback was received from two care givers of two children with severe scoliosis, one of whom underwent VBT, whilst the other received spinal fusion T4-L1. The feedback was supportive of VBT for the treatment of AIS and stressed that subsidised

treatment through the MBS would offer a new treatment option for children and families in the public health sector, who would otherwise be unable to afford it. The feedback highlighted that VBT is a less invasive and shorter procedure compared to spinal fusion, with less pain, faster recovery times, shorter hospital stays and less risk of post-operative complications, therefore reducing the state health costs. One carer outlined that after undergoing VBT, her child achieved modest correction of the spinal deformity and good spinal growth with improved mental health and lung capacity.

The disadvantage of VBT noted in the individual consultation feedback was the possibility of overcorrection and tether breakage. However, the feedback stressed that such instances are not prevalent, especially under the care of highly trained surgeons.

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

### *Description of proposed intervention*

VBT is a form of scoliosis surgery that aims to preserve spinal mobility, flexibility, and function. It is a minimally invasive procedure performed by an orthopaedic spinal surgeon. An assisting general (access) surgeon may also be required for anterior exposure of the spine. After the patient is administered general anaesthesia, the surgeon(s) will access the spine via thoracoscopic access or mini-thoracotomy (an anterior approach). The surgeons then use a fibre-optic video camera to help them place titanium screws into the vertebral bodies on the convex side of the coronal deformity. The screws are placed into the middle of the vertebral body with bicortical purchase under fluoroscopic guidance. A high-strength, braided polypropylene tether is then placed into the screw heads and sequentially secured to each screw after segmental compression. The tether is pulled taut, which then guides future growth. The technique achieves immediate post-operative partial correction of the spinal deformity. The pressure from the tether causes the vertebrae to grow denser and more slowly on the convex side of the curve, whilst the concave side of the spine continues to grow at a normal rate. As such, the spine gradually straightens as the patient grows.

### *Description of medical condition(s)*

AIS refers to scoliosis (Cobb angle  $\geq 10^\circ$ ) of unknown cause first identified in children when they are aged between 10 and 18 years (Horne 2014)<sup>10</sup>. The incidence of scoliosis is similar in males and females; however, females have up to a 10-fold greater risk of curve progression. Without treatment, there is progression of scoliosis and the extent of spinal curvature, with the rate of progression being greater for more severe curves at the time of diagnosis. Although AIS may not cause significant pain, it is associated with visible deformity, which is in turn associated with emotional distress and diminished self-image. Detrimental impacts on quality of life have been reported for self-image (and pain) domains for patients who do not undergo surgery for AIS<sup>11</sup>. Severe curvature (Cobb angle  $\geq 40^\circ$ ) can also lead to impaired pulmonary function (shortness of breath) due to rib deformity, which may affect the ability to perform daily activities<sup>12,13,14</sup>.

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<sup>10</sup> Horne JP, Flannery R, Usman S, 2014, 'Adolescent idiopathic scoliosis: diagnosis and management', *American family physician*, vol. 89, no. 3, pp. 193-8.

<sup>11</sup> Rushton PRP, Grevitt MP, 2013, 'Comparison of untreated adolescent idiopathic scoliosis with normal controls: a review and statistical analysis of the literature', *Spine*;38(9):778-785.

<sup>12</sup> Farady JA 1983, 'Current principles in the nonoperative management of structural adolescent idiopathic scoliosis', *Physical Therapy*; 63(4): 512-523.

<sup>13</sup> Karol LA, Johnston C, Browne RH, Madison M, 1993, 'Progression of the curve in boys who have idiopathic scoliosis', *The Journal of bone and joint surgery*; 75(12): 1804-1810.

<sup>14</sup> Maruyama T, Takeshita K, 2008, 'Surgical treatment of scoliosis: a review of techniques currently applied', *Scoliosis*; 3(1): 1-6.

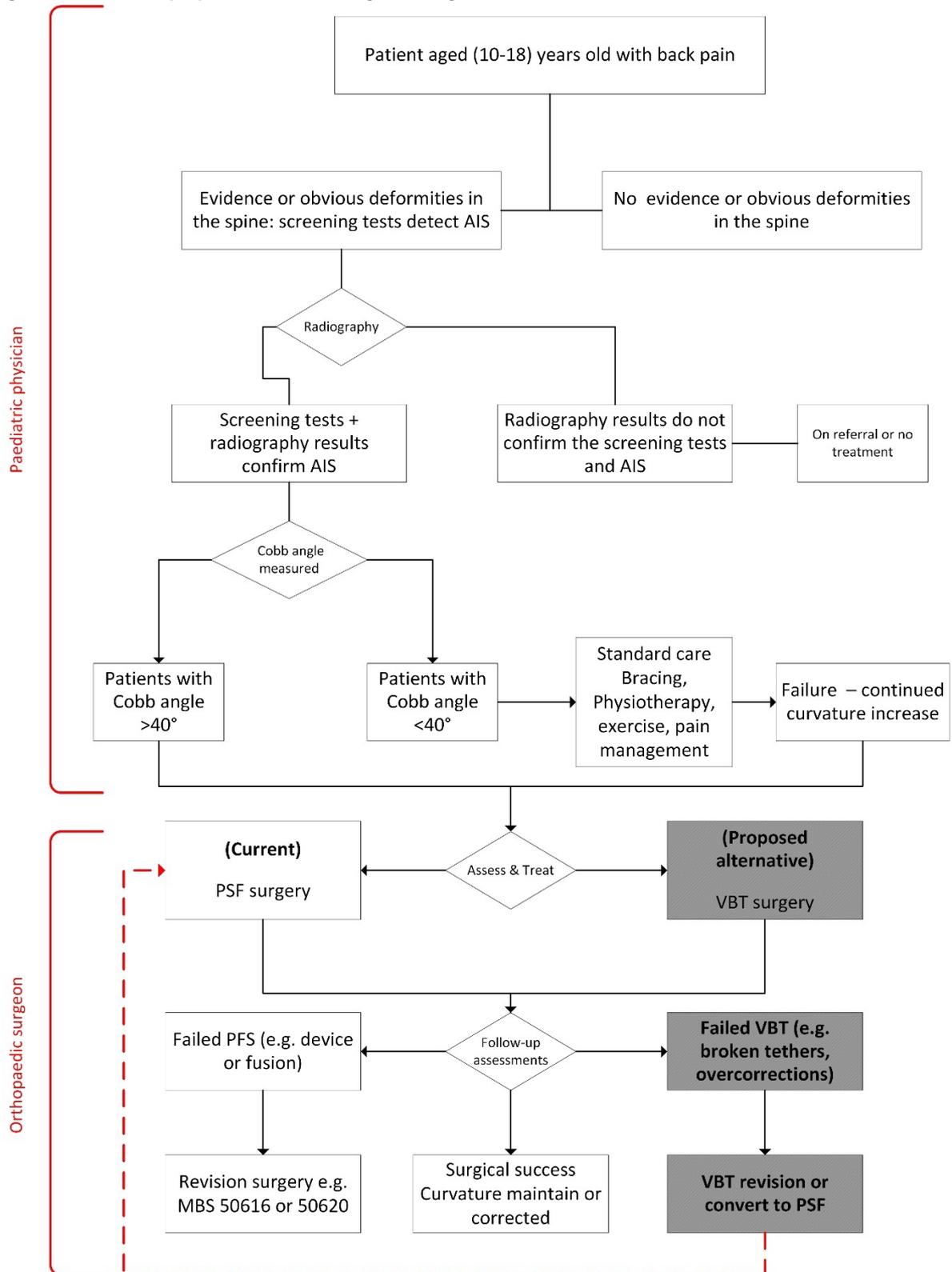
The proposed population is a skeletally immature child or adolescent aged 10-18 years with a Cobb angle of  $\geq 40^\circ$  who has failed standard care including external bracing. Severe AIS is defined internationally (including by Scoliosis Australia) as a Cobb angle  $\geq 40^\circ$ . Failure of external bracing can be defined by  $>5^\circ$  progression and/or intolerance to brace wear<sup>15</sup>. The current and proposed clinical management algorithm is summarised in Figure 1. Patients are treated according to the severity of their Cobb angle. Those with Cobb angles  $< 40^\circ$  are offered bracing, physiotherapy, exercise, and pain management. Those with Cobb angles  $\geq 40^\circ$  are offered surgical correction.

The commentary considered the clinical management algorithm is appropriate to the population and comparators specified, noting that a proportion of VBT patients will undergo subsequent PSF surgery.

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<sup>15</sup> US Food and Drug Administration, Summary of safety and probable benefit (SSPB) Vertebral Body Tethering System. 2019.

Figure 1 Current and proposed clinical management algorithm



Source: Ratified PICO, Figure 2, p. 14; ADAR Figure A.6.1, p. 29

## 9. Comparator

The comparator proposed in the ADAR is PSF, which is MBS funded (see Table 4).

Spinal fusion (typically done with a posterior approach, e.g. PSF) is the current approach for the treatment and management of AIS with a Cobb angle of  $\geq 40^\circ$ . A bone graft taken from

the patient, bone bank or an artificial substitute is utilised to promote fusion between two vertebrae, improve stability, correct a deformity and/or reduce pain (Tarpada, Morris & Burton 2017). The most common approach of spinal fusion, which involves metal screws, plates, and rods, is generally performed using the posterior approach. After general anaesthesia, an incision at the back of the spine is made, and pedicle screws are utilised, placed above and below the fused vertebrae, to provide extra support and strength to the purported spinal fusion. The pedicle screws are connected by the rod to prevent movement and promote healing. The screws and rod can be removed after the surgery if they cause pain and discomfort.<sup>16</sup>

PASC agreed that PSF is the appropriate comparator for VBT, with VBT hypothesised as a direct replacement. The commentary accepted this as the appropriate comparator; however, a percentage of patients that undergo the VBT procedure may require PSF surgery.

**Table 4 MBS items for posterior spinal fusion**

MBS item number	Category 3 – Therapeutic Procedures (Group T8 – Surgical Operations, Subgroup 15 – Orthopaedic, Subheading 20 – Spine Surgery For Scoliosis And Kyphosis In Paediatric Patients)
50608	SCOLIOSIS OR KYPHOSIS, in a child or adolescent, treatment by segmental instrumentation and fusion of the spine Fee: \$3,534.05
50604	Scoliosis or kyphosis, in a child or adolescent, spinal fusion for (without instrumentation) Fee: \$1,902.65
50640	SCOLIOSIS, in a child or adolescent, congenital, resection and fusion of abnormal vertebra via an anterior or posterior approach Fee: \$2,254.05

Source: Table 16, pp8-9 of the commentary

## 10. Comparative safety

The ADARs included three matched cohort studies of VBT vs. PSF (Mathew 2020; Newton 2020; Pehlivanoglu 2021). The ADAR included matched cohort studies were given an ‘acceptable’ rating, although it should be noted that one study, Mathew (2020) was a conference abstract only. Meta-analyses of the matched cohort studies are also presented for outcomes, where possible. The commentary included an additional study; a systematic review by Shin 2021. This meta-analysis included case series, retrospective cohorts, prospective cohorts and randomised controlled trials of VBT and PSF and used a single-arm meta-analysis approach.

The ADAR also supplemented comparative studies with the single arm FDA registration study, and a systematic review of PSF by Aghdasi (2020) to provide health-related quality of life data. No formal bias assessment of the FDA study or Aghdasi (2020) studies was conducted in the ADAR. The characteristics of the evidence base are summarised in Table 5.

Regarding the comparative studies, the ADAR noted that in Newton (2020), the VBT group was less skeletally mature (Sanders stage) compared with the PSF group, and in Mathew (2020), the PSF group had a higher thoracic Cobb angle than the VBT group. The impact of the former is ambiguous (particularly since not all patients reached skeletal maturity during the study). The impact of the latter may be in favour of PSF since these patients had a greater

<sup>16</sup> Deyo RA, Nachemson A, Mirza SK, 2004, 'Spinal-fusion surgery—the case for restraint', *The Spine Journal*; 4(5): S138-S42.

potential for Cobb angle correction. Overall, the commentary considered that despite matching, the comparative studies are at substantial risk of confounding.

**Table 5 Key features of the included evidence- commentary**

Study/ Country	N	Design/ duration of follow-up	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
<b>ADAR comparative studies</b>						
Pehlivanoglu (2021) Turkey	43	Retro CC, SC <u>Mean FU</u> 3.3 yrs. in both arms	Acceptable	Age 9 —14 years MT-TL curve 40°—60° Risser ≤ 2—Sanders ≤ 4 History of failed bracing <u>Matched:</u> age-gender- instrumented level-min FU	Radiographic outcomes HRQoL- SRS-22, SF-36 Functional outcomes (lumbar ROM, lumbar bending flexibility, trunk endurance, motor strength of trunk)	Yes
Newton (2020) United States	49	Retro CC, SC <u>Mean FU</u> VBT:3.4±1. 1 yrs.; PSF: 3.6±1.6 yrs.	Acceptable	Age 9—15 years MT curve 40°—67° Risser stage of ≤1 No prior spine surgery Surgery: 2011-2016 <u>Matched:</u> demographics	Complications Revision surgery Radiographic outcomes Clinical success HRQoL- SRS-22 Clinical measurements HC system outcomes	Yes (revision surgery)
Mathew (2020) United States [Conference abstract] (part of the FDA 2019 registration study)	60	Pro, CC, SC FU: 73% 1 year 33% 2 years	Acceptable	Paediatrics ≥10 years of age MT curve, Cobb ≥30° & ≤65° Sanders ≤5 or Risser ≤3 <u>Matched</u> 1:1 age- Risser sign- MT curve magnitude	Complications Revision surgery Radiographic outcomes Curve flexibility HC system outcomes	No
Meta-analysis	103 k=2	-	-	Newton (2020) Mathew (2020)	Complications Revision surgery	No
Meta analysis	92 2=2	-	-	Pehlivanoglu (2021) Newton (2020)	Radiographic outcomes HRQoL- SRS-22	Yes (utilities)
<i>Meta-analysis Shin (2021)</i>	1,280 k=24	<i>Included CS, retro, pro &amp; RCTs Mean FU VBT 33.7 months PSF 46.9 months</i>	Acceptable	<i>Included studies were human clinical outcomes study with follow-up of &gt;1 year; selective thoracic fusion or Lenke 1 or 2 curves; patient age of 10 to 18 years; AIS; undergoing primary surgical procedures</i>	<i>Radiographic outcomes Complications Revision surgery Conversion to PSF</i>	No
<b>ADAR non-comparative studies</b>						
<i>FDA study (2019)</i>	57	<i>Mean FU: 57 months</i>	<i>Not assessed</i>	<i>VBT, patients aged ≥10 years; AIS failed brace treatment defined as &gt; 5 degrees of progression and/intolerance to brace wear, Lenke 1; pre-operative Cobb ≥ 30 ° and ≤ 65 °; Sanders stage ≤ 5 or Risser sign ≤3</i>	<i>HRQoL- SRS-22</i>	<i>Yes (SA)</i>
Aghdasi (2020)	1,494	<i>Systematic review and meta- analysis (k=7, N=1494) Mean FU:</i>	Acceptable	<i>PSF, included studies provided SRS-22 data; performed spinal fusion using posterior pedicle screw instrumentation for AIS; and reported values for</i>	<i>HRQoL- SRS-22</i>	<i>Yes (SA)</i>

Study/ Country	N	Design/ duration of follow-up	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
		<i>Not reported</i>		<i>preoperative and postoperative means and SDs for the same patient cohort at 24- or &gt; 60-month follow-up</i>		

CC = case-control; CS = case series; FU = follow-up; HC = healthcare HRQoL = health related quality of life; pro = prospective; retro = retrospective; TL = thoracolumbar; MT = major thoracic; PSF = posterior spinal fusion; RCT = randomised controlled trial; SF-36 = short form-36; SA = sensitivity analysis; SC = single centre; SRS-22= Scoliosis Research Society -22; VBT = vertebral body tethering; yrs. = years

Source: compiled during the evaluation based on Tables B.4.1, B.4.2, B.4.3 of ADAR

Newton (2020) reported that (outside of revision procedures) neither surgical cohort experienced major, life-threatening, or debilitating complications. The peri-operative complications in the VBT group, for example, atelectasis, pleural effusion, were reported to be typical of thoracoscopic spine surgery. The ADAR concluded non-inferior safety based on no statistically significant differences in revision procedures, medical complications, or pleural effusion after a mean follow-up of 3.5 years (Newton 2020) and up to two years (Mathew 2020). However, revision procedures were statistically higher in the Newton (2020) study. The commentary considered that pooling the estimate of revision surgery with Mathew (2020), a conference abstract with limited follow-up, drives the difference to marginal levels and favours VBT. In addition, including the results by Shin (2021) also suggested there are significantly more revisions in patients who undergo VBT (Table 6).

**Table 6 Revision surgeries**

Study ID	VBT		PSF		OR (95% CI) P-value
	N	n (%)	N	n (%)	
Newton (2020)	23	7 (30)	26	0	<b>22.3 (1.2, 420.6)</b> <b>0.0437</b>
Mathew (2020)	30	1 (3)	30	0	2.0 (0.1, 63.0) 0.6866
Shin (2021)	211	<i>n=31</i> <i>14.1% (95% CI 5.6 to 22.6)</i>	312	<i>n=4</i> <i>0.6% (95% CI 0.0 to 2.3)</i>	<b>25.7 (95% CI 6.4 to 223.3)</b> <b>P&lt;0.0001</b>

n, number of patients experiencing event; N, total number of patients in treatment arm; OR, odds ratio; PSF, posterior spinal fusion; VBT, vertebral body tethering

Notes: Odds ratio calculated using Excel, applying correction to account for zero cells (0.5)\*. This is standard statistical practice and is recommended by Cochrane in their handbook. Commentary added figures are in *italics* and statistically significant figures are in **bold** text.

Source: Table 39, p60 of the commentary

Overall adverse event rates were not reported in the ADAR. The meta-analysis by Shin (2021) reported a statistically significant difference between VBT and PSF in terms of overall adverse events, favouring PSF (Table 7). The most common complications for VBT were tether breakage (n= 17; 7.5%), overcorrection (n = 17; 7.5%), and pulmonary complications (n = 11; 4.8%). The pooled complication rate excluding tether breakages for the VBT group was 17.4% (95% CI: 8.0% to 26.7%). The most common complications for PSF were neurological complications (n = 6; 0.5%), screw pull-out/loosening (n = 6; 0.5%), and infection (n= 4; 0.3%) (see Table 7). However, the commentary noted that availability of adverse event data for PSF was not available for all patients, increasing uncertainty in interpreting difference in risk between VBT and PSF.

Serious adverse events were not distinguished from overall adverse events in any of the included studies. In the FDA (2019) study, serious adverse events were reported in 8/57

(14%) patients, including overcorrection of instrumented curve (n=5, 8.8%), definite cord break (n=1, 1.8%), development of new curve (n=1, 1.8%), and spondylolisthesis (n=1, 1.8%).

**Table 7 Complications**

Study ID		VBT		PSF	
		N	%, (95% CI)	N	%, (95% CI)
<b>Overall Adverse Event Rate</b>					
Shin (2021)	< 36 months	211	11.8 (95%CI 4.4 to 18.6)	610	1.0 (95%CI 0.0 to 2.4)
	≥ 36 months	211	25.2 (95%CI 19.1 to 31.7)	610	2.9 (95%CI 0.5 to 5.3)
	Overall	211	26.0 (95%CI 12.0 to 40.0)	610	2.0 (95%CI 0.0 to 4.0)
<b>Risk difference PFS-VBT from Shin (2021)</b>					<b>24.0% (95% CI 18.1% to 30.1%)</b> <b>p&lt;0.0001</b>
Shin (2021)	Overall	N	n (%)	N	n (%)
		211	55 (26)	610	12 (2)
<b>Overall pooled OR (95% CI) for Shin (2021)</b>					<b>17.60 (95% CI 8.98 to 36.80)</b> <b>p&lt;0.0001</b>
<b>Infection Rate</b>					
Shin (2021)	Overall	N	n (%)	N	n (%)
		211	1 (0.44)	610	4 (0.31)
<b>Overall pooled OR (95% CI) for Shin (2021)</b>					<b>0.72 (0.01 to 7.34)</b> <b>p=0.77</b>
<b>Neurological Complications</b>					
Shin (2021)	Overall	N	n (%)	N	n (%)
		211	2 (0.88)	610	6 (0.46)*
<b>Overall pooled OR (95% CI) for Shin (2021)</b>					<b>0.96 (95% CI 0.09 to 5.44)</b> <b>p=0.96</b>
<b>Device Related Event, including tether breakage or screw pull-out/loosening</b>					
Newton (2020)	Overall	N	n (%)	N	n (%)
		23	12 (52)	26	NR
Shin (2021)	Overall	211	18 (7.9)	610	6 (0.46)*
<b>Risk difference PSF-VBT from Shin (2021)</b>					<b>7.5% (95% CI 3.7% to 11.4%)</b> <b>p=0.0338</b>
<b>Overall pooled OR (95% CI) for Shin (2021)</b>					<b>9.39 (95% 3.50 to 29.21)</b> <b>P&lt;0.0001</b>

n, number of patients experiencing event; N, total number of patients in treatment arm; OR, odds ratio; PSF, posterior spinal fusion; VBT, vertebral body tethering; **bold italics**, statistically significant.

\*Note this is the percentage reported in the paper, however, it appears incorrect if the denominator is 610 as per Supplementary Table 2 in the paper.

Overall pooled OR for Shin (2021) were calculated using the methods of Rothman (1979), Rothman (1986) and Rothman, Greenland and Lash (2008) as implemented in the cci command in Stata MP v16 for Mac. Significant results given in **bold**. Note Shin (2021) includes Newton (2020), so Newton was excluded from calculations. Source: Table 27, pp38-39 of the commentary

## 11. Comparative effectiveness

### Health Related Quality of Life

Patient-reported HRQoL was measured using the disease specific SRS-22. The MCIDs in the SRS-22 are > 0.2 for pain, > 0.08 for function, > 0.98 for self-image, and > 0.4 for other subcategories<sup>17,18</sup>. The ADAR random-effects meta-analyses of the post-operative SRS-22 scores reported by Newton (2020) and Pehlivanoglu (2021) showed no statistically significant differences between the VBT and PSF groups (Table 8) but claimed trends towards VBT in all domains. Clinical significance could not be demonstrated as only post-operative scores were available in meta-analysis.

Table 8 HRQoL – SRS-22 scores

Study ID	VBT		PSF		Mean difference (95% CI)	p-value <sup>a</sup>
	N	SRS-22 scores at final follow-up Mean (SD)	N	SRS-22 scores at final follow-up Mean (SD)		
<b>n</b>						
Newton (2020)	12	4.3 (0.4)	22	4.3 (0.4)	0.00 (-0.28, 0.28)	0.748
Pehlivanoglu (2021)	21	4.8 (1 <sup>b</sup> )		4.1 (1 <sup>b</sup> )	0.70 (0.10, 1.30)	NR
<b>Pooled result</b>	<b>33</b>	<b>4.52</b>	<b>44</b>	<b>4.27</b>		
Pooled result from random effects model: Chi-square for heterogeneity: p = 0.04, I <sup>2</sup> statistic = 76.80%					0.30 (-0.38, 0.98) <sup>c</sup>	0.39
<b>Mental Health</b>						
Newton (2020)	12	4.3 (0.6)	22	4.0 (0.6)	0.30 (-0.12, 0.72)	0.748
Pehlivanoglu (2021)	21	4.9 (1 <sup>b</sup> )		3.9 (1 <sup>b</sup> )	1.00 (0.40, 1.60)	NR
<b>Pooled result</b>	<b>33</b>	<b>4.59</b>	<b>44</b>	<b>3.97</b>		
Pooled result from random effects model: Chi-square for heterogeneity: p = 0.06, I <sup>2</sup> statistic = 71.54%					0.62 (-0.07, 1.30) <sup>c</sup>	0.08
<b>Pain</b>						
Newton (2020)	12	4.4 (0.6)	22	4.4 (0.6)	0.00 (-0.42, 0.42)	0.903
Pehlivanoglu (2021)	21	4.9 (1 <sup>b</sup> )		4.1 (1 <sup>b</sup> )	0.80 (0.20, 1.40)	NR
<b>Pooled result</b>	<b>33</b>	<b>4.63</b>	<b>44</b>	<b>4.31</b>		
Pooled result from random effects model: Chi-square for heterogeneity: p = 0.02, I <sup>2</sup> statistic = 80.85%					0.36 (-0.42, 1.14) <sup>c</sup>	0.37
<b>Satisfaction</b>						
Newton (2020)	12	4.3 (0.7)	22	4.7 (0.7)	-0.40 (-0.89, 0.09)	0.053
Pehlivanoglu (2021)	21	4.9 (1 <sup>b</sup> )		3.6 (1 <sup>b</sup> )	1.30 (0.70, 1.90)	NR
<b>Pooled result</b>	<b>33</b>	<b>4.59</b>	<b>44</b>	<b>4.17</b>		
Pooled result from random effects model: Chi-square for heterogeneity: p = 0.00, I <sup>2</sup> statistic = 95.30%					0.44 (-1.23, 2.10) <sup>c</sup>	0.61
<b>Self Image</b>						
Newton (2020)	12	4.2 (0.4)	22	4.4 (0.4)	-0.30 (-0.79, 0.19)	0.29
Pehlivanoglu (2021)	21	4.8 (1 <sup>b</sup> )		3.3 (1 <sup>b</sup> )	1.50 (0.90, 2.10)	NR
<b>Pooled result</b>	<b>33</b>	<b>4.45</b>	<b>44</b>	<b>3.86</b>		
Pooled result from random effects model: Chi-square for heterogeneity: p = 0.00, I <sup>2</sup> statistic = 95.52%					0.59 (-1.18, 2.35) <sup>c</sup>	0.51
<b>Total</b>						
Newton (2020)	12	4.2 (0.4)	22	4.4 (0.4)	-0.20 (-0.48, 0.08)	0.748
Pehlivanoglu (2021)	21	4.9 (1 <sup>b</sup> )		3.8 (1 <sup>b</sup> )	1.10 (0.50, 1.70)	<0.001
<b>Pooled result</b>	<b>33</b>	<b>4.53</b>	<b>44</b>	<b>4.13</b>		
Pooled result from random effects model: Chi-square for heterogeneity: p = 0.00, I <sup>2</sup> statistic = 93.27%					0.42 (-0.85, 1.69) <sup>c</sup>	0.52

CI, confidence interval; ID, identification; N, number of patients reporting data; NR, not reported; PSF, posterior spinal fusion; SD, standard deviation; SRS-22, Scoliosis Research Society 22-Item Questionnaire; VBT, vertebral body tethering.

Notes: Mean differences and pooled analysis calculated with Stata(v16) for the ADAR. Calculated figures are *in italics* and statistically significant figures are in **bold text**.

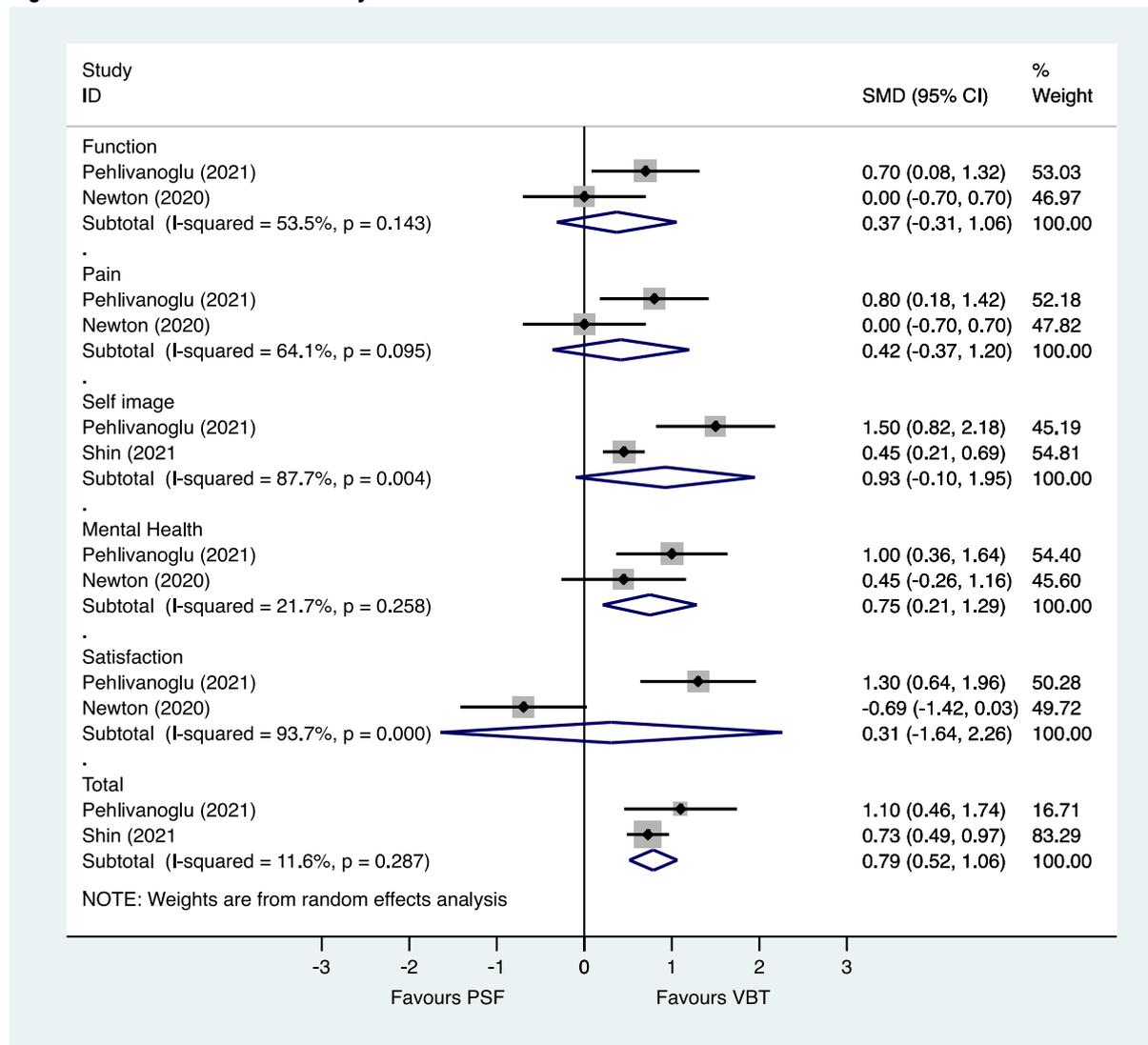
<sup>a</sup> As reported in publications

<sup>b</sup> As SD's were not reported in publication, SD=1 for each field was used in the calculation.

Source: ADAR Table B.6.7

The commentary performed an additional meta-analysis including the results of Shin (2021). The heterogeneity of SRS-22 scores was not reported in Shin (2021), and only post-operative SRS-22 scores were reported. Consistent with the ADARs meta-analysis, there were uncertainties related to the effect estimates of SRS-22, including the consistency of results, and whether any difference observed are clinically significant given the lack of pre-operative data. Nonetheless, only the mental health domain and total score were significantly better in those treated with VBT compared to PSF Figure 2.

**Figure 2 Random effects meta-analysis of SRS-22 in included studies**



Source: ADAR Commentary p.50, Figure 10.

The ADAR also included a supplementary analysis of a naïve comparison of single-arm studies which showed there were statistically significant improvements in the function and total SRS-22 scores in favour of VBT compared with PSF using the data from Aghdasi (2020) reported at 24 months (n=1,468). A statistically significant improvement in the function scores in favour of VBT compared with PSF was also demonstrated using the data from Aghdasi (2020), reported at ≥60 months (n=137).

### Functional outcomes

The ADAR presented additional functional efficacy outcomes based on the Pehlivanoglu (2021) study. Based on a single, small study (Pehlivanoglu 2021), it appears that average lumbar range of movement, average lumbar bending flexibility, average trunk endurance and average motor strength of trunk muscles are all statistically significantly better in those

undergoing VBT compared with PSF. However, the commentary considered given the lack of baseline characteristic data presented in this study, it is difficult to know whether the functional outcomes occur as a result of potential differences in the indications of VBT and PSF, an issue that the authors themselves highlight.

### *Clinical claim*

The clinical claim made in the ADAR is that VBT for the management of AIS is superior in terms of effectiveness as measured by HRQoL and functional outcomes, and non-inferior in terms of safety (adverse event rates) compared to PSF.

Consistent with the ratified PICO, the ADAR appropriately focused on the clinical claim for patient-relevant outcomes. For radiographic (surrogate) outcomes, the ADAR appropriately concluded that VBT was inferior to PSF due to statistically significant differences in favour of PSF (absolute change in Cobb angle, correction in Cobb angle, clinical success and other spinal curvature efficacy outcomes).

However, the commentary considered that VBT has uncertain safety compared to PSF in terms of adverse events, serious adverse events and other complications. The uncertainty is primarily due to low numbers in included studies, and the potential for confounding or missed reporting. For device related events, VBT appears inferior to PSF.

The commentary noted the clinical claim for superior efficacy in terms of HRQoL (SRS-22) is not strongly supported by the ADARs comparative studies, which the ADARs meta-analysis showed no statistically significant differences between the VBT and PSF groups (but numerical differences in favour of VBT). Clinical significance could also not be demonstrated either as only post-operative scores were available in meta-analysis. In addition, there was considerable heterogeneity in the ADARs meta-analysis (likely influenced by the small sample sizes in the included studies), the retrospective matched cohort studies were at substantial risk of confounding (despite matching), no pre-operative SRS-22 scores were reported for one study (Newton 2020) limiting any assessment against the MCID, and the estimates of variance were imputed for one study (Pehlivanoglu 2021) introducing even further uncertainty. Overall, this represented low to very-low certainty evidence.

The commentary also queried whether MSAC will accept the claim of superior efficacy in terms of HRQoL based on a naïve comparison (unadjusted for confounders) of single arm-studies representing very-low quality evidence. In addition, the ADAR included these studies despite its literature search being limited to comparative studies only, they did not undergo a formal risk of bias assessment and some applicability concerns as the FDA study for VBT included a proportion of patients with Cobb angles < 40 who would be ineligible as per the proposed MBS population.

Finally, the commentary queried whether MSAC will accept the claim of superior efficacy in terms of patient-relevant functional outcomes (not prespecified in the PICO), which were limited to a single matched cohort study with small patient numbers (n<30 in each group).

## **12. Economic evaluation**

The economic analysis presented in the ADAR uses a cost-utility analysis (CUA) on the basis of the clinical claim of superior effectiveness and non-inferior safety of VBT compared to PSF. The inputs used in the economic model are summarised in Table 9.

**Table 9 Summary of the economic evaluation**

<b>Perspective</b>	Australian healthcare system Including direct healthcare costs to patients, governments, health insurance agencies and any other part of society.
<b>Comparator</b>	PSF
<b>Type of economic evaluation</b>	Cost -utility analysis
<b>Sources of evidence</b>	Systematic review
<b>Time horizon</b>	6 years (mean age at time of procedure 12 years to skeletal maturity age 18 years)
<b>Outcomes</b>	Costs, and quality-adjusted life years
<b>Methods used to generate results</b>	Markov state-transition model
<b>Health states</b>	VBT: VBT index, VBT revision, PSF index procedure, dead PSF: PSF index, PSF revision, dead
<b>Cycle length</b>	1 year
<b>Discount rate</b>	5.0% for costs and health outcomes
<b>Software packages used</b>	Microsoft Excel

Source: ADAR Table D.3.1.

Over a six-year time horizon, the base case model for VBT is projected to cost \$84,328 and PSF is projected to cost \$72,504 including index and revision procedures, resulting in a cost increment of \$11,823 with VBT. Over this time horizon, VBT patients are expected to accrue 4.835 QALYs and PSF patients are expected to accrue 4.455 QALYs, representing a gain of 0.380 QALYs with VBT. The resulting incremental cost per QALY gained is \$31,104.

The modelled results were most sensitive to VBT and PSF QALY parameters. Consistent with a published CUA model by Polly (2021)<sup>19</sup>, the mean postoperative utility weightings are key sources of uncertainty in the ADAR economic model. Univariate sensitivity analyses were conducted on the key drivers and assumptions in the model (Table 10).

<sup>19</sup> Polly DW, Noelle Larson A., Samdani AF, et al, 2021, 'Cost-utility analysis of anterior vertebral body tethering versus spinal fusion in idiopathic scoliosis from a us integrated healthcare delivery system perspective', *ClinicoEconomics and Outcomes Research*; 13: 175-190.

**Table 10 Sensitivity analyses**

<b>Sensitivity analysis</b>	<b>Incremental cost (AUD)</b>	<b>Incremental QALYs</b>	<b>ICER (AUD)</b>
Base case	\$11,823	0.380	\$31,104
<b>Discount rate for costs and benefits (base case: 5.0%)</b>			
0.0%	\$13,811	0.426	\$32,449
3.5%	\$12,374	0.393	\$31,509
<b>Time horizon (base case: 6 years)</b>			
4 years	\$7,290	0.275	\$26,528
10 years	\$18,558	0.543	\$34,189
15 years	\$23,994	0.680	\$35,263
<b>Length of hospital stay associated with VBT revision (plausible upper limit) (base case: 2.5 days)</b>			
5 days	\$14,609	0.380	\$38,431
<b>Annual probability of VBT revision (FDA registration study) (base case: 7.39%)</b>			
2.92%	\$9,752	0.380	\$25,654
<b>Annual probability of PSF following VBT (FDA registration study) (base case: 3.76%)</b>			
0.84%	\$1,959	0.419	\$4,670
<b>Annual probability of PSF revision (Lykissas 2013) (base case: 0.00%)</b>			
0.48%	\$10,046	0.380	\$26,430
<b>Utility for VBT post-operation (FDA registration study) Utility for PSF post-operation 24 months and 60+ months (Aghdasi 2020) (base case: VBT = 0.889, PSF = 0.842)</b>			
VBT = 0.925, PSF = 0.875 (24 months)	\$11,823	0.236	\$50,031
VBT = 0.925, PSF = 0.900 (60 months)	\$11,823	0.119	\$99,158
<b>ESC multivariate sensitivity analyses</b>			
VBT = 0.925, PSF = 0.875 (24 months) AND VBT revision hospital stay = 5 days	\$14,609	0.236	\$61,816
VBT = 0.925, PSF = 0.900 (60 months) AND VBT revision hospital stay = 5 days	\$14,609	0.119	\$122,517

ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life year.

Source: ADAR Table D.6.1 1, and sensitivity analyses added in during ESC

### **13. Financial/budgetary impacts**

The financial analysis in the ADAR is based on the expectation that VBT will substitute for a proportion of PSF procedures. Specifically, the proportion of all PSF patients aged 10 – 18 years, and the substitution rate with PSF procedures. The commentary considered that the base case utilisation presented in the ADAR underestimate the utilisation of VBT as they do not account for the expected number of VBT revisions, or PSF after VBT procedures. In addition, consultation with Scoliosis Society of Australia indicated that around 60 VBT procedures are currently performed in the private sector each year. It is therefore expected that at least 60 VBT procedures would occur each year (this would be the lower bound estimate of uptake). Actual uptake may be higher due to lower out of pocket expenses for

patients, and the less invasive nature of the procedure compared to PSF, which will increase demand. The base case results have been adjusted (Table 11) to include and make financial estimates consistent with the economic analysis.

**Table 11 Number of VBT procedures - Uptake sensitivity**

Sensitivity	Year 1	Year 2	Year 3	Year 4	Year 5
ADAR estimate (Base case)	29	29	30	30	30
60 VBT per year (current VBT)	60	60	60	60	60
60 VBT per year plus 15% PSF substitution	89	89	90	90	90
60 VBT per year plus 30% PSF substitution	118	119	119	120	120
60 VBT per year plus 15% PSF substitution plus Eligible population limited to 10-16 years	83	83	83	84	84

VBT=Vertebral Body Tethering, PSF=Posterior Spinal Fusion

Source: Table 62, p102 of the commentary

The total MBS fees (75% benefit) per VBT index procedure are \$4,821 and per average VBT revision procedure are \$2,215 (based on the VBT revision procedure cost being identical to the PSF revision cost of MBS item 50616).

The financial implications to the MBS resulting from the proposed listing is summarised in Table 12. Patients who undergo VBT are expected to substitute the VBT index procedure directly for the PSF index procedure. Where revisions are estimated, these are assumed to occur in the same year as the index procedure. These revision procedures may occur in future years, in which case the timing of costs could vary. Using an alternative VBT uptake estimate, which accounts for patients who currently undergo VBT in the absence of MBS funding, results in a significantly higher financial cost of the VBT MBS listing, with net cost of \$309,348 in year 1 rising to \$364,797 in year 5 with a 75% MBS benefit This is due to:

- the larger number of VBT procedures funded by the MBS, compared to the base case presented in the ADAR, the majority of which were previously funded by patients, and
- the smaller number of avoided PSF procedures. This is due the patients who currently fund their VBT procedure, the MBS listing sees these costs being transferred from patients to government, with no change in the number of PSF procedures undertaken for this group of patients.

**Table 12 Net financial implications of VBT to the MBS including VBT revision and PSF after VBT procedures – Uptake sensitivity**

Sensitivity	Year 1	Year 2	Year 3	Year 4	Year 5
Base case	\$25,535	\$25,953	\$26,278	\$26,564	\$26,693
Base case (adjusted)	\$25,535	\$34,938	\$43,086	\$50,208	\$56,350
Eligible population limited to 10-16 years	\$20,081	\$27,476	\$33,883	\$39,484	\$44,314
60 VBT per year	\$41,796	\$56,262	\$68,514	\$78,976	\$88,215
60 VBT per year plus 15% PSF substitution	\$78,683	\$106,482	\$130,210	\$150,636	\$168,526
60 VBT per year plus 30% PSF substitution	\$104,218	\$141,421	\$173,296	\$200,844	\$224,877
60 VBT per year plus 15% PSF substitution plus Eligible population limited to 10-16 years	\$73,229	\$99,019	\$121,007	\$139,911	\$156,490
60 VBT per year plus 15% PSF substitution plus Eligible population limited to 10-16 years – assume 60 VBT per year do not result in an avoided PSF procedure (no substitution from PSF).	\$309,348	\$327,541	\$342,462	\$354,847	\$364,797

VBT=Vertebral Body Tethering, PSF=Posterior Spinal Fusion

The 75% benefit is applied to all costs presented in this table.

Source: Constructed during the evaluation based on Attachment 3 Financial Analysis workbook (Table 8, pxxix of the commentary).

The financial impact of the prosthesis for private health insurers is summarised in Table 13.

**Table 13 Net change in prosthesis costs for private health insurers**

Parameter	Year 1 2022	Year 2 2023	Year 3 2024	Year 4 2025	Year 5 2026
Expected utilisation of VBT (MBS)	29	29	30	30	30
Reported in ADAR (excludes VBT revision costs and PSF after VBT)	-\$182,963	-\$185,974	-\$188,328	-\$190,390	-\$191,301
Including VBT revisions and PSF after VBT, using ADAR resources (no prostheses for VBT revision)	-\$182,963	-\$132,901	-\$85,252	-\$40,341	\$2,827
Including VBT revisions and PSF after VBT, using Polly (2021) VBT revision prostheses requirements (50% of revisions requiring a VBT cord, 2 vertebral body screw and 2 anchors)	-\$182,963	-\$108,964	-\$42,034	\$18,399	\$74,084

MBS, Medicare Benefits Schedule; PSF, posterior spinal fusion; VBT, vertebral body tethering

Source: Table 76, p114 of the commentary

## 14. Key issues from ESC to MSAC

ESC key issue	ESC advice to MSAC
Clinical claim of non-inferior safety is uncertain	VBT has uncertain patient selection criteria, and higher complication and revision rates compared to the comparator, PSF. In addition, there are no data on the long-term complications of VBT.
Clinical claim of superior effectiveness is not supported by the data	Comparative studies show that VBT may achieve non-inferior curve correction but did not demonstrate clinically or statistically significant differences in HRQoL and were considered at substantial risk of selection bias and confounding. In addition, the meta-analysis results has substantial heterogeneity, limiting interpretation of results. Superior functional outcomes (not included in Ratified PICO) were presented from one very small study which did not measure baseline data.
Uncertain economic modelling	Evidence used to inform model inputs is uncertain as it is informed from low-very low quality evidence with risk of bias due to study design (studies are retrospective observational studies), small studies, and short follow-up. In particular: <ul style="list-style-type: none"> <li>•High level of uncertainty in utility values used in the model, which is key model driver</li> <li>•High level of uncertainty in transition probabilities and assuming continuing effects (i.e. HR-QoL improvements)</li> <li>•Moderate level uncertainty in model structure and assumptions</li> <li>•The costs of revisions used in the economic model may be incorrect.</li> </ul>
MBS item	The ADAR did not sufficiently justify the proposed fee or the need for a new MBS item.
Financial impact	The financial estimates may have underestimated the number of VBTs that are currently performed and did not properly account for VBT revisions or PSF after VBT.
Out-of-pocket costs	The applicant's device is currently not on the Prosthesis List, which will likely result in high out-of-pocket costs to consumers.

### ESC discussion

ESC noted that this application, from Zimmer Biomet, was for a new Medicare Benefits Schedule (MBS) item number for funding vertebral body tethering (VBT) for adolescent idiopathic scoliosis (AIS).

ESC noted that the public consultation feedback was generally supportive of the application, but the Spine Society of Australia (SSA) raised some concerns (see Section 5). ESC also noted positive consumer feedback about the procedure, with some parents considering going overseas to access VBT treatment for their child. Supportive feedback for VBT included that the patient is more flexible after the procedure, that the procedure allows for natural correction as the patient grows, and the faster recovery time and less scarring after surgery compared with posterior spinal fusion (PSF).

ESC noted the pre-ESC response, which indicated that spinal surgeons in Australia are already claiming VBT using one of the existing MBS item numbers 51021 to 51026, and 51165. ESC noted all new spinal surgery items are located within sub-group 17 of group T8 on the MBS (items 51011 to 51171). Items 51021 to 51026 are intended for spinal instrumentation at any level with the appropriate item determined by the number of motion

segments instrumented and 51165 can be used by either the primary or approach surgeon for anterior approach to 2 or more motion segments.

ESC noted that the proposed new MBS item for the index procedure (see Table 2) and modified MBS item 50616 for a revision item (see Table 3) does not provide a new technology, procedure or device type, or cover a treatment gap. ESC also noted that a new and specific item for VBT would encompass procedures where screws are removed (but not replaced) and tethers are divided. ESC noted that, if screws are then replaced, the proposed descriptor does not exclude using MBS items 51020 to 51026. The approach using MBS item 51165 (anterior exposure of spine) could continue as done currently. The SSA proposed using MBS 51021–51025 (alongside 51165) as appropriate alternative items, which the applicant agreed to. However, ESC queried whether it is reasonable to have a duplicate set of MBS items for VBT, and if it is necessary to have new items for tether and screw removal when this is not a significant part of revisions.

ESC noted that the commentary proposed amendments to the new MBS item, which the pre-ESC response largely agreed to (see Section 4). ESC also noted that MSAC may want to consider which assessment tool is most appropriate or whether type or number of assessment tool(s) should be unspecified; as correct patient selection and assessment of skeletal maturity is crucial for this procedure, in practice multiple tools are often used.

ESC considered that an upper age limit may not be necessary, as skeletal maturity is the most important factor for patient selection, not chronological age. ESC queried whether a lower age limit is necessary. ESC noted that the application is for AIS, so patients under the age of 10 would not be considered for this procedure. Some patients may have accelerated skeletal age and rare syndromes that result in precocious puberty, but this is rare.

ESC noted that the proposed fee is based on MBS item 50608 (the main MBS item for the comparator, PSF), but considered the applicant-developed assessment report (ADAR) did not sufficiently justify the additional cost or the need for a new MBS item number.

ESC considered the proposed clinical management algorithm to be too simplistic. In particular, that the clinical management algorithm does not identify how patients will be chosen as potential candidates for VBT. The ADAR focused on comparing VBT to PSF, but ESC considered that the overlap of patients who would choose between VBT or PSF may be small. ESC therefore considered that VBT would not replace PSF as an option for many patients.

ESC noted that correct patient selection is critical for VBT, and the most important criterion is skeletal maturity of the patient<sup>20</sup> (Alanay et al. *Spine* 2020). Other important selection criteria include Cobb angle, spinal flexibility, type and rotation of curve and patient age. ESC noted that there are differences in these criteria to select patients in the literature. For example, patients with a Cobb angle of <40° are considered for VBT overseas (e.g. patients recruited in FDA study), but in Australia such patients would be braced. ESC noted the challenges of prescribing strict patient criteria in the MBS item at this time.

ESC noted the ADARs evidence base consisted of three small single centre case-control studies, supplemented with two single-arm studies. The commentary included a recently

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<sup>20</sup> Alanay A, Yucekul A, Abul K, Ergene G, Senay S, Ay B, Cebeci BO, Yalinay Dikmen P, Zulemyan T, Yavuz Y, Yilgor C. Thoracoscopic Vertebral Body Tethering for Adolescent Idiopathic Scoliosis: Follow-up Curve Behavior According to Sanders Skeletal Maturity Staging. *Spine (Phila Pa 1976)*. 2020 Nov 15;45(22):E1483-E1492. doi: 10.1097/BRS.0000000000003643. PMID: 32756290.

published meta-analysis (Shin 2021) after the ADAR was published. ESC agreed with the commentary who considered that the matched case-control studies were at substantial risk of both selection bias and confounding. ESC considered that the evidence base was low to very low quality for most outcomes, limiting confidence in the estimates of effect size. ESC also considered that one of the studies included in the evidentiary base was not peer-reviewed but a conference abstract of a single arm of a multi-arm study, and therefore not appropriate to include.

ESC noted the pre-ESC response acknowledged the shortcomings of the comparative matched cohort studies.

In terms of comparative safety, ESC noted that incorrect patient selection can lead to overcorrection (21.1% , FDA 2019<sup>21</sup>), which may or may not require revision. ESC noted that overcorrection is not an issue with PSF. ESC noted the other potential adverse events from VBT included:

- cord breakage (52%, Newton 2020<sup>22</sup>)
- screw migration (5.3%, FDA 2019) – although this is not specific to VBT
- re-operation rates (14.1% VBT vs 0.6% PSF, Shin et al. 2021<sup>23</sup>; 30% VBT vs. 0% PSF, Newton 2020; see Table 6).

In addition, ESC agreed with the commentary who noted that including the conference abstract in the meta-analysis of revision rates favoured VBT. ESC noted the high rates of conversion using PSF after VBT, which ranged from 10.5% Miyanji et al. (2020)<sup>24</sup> to 26% (Newton 2020). ESC also noted that, if patients need to undergo PSF after a VBT procedure, it will be more difficult because new pedicle screws will on occasion be obstructed by the vertebral body screws left in situ by the index surgical procedure.

Overall, ESC agreed with the commentary and considered that VBT has uncertain safety for all outcomes except revisions (where VBT is inferior). ESC also noted there are no data on the long-term complications of VBT.

In terms of comparative effectiveness, ESC noted that, at 36 months post-surgery, curve correction for VBT vs. PSF was similar (VBT: 22.5 (95% CI: 14.1-30.9); PSF: 22.7 (95% CI: 19.6- 25.8), Shin et al. 2021). ESC noted that the ADARs superiority clinical claim focused on patient-reported outcome measures (PROMs) for HRQoL (Scoliosis Research Society 22-item [SRS-22]). However, ESC noted the ADARs meta-analysis of case-control studies did not demonstrate clinically or statistically significant differences in SRS-22. ESC noted that the ADARs meta-analysis and commentary's meta-analysis of post-operative SRS-22 scores (including Shin 2021) were impacted by considerable heterogeneity, which significantly limited interpretation of results. Overall, ESC considered that there was no difference in SRS-22 total scores.

ESC also noted that the ADARs clinical claim of superiority focused on functional measures, which were not ratified by PASC in the PICO. In the pre-ESC response, the applicant noted

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<sup>21</sup> US Food and Drug Administration, Summary of safety and probable benefit (SSPB) Vertebral Body Tethering System. 2019.

<sup>22</sup> Newton, P.O., et al., Anterior Spinal Growth Modulation in Skeletally Immature Patients with Idiopathic Scoliosis: A Comparison with Posterior Spinal Fusion at 2 to 5 Years Postoperatively. *J Bone Joint Surg Am*, 2020. 102(9): p. 769-777.

<sup>23</sup> Shin, M., et al., Complications, Reoperations, and Mid-Term Outcomes Following Anterior Vertebral Body Tethering Versus Posterior Spinal Fusion: A Meta-Analysis. *JB JS Open Access*, 2021. 6(2).

<sup>24</sup> Miyanji et al *Bone Joint J* 2020;102-B(12):1703–1708.

that these measures were not considered by PASC because they had not yet been published. However, ESC considered the improved flexibility scores for VBT compared to PSF may be expected, as spinal fusion is a procedure that will naturally result in a loss of flexibility.

ESC noted that the economic evaluation was a cost-utility analysis.

In terms of model structure, ESC noted that the health states did not include a transition probability from PSF index to PSF revision, which was not justified. ESC also noted that only one VBT revision was allowed for, which was not justified, but noted that this was likely to have a minor impact on the incremental cost-effectiveness ratio (ICER). ESC also noted that the model did not include post-surgery complications, and it assumed that resource use relating to management of complications is similar, and disutilities are captured in the post-operative utility values. ESC noted that this had an uncertain impact on the ICER, as there are no long-term data on the complications of VBT. Finally, ESC noted that the model assumed constant transition probabilities throughout the model's time horizon, and that the impact of this on the ICER was uncertain given the short follow-up in Newton (2020), which informed most model inputs.

ESC considered that the mapping algorithm used to convert SRS-22 data to utility values was appropriate. However, ESC noted issues with the sources of the SRS-22 scores data from Newton (2020) and Pehlivanoglu (2021)<sup>25</sup>, in that they were retrospective observational studies, with short follow-up time (3.5 years) and small sample size, and differences in skeletal maturity (Newton 2020) or lack of data on skeletal maturity Pehlivanoglu (2021). There was also substantial heterogeneity in the reported meta-analysis ( $I^2 > 75\%$ ) used to inform utility values. ESC also noted that the same utility values were used for index and revision procedures, and that post-operative utility values were based on reported SRS-22 data at the time of final follow-up for all types of patients. ESC noted that this does not capture the impact of the interventions on quality of life across the follow-up time.

In addition, ESC noted that, without longer-term comparative SRS-22 data, the model assumes that benefits will continue to accrue throughout the model time horizon and beyond the time frame for which there are data, thus the model assumes that quality of life improvements will continue to improve. These uncertainties impact the ICER, which is highly sensitive to the modelled utility values and assumptions.

ESC noted that the economic model included a significantly lower cost for VBT revisions than VBT index procedures, as it assumed no prostheses cost for revisions. The commentary included the cost of new cords using a 50% VBT revision rate (Polly 2021)<sup>26</sup>, which led to a 32% increase over the base case ICER of \$31,104. ESC also noted that the economic model assumed a length of stay of 5 days for VBT and PSF index procedures and PSF revision, and 2.5 days for VBT revision; however, this was based on clinical expert opinion and was not supported by published data. The commentary noted that, if 5 days was used for VBT revision procedure, this would lead to a 24% increase over the base case ICER. ESC considered the base case ICER to be uncertain, with multivariate sensitivity analysis showing the ICER reaching \$122,517 when using other plausible estimates for VBT revision length of stay and utility values from Aghdasi (2020)<sup>27</sup> (see Table 10).

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<sup>25</sup> Pehlivanoglu et al Spine Deformity 2021 Jul;9(4):1175-1182.

<sup>26</sup> Polly DW, Noelle Larson A., Samdani AF, et al, 2021, 'Cost-utility analysis of anterior vertebral body tethering versus spinal fusion in idiopathic scoliosis from a us integrated healthcare delivery system perspective', ClinicoEconomics and Outcomes Research; 13: 175-190.

<sup>27</sup> Aghdasi, B., et al., Patient-reported Outcomes Following Surgical Intervention for Adolescent Idiopathic Scoliosis: A Systematic Review and Meta-Analysis. Clin Spine Surg, 2020. 33(1): p. 24-34.

ESC noted the multiple data sources used for the financial impact. The base case financial impact was ~\$25,500 in Year 1 to ~\$26,700 in Year 5, but ESC considered that these numbers could be underestimated. The base case was based on the number of PSF procedures and assumed a substitution rate of 15% of PSF with VBT, resulting in 30 patients per year receiving VBT. However, the 15% substitution rate was derived from expert opinion, not published data. ESC considered this substitution rate could be too low, as it did not consider VBT revisions or PSF after VBT. Based on current uptake of VBT in the private sector, the commentary revised the patient numbers (see Table 11) that would undergo VBT (including revisions), resulting in a net cost to the MBS of ~\$309,000 in Year 1 to ~\$365,000 in Year 5.

ESC noted the applicant's pre-ESC response to other issues.

ESC noted the applicant's device is currently not on the Prosthesis List, which may result in high out-of-pocket costs to consumers.

ESC noted the advances in this field of study and the continual emergence of new clinical data. The criteria for using VBT are constantly evolving, making health technology assessment difficult. For example, various studies are conflicted about which Cobb angle to use when selecting patients for VBT (some use a Cobb angle of >30°). ESC noted that VBT is still undergoing a learning curve<sup>28</sup>.

In addition, ESC noted that there is an upcoming randomised controlled trial (RCT) comparing VBT and PSF in skeletally immature patients with AIS (Cobb angle 40-60; age 10-16 years, selective thoracic fusion feasible; [NCT04590807](#)). The estimated primary completion date is December 2023 (study completion date: 2025). ESC considered that although it may represent higher quality evidence and outcomes were powered for assessing HRQoL, it might not add substantial value to MSAC decision making, as it was a second-stage US Food and Drug Administration (FDA) study with only 70 patients due to enrol.

ESC considered that if MSAC does not support public funding of VBT that MSAC may wish to consider, in consultation with spinal surgeons, whether the MBS items currently being used to claim VBT need to be reviewed to exclude this use. In addition, ESC noted that in other jurisdictions, there is divergent surgical views of this procedure with some countries limiting its use. ESC noted the commentary (Herring 2020)<sup>29</sup> from a large US spinal centre, which noted the unfavourable results for VBT after reviewing the results of Newton 2020. VBT is not undertaken in the UK National Health Service by policy decision (2019)<sup>30</sup>, and the British Scoliosis Society does not currently recommend VBT (2016)<sup>31</sup>.

## 15. Other significant factors

Nil

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<sup>28</sup> Mathew S, Larson AN, Potter DD, Milbrandt TA. Defining the learning curve in CT-guided navigated thoracoscopic vertebral body tethering. *Spine Deform*. 2021 Nov;9(6):1581-1589. doi: 10.1007/s43390-021-00364-w. Epub 2021 May 18. PMID: 34003460

<sup>29</sup> Herring JA. What Is the Role of Anterior Vertebral Tethering?: Commentary on an article by Peter O. Newton, MD, et al.: "Anterior Spinal Growth Modulation in Skeletally Immature Patients with Idiopathic Scoliosis. A Comparison with Posterior Spinal Fusion at 2 to 5 Years Postoperatively". *J Bone Joint Surg Am*. 2020 May 6;102(9):e41. doi: 10.2106/JBJS.20.00123.

<sup>30</sup> <https://www.england.nhs.uk/commissioning/publication/vertebral-body-tethering-for-scoliosis-age-8-18-years/>

<sup>31</sup> <https://britscoliosis.org.uk/resources/Documents/British%20Scoliosis%20Society%20VBT%20Position%20Statement.pdf>

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

The applicant had no comment.

**17. Further information on MSAC**

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