

# Medical Services Advisory Committee (MSAC) Public Summary Document

## *Application No. 1719 - Insertion of a bioabsorbable implant for nasal airway obstruction due to lateral wall insufficiency*

**Applicant:** Stryker Australia Pty Ltd

**Date of MSAC consideration:** 30-31 March 2023

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 for the insertion of a bioabsorbable implant (LATERA®) for the treatment of nasal airway obstruction (NAO) due to lateral wall insufficiency (LWI) was received from Stryker Pty Ltd by the Department of Health and Aged Care.

The clinical claim in the Applicant Developed Assessment Report (ADAR) is that the insertion of LATERA for the treatment of NAO due to LWI has:

- non-inferior clinical safety and effectiveness compared to rhinoplasty
- inferior safety and superior clinical effectiveness compared to conservative treatment (i.e. breathe right strips).

### **2. MSAC's advice to the minister**

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC supported the creation of new Medicare Benefits Schedule (MBS) items for the insertion and removal of a bioabsorbable implant for nasal airway obstruction (NAO) due to lateral wall insufficiency (LWI). MSAC considered insertion of the bioabsorbable implant would provide patients with a minimally invasive alternative treatment with likely non-inferior safety and effectiveness compared to the primary comparator, functional rhinoplasty. MSAC considered the bioabsorbable implant had inferior safety and probably superior effectiveness compared to conservative management. MSAC noted the uncertainty of the evidence and that there was limited evidence for safety of the LATERA implant beyond 2 years. However, MSAC considered there is an unmet clinical need for a small subgroup of patients who are managed conservatively due to being unable or unwilling to undergo functional rhinoplasty surgery or have failed functional rhinoplasty surgery. MSAC considered the results of the economic analyses were uncertain but indicated that insertion of the bioabsorbable implant to treat NAO due to LWI was cost-effective compared to functional rhinoplasty. MSAC considered the financial estimates to be uncertain and likely underestimated, and that the claimed cost savings may not be realised, but that the overall potential financial impact to the Australian health care system was modest. MSAC considered that utilisation should be reviewed after 2 years.

Category 3 – THERAPEUTIC PROCEDURES

MBS item XXXX

Unilateral insertion of bioabsorbable implant for nasal airway obstruction due to lateral wall insufficiency confirmed by positive modified Cottle manoeuvre and the patient has a self-reported NOSE Scale score of greater than or equal to 55 if the indicated surgery is:

- (i) Provided by otolaryngologist and specialist plastic surgeons, who have undergone the Australian Medical Council (AMC) accredited training program
- (ii) photographic and/or NOSE scale evidence demonstrating the clinical need for this service is documented in the patient notes.

(anaes)

Fee: \$198.95 Benefit: 75% = \$149.20; 85% = \$169.10

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- (ii) Photographic and/or NOSE scale evidence demonstrating the clinical need for this service is documented in the patient notes.

(anaes)

Fee: \$298.43 Benefit: 75% = \$223.82; 85% = \$253.67

**Consumer summary**

This application from Stryker Australia Pty Ltd requested Medicare Benefits Schedule (MBS) listing for the insertion of a bioabsorbable implant (LATERA®) for nasal airway obstruction due to lateral wall insufficiency.

People who have nasal airway obstruction have trouble breathing through their nose. There can be many reasons for this, but this application focuses on lateral wall insufficiency. This means that the outside wall of the nostril collapses when the person breathes, which makes the nostril smaller, so it is harder to breathe. This can happen in one nostril or both nostrils. People with this condition can take medication or attach temporary strips to their nose to help their breathing, but it does not work for everyone. If it does not work, people can have surgery on their nose (called functional rhinoplasty) to help fix the problem.

LATERA is a small synthetic rod that is implanted within the outside wall of the nostril. It is attached to the bone in the nose and supports the nostril to stay open, making it easier for the person to breathe. The implant is absorbed over time and the body replaces it with a type of harder tissue that gives ongoing support to the nostril.

MSAC reviewed the evidence and considered that LATERA is just as safe and just as effective as functional rhinoplasty surgery. MSAC considered that LATERA is not as safe as non-operative management but is probably more effective. LATERA would be an option for people who are not getting better with medication or attaching temporary strips to their nose, who cannot or do not want to have surgery, or who have had surgery but have not improved. LATERA might also save the health system money.

## Consumer summary

### MSAC's advice to the Commonwealth Minister for Health and Aged Care

MSAC supported MBS listing for the insertion of a bioabsorbable implant for nasal airway obstruction due to lateral wall insufficiency. The implant gives patients another treatment option that is less invasive than surgery but just as safe and effective, and it might save the health system money.

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

MSAC noted that the application sought MBS listing of services for the insertion of a bioabsorbable implant (LATERA®) for the treatment of NAO due to LWI. MSAC noted that the applicant had also submitted an application to the Prostheses List Advisory Committee seeking listing of the LATERA implant on the Prostheses List (PL).

MSAC confirmed that the item descriptors for implantation should specify a nasal obstruction symptom evaluation (NOSE) score of  $\geq 55$ , in line with the clinical evidence, and that evidence of this should be documented in the patient notes. The items should specify once per lifetime per nostril, be restricted to use by otolaryngology head and neck surgeons and plastic surgeons and should include "(anaes)" to allow claiming of anaesthesia where required. MSAC considered the restriction to otolaryngology head and neck surgeons and plastic surgeons and the requirement for clinical evidence of need in the patient record should reduce the risk of misuse of the procedure in a broader population who may seek to undergo the procedure for cosmetic reasons. MSAC noted that the most common complication following LATERA is implant retrieval/extrusion/migration (9% of patients), and therefore advised the Department that an MBS item number for revision or removal would be required.

MSAC noted the proposed clinical management algorithm. This had been modified from the ratified PICO confirmation to allow patients to receive LATERA either as a second-line intervention after failed conservative management, or as a third-line intervention after failed functional rhinoplasty. MSAC considered that this modification was reasonable noting that in one of the LATERA studies<sup>1</sup>, 59% of patients had received prior nasal surgery of which 13% had previously undergone functional rhinoplasty.

MSAC noted the applicant's proposed comparators of functional rhinoplasty (primary) and conservative management (secondary). MSAC noted advice from ESC that conservative management was not an appropriate comparator, as patients would be eligible for LATERA only after they had failed conservative management. However, MSAC accepted the applicant's pre-MSAC response that the comparison against conservative management is relevant because not all patients whose symptoms continue despite conservative management are able to or will elect to undergo a functional rhinoplasty. MSAC also noted the advice from ESC that the primary comparator should be restricted to partial rhinoplasty only (MBS item 45632), as the other two rhinoplasty MBS items (45641 and 45644) are for total rhinoplasty that involves correction of all bony and cartilaginous elements of the external nose. However, the applicant's pre-MSAC response stated that "limiting the comparator to MBS item 45632 would infer that LATERA is only used for external valve collapse (alar rim) for which MBS code 45632 is typically used. Neither the TGA (Therapeutic Goods Administration) approved indication nor the evidence base for LATERA limits use to alar rim." Hence, the applicant pre-MSAC response claimed it was incorrect to suggest that all future candidates for LATERA currently receive partial rhinoplasty.

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<sup>1</sup> LATERA-RCT: [NCT03400787](https://clinicaltrials.gov/ct2/show/study/NCT03400787) - Latera Randomized Controlled Trial (RCT) - Latera® Absorbable Nasal Implant vs. Sham Control for Lateral Nasal Valve Collapse

“While correcting the underlying anatomical issues for these patients may not necessarily involve manipulation of bones, they often require grafting of cartilaginous tissues (MBS items 45641 and 45644)”. MSAC confirmed that the appropriate primary comparator should include all three MBS items for functional rhinoplasty, as stated in the ratified PICO confirmation.

MSAC considered the evidence comparing LATERA with functional rhinoplasty were uncertain due to naive indirect comparisons using low-quality evidence with a moderate to high risk of bias. However, MSAC noted that the evidence for functional rhinoplasty (which is the current gold standard) in this population was also of low-quality with a moderate to high risk of bias. Regarding comparative safety, MSAC considered that LATERA had inferior safety compared with conservative management, and at least non-inferior safety compared with functional rhinoplasty where this is performed without any adjunct procedures. MSAC noted that the long-term safety of LATERA beyond 2 years is unknown. Regarding comparative effectiveness, MSAC noted that the claims of non-inferior effectiveness compared with functional rhinoplasty, and superior effectiveness compared with conservative management, were uncertain. However, MSAC noted that patients showed greater improvements in the NOSE score outcome with LATERA compared with functional rhinoplasty at 12 months and at 24 months.

MSAC noted the economic evaluation. The ADAR presented a cost-minimisation analysis that compared LATERA with functional rhinoplasty, which demonstrated cost savings for LATERA, including in the sensitivity analyses requested by ESC. MSAC noted the pre-MSAC response presented an additional cost-minimisation analysis with a 2-year time horizon that captured revisions and subsequent surgery (presented in Table 21), and this still demonstrated that LATERA resulted in incremental cost savings. MSAC agreed with the pre-MSAC response that an 80% response rate does not equate to a 20% revision rate, as non-response is not synonymous with reintervention, and is not a valid assumption for analysis. The ADAR also presented a cost-utility analysis compared with conservative management. MSAC noted and agreed with the concerns raised by ESC and the commentary, including that this analysis assumed the comparator had zero cost, used utility values from septorhinoplasty with a different population to the LATERA studies, did not include revision rates or safety costs, and provided no evidence to support the 5-year time horizon.

MSAC noted the estimated financial and budgetary impacts. MSAC considered that the financial estimates provided were highly uncertain and likely underestimated, as the estimates do not include revision or subsequent rhinoplasty, evidence to support the estimated uptake of LATERA, potential use of LATERA beyond the evidence base, or NOSE score severity. The rate of bilateral implantation may be an underestimate. MSAC also noted that sensitivity analyses requested by ESC indicate that the cost savings reported in the ADAR may not be realised.

MSAC noted that the cost of LATERA appears to be higher than other comparable bioabsorbable implants on the PL, although the pre-MSAC response argued that there are no comparable implants on the PL. MSAC confirmed that the LATERA procedure should be categorised as type C, as the procedure was designed to be used in consulting rooms. MSAC noted that, if LATERA is listed on the PL, this may provide a financial incentive to perform the procedure in hospitals. However, MSAC agreed with ESC that clinical factors, not financial incentives, should be used to determine the appropriate setting for the procedure. It was also noted that type C procedures can be performed in hospital if clinically indicated and with a clinician’s certificate.

Overall, MSAC considered that LATERA offers patients a minimally invasive alternative to rhinoplasty that is likely to be non-inferior in both safety and effectiveness. There is a clinical need in a small subset of patients who are unable or unwilling to undergo rhinoplasty, or who have failed rhinoplasty. LATERA has inferior safety and probably superior effectiveness compared with conservative management. The financial impacts are modest. MSAC advised that utilisation of the item should be reviewed after 2 years.

## 4. Background

MSAC has not previously considered LATERA for the treatment of NAO due to LWI.

## 5. Prerequisites to implementation of any funding advice

The LATERA bioabsorbable nasal implant used in the proposed service is included on the Australian Register of Therapeutic Goods (ARTG) (Table 1).

**Table 1 Bioabsorbable nasal implant listed on the ARTG**

<b>Product name &amp; Sponsor</b>	<b>ARTG summary</b>	<b>Functional description</b>	<b>Intended purpose</b>
LATERA Absorbable Nasal Implant Stryker Australia Pty Ltd	<b>ARTG ID:</b> 389271 <b>Start date:</b> 31/05/2022 <b>Category:</b> Class III <b>GMDN:</b> 62157 Nasal implant, synthetic polymer, bioabsorbable	The LATERA Absorbable Nasal Implant is used as part of the LATERA Absorbable Nasal Implant System where the implant is inserted into the upper and/or lower lateral nasal cartilage using the delivery device to provide support to the cartilage by reinforcing the nasal wall. The implant is composed of a polymer. The implant is absorbed by the body over a period of approximately 18 months, during which the implant is replaced with tissue fibres that provide ongoing nasal wall support.	LATERA Absorbable Nasal Implant is indicated for supporting upper and lower lateral nasal cartilage
Nasal implant introducer Stryker Australia Pty Ltd	<b>ARTG ID:</b> 346524 <b>Start date:</b> 23/10/2020 <b>Category:</b> Class IIa <b>GMDN:</b> 62156 Nasal implant introducer	–	Intended to aid in the surgical implantation of the nasal implant.

Source: Table 1, pg 20-21 of MSAC 1719 ADAR

Abbreviations: ARTG ID= Australian Register of Therapeutic Goods identification; GMDN= Global Medical Device Nomenclature

## 6. Proposal for public funding

The ADAR proposed MBS item descriptors for the unilateral and bilateral insertion of bioabsorbable implants for NAO due to LWI, are presented below. Modifications suggested by the commentary are included in italics.

**Table 2 Proposed item descriptor for the insertion of one bioabsorbable nasal implant modified by the commentary**

Category 3 – THERAPEUTIC PROCEDURES
<p><b>MBS item XXXX</b></p> <p>Unilateral insertion of bioabsorbable implant for nasal airway obstruction due to lateral wall insufficiency confirmed by positive modified Cottle manoeuvre and the patient has a self-reported NOSE scale score of greater than <del>45</del> or equal to 55 if:</p> <p>(a) <i>the indicated surgery is:</i></p> <p>(i) <i>Provided by otolaryngologist and specialist plastic surgeons, who have undergone the Australian Medical Council (AMC) accredited training program</i></p> <p>(ii) <i>photographic and/or NOSE scale evidence demonstrating the clinical need for this service is documented in the patient notes.</i></p> <p>Fee: \$198.95 Benefit: 75% = \$149.20; 85% = \$169.10</p> <p><b>MBS item XXXX</b></p> <p>Bilateral insertion of bioabsorbable implant for nasal airway obstruction due to lateral wall insufficiency confirmed by positive modified Cottle manoeuvre and the patient has a self-reported NOSE scale score of greater than <del>45</del> or equal to 55) if:</p> <p>(a) <i>the indicated surgery is:</i></p> <p>(i) <i>Provided by otolaryngologist and specialist plastic surgeons, who have undergone the Australian Medical Council (AMC) accredited training program</i></p> <p>(ii) <i>Photographic and/or NOSE scale evidence demonstrating the clinical need for this service is documented in the patient notes</i></p> <p>(iii) <i>in patients contra-indicated to general anesthetic</i></p>

Source: Table 6, pg 44 of MSAC 1719 ADAR

Note: Commentary suggestions and additions proposed are shown in *italics* and deletions are in ~~strikethrough~~.

The ADAR proposed the MBS item descriptors be aligned with the existing MBS items for rhinoplasty procedures (MBS items 45632, 45641 and 45644). The proposed items require NAO due to LWI to be confirmed by a positive modified Cottle manoeuvre and the patient must have a self-reported NOSE scale score of greater than 45. For reference Table 3 displays NOSE score categorisations.

**Table 3 NOSE Score Severity Classification**

Severity class	NOSE score range
Mild	Range: 5-25
Moderate	Range: 30-50
Severe	Range: 55-75
Extreme	Range: 80-100

Reference: Stewart 2004<sup>2</sup>

The proposed MBS population is broader (i.e., NOSE scale score >45) than the patient population included in the clinical evidence (i.e., NOSE scale score ≥55). This creates uncertainty in the applicability of the clinical evidence and the treatment effect reported to the proposed MBS population. As the clinical evidence for LATERA only included patients with a NOSE scale score of 55 or greater, the commentary proposed amending the MBS item descriptors to increase the

<sup>2</sup> Stewart MG, Witsell DL, Smith TL et al. (2004) Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. *Otolaryngol Head Neck Surgery*.130(2):157-63.

NOSE threshold from >45 to ≥55. The applicant pre-ESC response acknowledged that no data exists for those with a NOSE score of 45-54, given the NOSE score eligibility in the trials was ≥55 and consider that it would be reasonable to update the MBS item descriptor to ≥55 should MSAC consider this more appropriate.

The commentary noted PASC advice that the service can be provided by ear nose throat (ENT) specialists and Specialist Plastic surgeons who undergo the Australian Medical Council (AMC) accredited training program. Therefore, the commentary proposed amending the item to restrict the service to 'otolaryngologists and specialist plastic surgeons who have undergone the AMC accredited training program'. The commentary also noted that MSAC may wish to consider limiting the total number of LATERA treatment(s) per patient.

The ADAR proposed an MBS item fee of \$198.95 for unilateral LATERA insertion based on expert opinion that the duration and complexity of the LATERA procedure is similar to a core biopsy (citing MBS items 50200 and 52180). The ADAR proposed an MBS fee of \$298.43 for bilateral LATERA insertion, based on the concept of the Multiple Operation Rule<sup>3</sup> (i.e., \$198.95\*1.5).

### **Other funding**

An application for listing the LATERA bioabsorbable implants, including the LATERA implantation device, on the Prostheses List (PL) has been submitted for consideration by the Prosthesis List Advisory Committee (PLAC) in September 2021. Therefore, the cost of the LATERA implants is currently an out-of-pocket (OOP) cost borne by the patients. The commentary noted that consumers may be concerned about the invasiveness and general anaesthesia requirement of rhinoplasty and while LATERA could provide patients with an alternative procedure to treat NAO due to LWI thereby increasing patient choice, the potential OOP costs may present a barrier to many consumers. It is also noted, that a successful PL listing and subsequent Private Health Insurance (PHI) coverage would result in the reimbursement of LATERA device costs in the hospital setting but not in the consulting room setting.

## **7. Population**

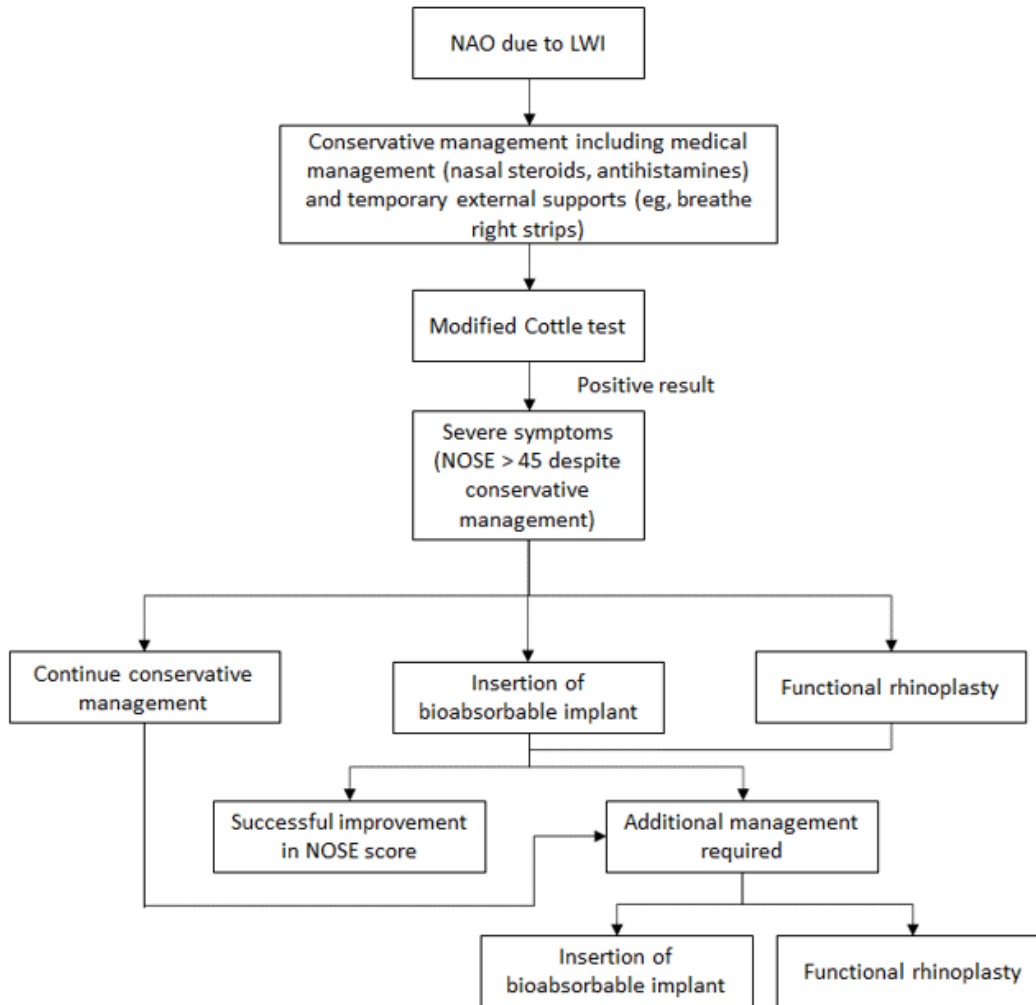
The proposed population, NAO due to LWI, is a subgroup of patients with NAO. This subgroup is confirmed by a positive modified Cottle manoeuvre and a self-reported NOSE scale score of greater than 45.

The ADAR stated that the insertion of LATERA to treat NAO due to LWI would be used in the proposed population as an alternative to the comparators (i.e., rhinoplasty or conservative management). LATERA is also a nexus to definitive surgical treatment (i.e., revision surgery). The proposed management algorithm for patients with NAO due to LWI, including insertion of LATERA as a treatment option, is shown below (Figure 1).

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<sup>3</sup> [MBS Note TN.8.2 Multiple Operation Rule](#)

Figure 1 Proposed management algorithm with the introduction of the proposed service



Source: Figure 12 p42 of MSAC 1719 ADAR

## 8. Comparator

The comparators are functional rhinoplasty (primary) and conservative management (secondary).

### Functional rhinoplasty (primary comparator)

Functional rhinoplasty is the gold standard treatment for NAO due to LWI. Functional rhinoplasty involves treatment of the internal valve (reflecting the point of maximum narrowing of the internal nasal airway) and the external valve, with the external valve collapse reflecting a dynamic process. The components of the internal valve, or point of maximum narrowing of the nasal airway, include the anterior inferior turbinate and the septum as well as the relationship of the upper lateral cartilage and the septum. These three components are examined and treated as necessary including septoplasty to correct a deviated septum, turbinate reduction and functional rhinoplasty involving grafts.

The main functional rhinoplasty strategies reportedly used in the management of NAO due to dynamic collapse or LWI, consistent with the proposed population, include the following:

- Alar batten grafts
- Butterfly grafts



- Lateral crural strut grafts
- Lateral nasal wall suspension (suture technique).

Functional rhinoplasty is often performed with concomitant procedures such as septoplasty, septorhinoplasty, turbinate reduction, and graft harvesting from the septum when addressing multiple aetiologies, however the comparator for this intervention is functional rhinoplasty alone, without adjuncts.

Table 4 describes the three MBS item numbers for the provision of functional rhinoplasty for the treatment of NAO.

In brief, MBS item 45632 is for partial rhinoplasty involving the correction of cartilage only (i.e., correction of one or both lateral cartilages, one or both alar cartilages or one or both lateral cartilages and alar cartilage). The other two rhinoplasty MBS items are for total rhinoplasty that involves correction of all bony and cartilaginous elements of the external nose. MBS item 45641 is for total rhinoplasty with or without autogenous cartilage or bone graft from a local site (nose) and MBS item 45644 is for total rhinoplasty with autogenous bone or cartilage graft obtained from distant donor site. MBS items 45632, 45641 and 45644 for rhinoplasty were introduced on the MBS from 01 December 1991.

### **Conservative management (secondary comparator)**

Conservative management was included in the ratified PICO as the comparator for the population that meets eligibility for rhinoplasty, but who elect not to have the procedure or have a contraindication to the procedure. Conservative management includes medical management (nasal steroids, antihistamines) and temporary external supports (e.g., Breathe Right strips).

**Table 4 MBS items claimed for the comparator services**

Category 3 – THERAPEUTIC PROCEDURES
<p><b>MBS item 45632</b>  Rhinoplasty, partial, involving correction of one or both lateral cartilages, one or both alar cartilages or one or both lateral cartilages and alar cartilages, if:  (a) the indication for surgery is:  (i) airway obstruction and the patient has a self-reported NOSE Scale score of greater than 45; or  (ii) significant acquired, congenital or developmental deformity; and  (b) photographic and/or NOSE Scale evidence demonstrating the clinical need for this service is documented in the patient notes  Multiple Operation Rule  (Anaes.)  Fee: \$541.20 Benefit: 75% = \$405.90 85% = \$460.05</p>
<p><b>MBS item 45641</b>  Rhinoplasty, total, including correction of all bony and cartilaginous elements of the external nose, with or without autogenous cartilage or bone graft from a local site (nasal), if:  (a) the indication for surgery is:  (i) airway obstruction and the patient has a self-reported NOSE Scale score of greater than 45; or  (ii) significant acquired, congenital or developmental deformity; and  (b) photographic and/or NOSE Scale evidence demonstrating the clinical need for this service is documented in the patient notes  Multiple Operation Rule  (Anaes.)  Fee: \$1,126.95 Benefit: 75% = \$845.25</p>
<p><b>MBS item 45644</b>  Rhinoplasty, total, including correction of all bony and cartilaginous elements of the external nose involving autogenous bone or cartilage graft obtained from distant donor site, including obtaining of graft, if:  (a) the indication for surgery is:  (i) airway obstruction and the patient has a self-reported NOSE Scale score of greater than 45; or  (ii) significant acquired, congenital or developmental deformity; and  (b) photographic and/or NOSE Scale evidence demonstrating the clinical need for this service is documented in the patient notes  Multiple Operation Rule  (Anaes.) (Assist.)  Fee: \$1,352.55 Benefit: 75% = \$1,014.45</p>

Source: MBS online: <http://www.mbsonline.gov.au/internet/mbsonline/publishing.nsf/Content/Home>

## 9. Summary of public consultation input

Consultation input was received from four individual health professionals, including two plastic surgeons and two Ear, Nose and Throat (ENT) surgeons. The input was mostly supportive of public funding for the service and agreed there is a clinical need for a minimally invasive procedure for patients with NAO due to LWI.

The health professionals stated that the main benefit of the proposed service is a simple, quick, office procedure that provides structural support of the lateral wall and compared to rhinoplasty, the service is less invasive, does not require grafts or manipulation of bones/cartilages and would have a quicker post-procedural recovery time. Feedback also stated that a further benefit to the proposed service is a reduced requirement for surgery. However, one respondent did express that longevity is a concern and that the natural history of absorbable implants is that the effect wears off with time.

The health professionals largely agreed with the proposed population, intervention, and the primary comparator (functional rhinoplasty) in the application form and PICO Confirmation. Respondents also considered that conservative management could also be an appropriate comparator for patients that meet eligibility for a rhinoplasty but who are contraindicated or choose not to have the procedure. Input largely agreed with the proposed service descriptor however, one respondent considered that a positive Cottle manoeuvre is a fairly non-discriminatory test, because in most people it is positive, and that if it is negative, the obstruction is likely static and will not be affected by the device.

Three respondents agreed with the clinical claim for LATERA versus functional rhinoplasty and conservative management. However, one respondent disagreed with the clinical claim and stated that there are no comparisons versus well performed rhinoplasty and that rhinoplasty does a lot more than the device can do. The respondent further stated that overall, for select cases, the proposed service may work. The respondent also noted that the implant may be very useful in certain circumstances of valve collapse with no other issues but stated that the effect is unlikely to be permanent and that longer term studies are needed for this. The respondent also considered that Specialist Plastic Surgeons do a large number of rhinoplasties in Australia, and disagreed with using rhinologists as the reference group. The feedback further stated that Rhinoplasty surgeons would be the group that carry out the most rhinoplasties and consists of Specialist Otolaryngologist Head and Neck surgeons and Specialist Plastic surgeons.

## 10. Characteristics of the evidence base

### LATERA versus functional rhinoplasty

No comparative evidence for LATERA versus functional rhinoplasty (when used alone i.e., without any adjunct procedures) was identified. Therefore, the comparison of LATERA versus rhinoplasty was informed by a naïve indirect comparison of LATERA (alone) versus rhinoplasty (alone), based on three LATERA studies (LATERA-RCT<sup>4</sup>, LATERA-OFFICE<sup>5</sup>, Trial 4350-001<sup>6</sup>) and six rhinoplasty studies (Most 2006<sup>7</sup>, Tan 2012<sup>8</sup>, Palesy 2015<sup>9</sup>, Rao 2016<sup>10</sup>, Taha 2021<sup>11</sup>, Sainio 2022<sup>12</sup>).

Table 5 summarises the key features of the evidence for LATERA versus functional rhinoplasty.

The LATERA-RCT compared LATERA versus sham, therefore the LATERA arm of the LATERA-RCT was used only in the naïve comparison. As there was no direct comparative evidence for LATERA versus functional rhinoplasty, the evidence supporting the ADAR's claims is comprised of single

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<sup>4</sup> [NCT03400787](#) - Latera Randomized Controlled Trial (RCT) - Latera® Absorbable Nasal Implant vs. Sham Control for Lateral Nasal Valve Collapse

<sup>5</sup> [NCT02964312](#) - Spirox Latera™ Implant Support of Lateral Nasal Wall Cartilage (LATERAL-OFFICE) Study

<sup>6</sup> [NCT02188589](#) - Evaluation of an Absorbable Implant for the Treatment of Nasal Valve Collapse

<sup>7</sup> Most SP (2006) Analysis of outcomes after functional rhinoplasty using a disease-specific quality-of-life instrument. *Archives of Facial Plastic Surgery*. 8(5): 306-309.

<sup>8</sup> Tan S & Rotenberg B (2012) Functional outcomes after lateral crural J-flap repair of external nasal valve collapse. *Annals of Otolaryngology, Rhinology and Laryngology*. 121(1): 16-20.

<sup>9</sup> Palesy T, et al. (2015) Airflow and patient-perceived improvement following rhinoplastic correction of external nasal valve dysfunction. *JAMA Facial Plastic Surgery*. 17(2): 131-136.

<sup>10</sup> Rao N & Toriumi D (2016) Three-dimensional analysis of rhinoplasty with composite grafts. *Otolaryngology - Head and Neck Surgery* (United States) 155: P177.

<sup>11</sup> Taha MA, et al. (2021) Costal Cartilage Lateral Crural Strut Graft for Correction of External Nasal Valve Dysfunction in Primary and Revision Rhinoplasty. *Ear, Nose & Throat Journal*. 0(0).

<sup>12</sup> Sainio S, et al. (2022) Effect of alar nasal valve stent on nasal breathing. *American journal of otolaryngology*. 43(4):103473. 3

arm studies with historical controls only, with significant differences in populations between the intervention and control groups.

The LATERA studies included some patients who had received prior nasal surgery. In the LATERA-RCT, 59% of participants had received prior nasal surgery. Trial 4350-001 reported previous nasal surgeries include septoplasty, conchotomy, septorhinoplasty, functional rhinoplasty, infundibulotomy, turbinoplasty, and minor outer skin resection of 66% (19/30). No subgroup analysis of patients who had or had not received prior nasal surgery was presented.

A comparison of LATERA and rhinoplasty, when used with adjunct procedures, was presented based on a retrospective non-randomised comparative cohort study (Olson 2021<sup>13</sup>). In Olson 2021, LATERA was performed in combination with septoplasty and turbinate submucous reduction (SMR) and rhinoplasty was performed in combination with lateral crural strut graft, bilateral spreader grafts or unilateral spreaders graft. This comparison is likely confounded by the adjunct procedures, so it is difficult to distinguish which intervention is causing the effect, although Olson 2021 is presented in the ADAR for completeness, it is not used in the meta-analysis or economic model.

**Table 5 Key features of the included evidence, LATERA vs. functional rhinoplasty**

References	N	Design/duration	Risk of bias	Patient population*	Outcome(s)	Use in modelled evaluation
<b>LATERA vs. functional rhinoplasty</b>						
LATERA-RCT	137 #	RCT, sham control, MC, SB; 3 months	Moderate <sup>a</sup>	Severe to extreme NOSE score	NOSE score, AEs, VAS	Response
LATERA-OFFICE	166	Single arm, prospective; 6 months	Moderate <sup>a</sup>	Severe to extreme NOSE score	NOSE score, AEs, VAS, ESS	Not used
Trial 4350-001	30	Prospective, MC, single arm, first-in-man; 24 months	Moderate <sup>a</sup>	Severe to extreme NOSE score	NOSE score, AEs, VAS	Not used
Most 2006	41(14) <sup>c</sup>	Prospective case series; 338 days <sup>f</sup>	Moderate <sup>a</sup>	Moderate to severe NOSE score	NOSE score	Not used
Palesy 2015	19	Prospective case series; 6 months	Moderate <sup>a</sup>	Moderate to extreme NOSE score	NOSE score, VAS	Not used
Rao 2016	50	Poster; Retrospective chart review; 13.6 months	High <sup>a</sup>	Severe NOSE score	NOSE score	Not used
Taha 2021	26	Prospective cohort study; 14.58 months	Moderate <sup>a</sup>	Moderate to extreme NOSE score	NOSE score	Not used
Tan 2012	15	Prospective case series; 13 months	Moderate <sup>a</sup>	Extreme NOSE score	NOSE score	Not used
Sainio 2022	20	Prospective, observational study; 12 months	Moderate <sup>a</sup>	Severe NOSE score	NOSE score	Not used

<sup>13</sup> Olson MD & Barrera JE (2021) A comparison of an absorbable nasal implant versus functional rhinoplasty for nasal obstruction. *American Journal of Otolaryngology - Head and Neck Medicine and Surgery*. 42(6).

Naïve IC	202	Included LATERA-RCT; LATERA-OFFICE; Trial 4350-001 assessed change in NOSE scores at 1 month	NOSE score
	223	Included LATERA-RCT; LATERA-OFFICE; Trial 4350-001 vs. Most 2006, Sainio 2022 assessed change in NOSE scores at 3 months	
	227	Included LATERA-RCT; LATERA-OFFICE; Trial 4350-001 vs. Palesy 2015, Sainio 2022 at 6 months	
	294	Included LATERA-RCT; LATERA-OFFICE; Trial 4350-001 vs. Taha 2021, Tan 2012, Rao 2016, Most 2006, Sainio 2022 at 12 months	
	143	Included LATERA-RCT; LATERA-OFFICE; Trial 4350-001 at 18 months	
	133	Included LATERA-RCT; LATERA-OFFICE; Trial 4350-001 at 24 months	
	NS	Included LATERA-RCT and LATERA-OFFICE at 24 months (last FU) vs. Most 2006, Palesy 2015, Taha 2021, Tan 2012, Rao 2016, Sainio 2022	

**Comparison of LATERA vs rhinoplasty with adjunct treatments**

Olson 2021	90	Prospective, observational study; 146.6 days	<i>High</i> <sup>b</sup>	Moderate to extreme NOSE score	NOSE score	Not used
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Source: Commentary Table 4, pg 74 of MSAC 1719 ADAR+inline commentary  
 Abbreviations: AE= adverse event; FU= follow up; IC= Indirect Comparison; NOSE= Nasal Obstruction Symptoms Evaluation; NS= not stated; PP= per protocol; RCT= randomised controlled trial; VAS= Visual Analogue Scale  
 Note:  
 a Risk of bias assessment was based on the National Heart, Lung, and Blood (NHLBI) Study Quality Assessment Tools for RCTs or before and after studies.  
 b Risk of bias assessment was based on the NHLBI Study Quality Assessment Tools for Observational Cohort and Cross-Sectional Studies.  
 c There were n = 41 patients in the total cohort however only n = 14 of these were applicable to the MSAC ADAR 1719 population: Spreader Grafting Without Turbinate Reduction (n = 7) and External Valve Suspension (n = 7)  
 d 338 days for spreader grafting without turbinate reduction; 110 days for external valve suspension  
 \*NOSE patients are categorised as follows: Mild (range, 5-25), Moderate (range, 30-50), Severe (range, 55-75), Extreme (range, 80-100) nasal obstruction. [Response: % with at least 1 NOSE class improvement; or ≥20% reduction in NOSE score from baseline]  
 Italics represent correction during commentary. LATERA-OFFICE and Trial 4350-001 could be moderate not low risk of bias  
 # LATERA-RCT intervention arm only was analysed in the meta-analysis. At 6 months the arm contained 65 patients, at 12 months 5825 patients and at 24 months 43 patients

**LATERA versus conservative management**

The comparison of LATERA versus conservative management was informed by a direct comparison informed by one randomised clinical trial (RCT; the LATERA-RCT), where LATERA was compared to sham (a proxy for conservative management).

In addition, single arm studies (LATERA OFFICE, LATER-OR, Trial 4350-001 and Saadat 2018<sup>14</sup>), were presented as additional evidence to support the use of LATERA alone or in combination with adjunct procedures, and to provide longer-term evidence for the safety and effectiveness of LATERA (up to 24 months).

Table 6 summarises the key features of the evidence for LATERA versus conservative management (sham surgery as proxy).

In the LATERA-RCT, 137 patients underwent either the LATERA (n=71) or sham procedure (n=66). At 3 months, patients in the sham arm were able to cross-over and undergo the LATERA procedure (cross-over arm). The sham procedure was identical to the LATERA procedure, except the implant was not deployed (i.e., patients in sham arm had a cannula inserted into the nasal

<sup>14</sup> Saadat, D., et al. (2018) Less invasive procedure for the treatment of nasal obstruction: impact on daytime drowsiness. *Sleep* 41: A208.

lateral wall). The primary outcome was the self-reported response NOSE score. The key inclusion criteria were:

- NOSE scores  $\geq 55$  (severe, extreme)
- failure to benefit from at least four weeks of conservative management (e.g., nasal steroids or antihistamines), as evidenced by lack of efficacy or tolerability.

There were no significant baseline and demographic differences between the treatment and sham arms except for a slightly lower VAS score in the sham arm (LATERA: mean (SD) 76.6 (12.9) vs sham: 71.2 (15.8);  $p=0.038$ ). The baseline NOSE scores were balanced between groups (LATERA mean (SD) (77.4 (13.1) vs sham: 77.7 (15.1);  $p=0.888$ ), reflecting a population of people with persistent severe to extreme nasal obstruction.

**Table 6 Key features of the included evidence, LATERA vs. conservative management**

References	N	Design/duration	Risk of bias	Patient population*	Outcome(s)	Use in modelled evaluation
<b>LATERA vs. Sham</b>						
LATERA-RCT	137	RCT, sham control, MC, SB; 3 months	<i>Moderate</i> <sup>a</sup>	Severe to extreme NOSE score	NOSE score, AEs, VAS	Response <sup>b</sup>
Meta-analysis	127 <sup>c</sup>	Included LATERA-RCT assessed change from baseline in NOSE score – PP at 1 and 3 months				NOSE score
<b>Additional LATERA evidence</b>						
LATERA-OR <sup>d</sup>	113	Single arm, prospective; 24 months	<i>Moderate</i> <sup>a</sup>	Severe to extreme NOSE score	NOSE score, AEs, VAS	Not used
Saadat 2018	188	Conference abstract; Single arm, prospective; 3 months	<i>High</i> <sup>a</sup>	Severe to extreme NOSE score	NOSE Score and ESS	Not used

Source: Commentary Table 9, pg 76 of MSAC 1719 ADAR+inline commentary. Italics represent correction during commentary.

Abbreviations: AE= adverse event; FU= follow up; IC= Indirect Comparison; NOSE= Nasal Obstruction Symptoms Evaluation; NS= not stated; PP= per protocol; RCT=randomised controlled trial; VAS= Visual Analogue Scale

Note:

a Risk of bias assessment was based on the National Heart, Lung, and Blood (NHLBI) Study Quality Assessment Tools for RCTs or before and after studies.

b NOSE score response

c Per protocol assessed at (1 month and) 3 months

d LATERA-OR investigated LATERA with adjunct procedures (i.e. septoplasty and inferior turbinate reduction) and therefore not included in the naive IC

\*NOSE patients are categorised as follows: Mild (range, 5-25), Moderate (range, 30-50), Severe (range, 55-75), Extreme (range, 80-100) nasal obstruction. [Response: % with at least 1 NOSE class improvement; or  $\geq 20\%$  reduction in NOSE score from baseline]

# LATERA-RCT intervention arm only was analysed in the meta-analysis. At 6 months the arm contained 65 patients, at 12 months 58 patients and at 24 months 43 patients

Italics represent correction during

The commentary agreed with the ADAR that the LATERA-RCT had a moderate risk of bias, noting the LATERA-RCT outcomes were analysed on a per protocol basis, not intention-to-treat. The commentary noted that the additional LATERA studies (LATERA-OFFICE, LATERA-OR, Trial 4350-001 and Saadat 2018) were open label (unblinded) studies that are prone to selection bias and confounding (when LATERA performed with adjunct procedures) and all of the effectiveness outcomes were subjective. Therefore, the commentary considered the risk of bias was moderate to high not low to moderate for these studies. The commentary agreed with the ADAR that all single arm studies of functional rhinoplasty were at a moderate risk of bias, except Rao 2016

(high risk), with potential for selection bias and confounding issues that are prevalent in single arm studies due to lack of randomisation.

Areas of uncertainty in the evidence for both LATERA vs functional rhinoplasty and conservative management are:

- The patients enrolled in the trials were narrower than those for whom listing is sought.
- The LATERA-RCT mean NOSE score at baseline is 77. The study eligibility criteria is NOSE  $\geq 55$  (NOSE score severe: range 55-75) although the requested MBS item descriptor NOSE  $>45$  which is lower than the study inclusion criteria (see Table 7).
- There is no evidence for LATERA for patients with a NOSE score of 45-55 nasal obstruction, consistent with the proposed MBS item descriptor (see Table 7).
- The inclusion of high severity patients in the LATERA studies would likely have impacted the effectiveness results as patients with more extreme severity generally have a larger treatment effect.

**Table 7 NOSE score of proposed MBS item, study eligibility and MSAC 1719 ADAR evidence**

Outcome	ADAR Proposed MBS item descriptor based on MBS item descriptor 45631;45641;45644	LATERA-RCT NCT03400787 study eligibility	LATERA-RCT NCT03400787 Baseline NOSE score, mean (SD); (Range)	LATERA-RCT NCT03400787 Mean (95% CI)
NOSE Score	$>45$	$\geq 55$	77.4 (13.4) (Range: 55-100) <sup>a</sup>	77.4 (75.14, 79.66) <sup>b</sup>

Source: Commentary Table 16, pg 89 of MSAC 1719 ADAR+inline commentary

a Reference: LATERA RCT Final Clinical Study Report p 53 to 57

b Calculated post hoc by the commentary

## 11. Comparative safety

### LATERA versus functional rhinoplasty

Due to limited safety data from the included rhinoplasty studies, the ADAR did not present a naïve indirect comparison for safety. The ADAR discussed safety data from the LATERA RCT, LATERA office and Trial 4350-001 studies and reported that implant retrieval/ extrusion/ migration, foreign body sensation, implant palpable/bumps on nose followed by discomfort and pain were the most commonly reported adverse events up to 24 months as shown in Table 8 and Table 9

Of the safety data available from the functional rhinoplasty studies, Tan 2012 and Most 2006 reported no complications post-surgery. Sainio 2022 reported one infection, one abscess and one re-surgery using an alar stent 13 months later. Palesy 2015, Taha 2021 and Rao 2016 did not report safety results.

Olson 2021, which compared LATERA vs rhinoplasty with adjunct treatments, reported no extrusions or other implant-related complications for either intervention.

Regarding revision rates, the ADAR suggested similar rates of revision could be expected due to LATERA and rhinoplasty achieving similar symptom control. However, the commentary suggested the revision rates could be from 5% for functional rhinoplasty (Sainio 2022) and up to ~10% based on the reported rates of implant retrieval/extrusion/migration in the LATERA-RCT study. Longer-term studies ( $> 24$  months) are needed to determine the longevity of the response to LATERA and if revision or subsequent intervention may be required.

In the absence of further data, the ADAR concluded that the comparative safety of LATERA is at least non-inferior to functional rhinoplasty when performed without adjunct procedures.

### LATERA versus conservative management

The LATERA-RCT, which compared LATERA versus sham, reported 10 serious adverse events in 10 participants over the duration of the study (24 months) but stated none were related to the device or study procedure. Device and procedure related adverse events reported in the LATERA-RCT study are summarised in Table 8. One cross over participant had bilateral nasal repair (0.9%), no other revisions were reported. The most commonly occurring non-serious adverse events included device migration/extrusion/retrieval (9%), pain or discomfort (4.5%), bumps on the nose (3.6%) and foreign body sensation (3.6%). The majority of device migration /extrusion events were mild in severity (80%) with remaining events moderate (20%), and the majority occurred within 10 days of the procedure (50%).

**Table 8 Summary of LATERA-RCT device-/procedure-related adverse events over 24 months**

Adverse events	LATERA (N=71)		Crossover (N=40)		All participants (N=111)	
	Event, n	Participants, n (%)	Event, n	Participants, n (%)	Event, n	Participants, n (%)
Device migration/extrusion/retrieval	7	7 (9.9)	3	3 (7.5)	10	10 (9.0) <sup>b</sup>
Pain or discomfort	3	3 (4.2)	2	2 (5.0)	5	5 (4.5)
Bumps on nose	3	3 (4.2)	1	1 (2.5)	4	4 (3.6)
Foreign body sensation	3	3 (4.2)	1	1 (2.5)	4	4 (3.6)
Headache	2	2 (2.8)	0	0	2	2 (1.8)
Inflammation	2	2 (2.8)	1	1 (2.5)	3	3 (2.7)
Pin prick/pinching sensation	2	2 (2.8)	0	0	2	2 (1.8)
Vasovagal response	2	2 (2.8)	0	0	2	2 (1.8)
Skin puncture with device delivery needle (not implant)	1	1 (1.4)	0	0	1	1 (0.9)
Bilateral nasal repair	0	0	1	1 (2.5)	1	1 (0.9)
<b>Total</b>	<b>25</b>	<b>18 (25.4)<sup>a</sup></b>	<b>9</b>	<b>8 (20)<sup>a</sup></b>	<b>34</b>	<b>26 (23.4)<sup>a</sup></b>

Source: Commentary Table 10, pg 118 of MSAC ADAR 1719+inline commentary

Notes:

a The total for participants is not the sum of the rows because one participant may have experienced more than one event.

b Note, based on data in Appendix 12.2, it was found that these 10 events were experienced by nine patients, because one patient experienced two of these events. Thus the proportion of patients experiencing at least one device migration/extrusion/retrieval was 8.1% (9/111).

Based on the safety data from the other LATERA studies (Table 9) there were no serious adverse events related to the procedure or implant. All the non-serious adverse events occurring over 24 months were mild to moderate in severity and resolved without clinical sequelae or were ongoing but stable at study completion. The most commonly occurring adverse events included implant retrieval/extrusion/migration (range, 3.1% to 4.7%), foreign body sensation, implant palpable/bumps on nose, infection and skin irritation/inflammation.



**Table 9 Summary of Device-/Procedure-related AEs in LATERA studies**

Adverse events, n (%)	LATERA-OFFICE (N=166)		LATERA-OR (N=113)		Trial 4350-001 (N=30)
	6 months	24 months	6 months	24 months	6 months
<b>Number of implants</b>	<b>319</b>		<b>224</b>		<b>56</b>
<b>Follow-up</b>	<b>6 months</b>	<b>24 months</b>	<b>6 months</b>	<b>24 months</b>	<b>6 months</b>
Implant retrieval/extrusion/migration	14/319 (4.4)	15/319 (4.7)	7/224 (3.1)	7/224 (3.1)	3/56 (5.4)
Foreign body sensation	6/319 (1.9)	6/319 (1.9)	0	0	0
Implant palpable/bumps on nose	5/319 (1.6)	5/319 (1.6)	1/224 (0.4)	2/224 (0.9)	0
Infection	5/319 (1.6)	5/319 (1.6)	2/224 (0.9)	2/224 (0.9)	0
Skin irritation/inflammation	1/319 (0.3)	1/319 (0.3)	1/224 (0.4)	1/224 (0.4)	1/56 (1.8)
Discomfort/pain	2/319 (0.6)	4/319 (1.3)	0	0	0
Mucous production/postnasal drip	2/319 (0.6)	2/319 (0.6)	0	0	0
Haematoma	1/319 (0.3)	1/319 (0.3)	0	0	1/56 (1.8)
Loss of smell/taste	1/319 (0.3)	1/319 (0.3)	0	0	0
Unintended perforation of the skin	0	1/319 (0.3)	0	0	0
Implant bent/fractured	0	0	1/224 (0.4)	1	0
Headache	NR	NR	NR	NR	NR
Pin pricking/pinching sensation	NR	NR	NR	NR	NR
Vasovagal response	NR	NR	NR	NR	NR
Skin puncture with device delivery needle (not implant)	NR	NR	NR	NR	NR
Bilateral nasal repair	NR	NR	NR	NR	NR
<b>Total</b>	<b>37/319 (11.6)</b>	<b>41/319 (12.9)</b>	<b>12/224 (5.4)</b>	<b>13/224 (5.8)</b>	<b>5/56 (8.9)</b>

Source: Commentary Table 11, pg 119 of MSAC 1719 ADAR+inline commentary  
Abbreviations: NR= not reported

The ADAR concluded that the LATERA adverse events were typically localised with mild to moderate intensity and transient in nature. However, owing to lack of data the ADAR concluded that the comparative safety of LATERA is inferior to conservative management.

### Extended harms assessment

A scan of the literature by the commentary identified Wakefield 2020<sup>15</sup> which reviewed the FDA sponsored database, 'manufacturer and user facility device experience' (MAUDE) between 2016 and 2019 for LATERA adverse events. The authors found cases of infection, were second to implant removal. The authors further mentioned the likelihood of under reporting on outcomes associated with absorbable implants.

<sup>15</sup> Wakefield C, Eggerstedt M, Tajudeen B, et al. (2020) Adverse Events Associated with Absorbable Implants for the Nasal Valve: A Review of the Manufacturer and User Facility Device Experience Database. *Facial Plastic Surgery & Aesthetic Medicine* 22(5)

## 12. Comparative effectiveness

### LATERA versus functional rhinoplasty

The ADAR presented a series of naïve indirect comparisons between LATERA and rhinoplasty for the NOSE score outcome at months 1, 3, 6, 12, 18, 24 and baseline to last follow up (FU) in the severe and extreme population for LATERA and a broader, moderate to extreme population for rhinoplasty (see Table 10 and Figure 2).

The pooled mean change in NOSE score was -43.68,  $p=0.76$  for LATERA versus -38.58,  $p=0.08$  for functional rhinoplasty at 12 months. The pooled mean change in NOSE scores was -45.59,  $p=0.76$  for LATERA versus -36.74,  $p=0.05$  for rhinoplasty at 24 months (last follow up).

Given there was no common reference arm (i.e., placebo or active treatment) there is a high potential for confounding due to differences in aetiological factors across single arms of different studies.

The commentary noted there is substantial heterogeneity<sup>16</sup> which approaches significance in the LATERA studies at 1 month and in the pooled studies of functional rhinoplasty therefore demonstrating inconsistency across studies. Regarding lost to follow up, at 24 months in LATERA-RCT there was 60% lost to follow up and the small number of patients increases uncertainty. LATERA-RCT intervention arm only was analysed in the meta-analysis (i.e. the cross-over arm from the LATERA-RCT was not included). The LATERA arm contained 71, 65, 58 and 43 patients at 0, 6, 12 and 24 months respectively, although it is noted that the lost to follow up included patients that crossed over to undergo the LATERA procedure. There was no formal statistical testing presented for effect sizes such as Cohens  $d$  small ( $d = 0.2$ ), medium ( $d = 0.5$ ), and large ( $d = 0.8$ ) for standard mean difference (SMD).

The rhinoplasty studies did not provide standard deviation (SD) therefore conversion to standard error (SE) and 95% confidence interval (CI) could not be undertaken. Sensitivity analysis for LATERA OFFICE and Trial 4350-001 vs. Taha 2021-primary, Taha 2021-revision at 12 months could be conducted with and without Palesy 2015 (6 months). The CI around the point estimate in Taha 2021-primary appears to be more precise than the LATERA studies. Of note, the CI for LATERA-OFFICE, Trial 4350-001, Taha 2021-primary and Taha 2021 revision appear to all crossover demonstrating non-inferiority in the current analysis (-43.68 (-47.59, -39.78),  $I^2=0\%$ ,  $p=0.76$  vs -38.58 (-49.48, -27.68),  $I^2=67\%$ ,  $p=0.08$  at 12 months).

Additionally, the ADAR also presented the findings of Olson 2021 (a retrospective study that compared LATERA+adjunct procedures versus rhinoplasty+adjunct procedures) which reported the change in NOSE scores was similar for both groups (LATERA: -40.5 vs functional rhinoplasty -40.3). The ADAR stated this confirmed the non-inferiority of LATERA versus rhinoplasty when used with adjunct septoplasty and inferior turbinate SMR procedures.

The commentary highlighted that there is limited applicability of the three single-arm studies on LATERA due to the inconsistency between the presented evidence (i.e. patients in the LATERA studies had a NOSE score of  $\geq 55$ ) and the ADAR proposed MBS item descriptor (NOSE score of

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<sup>16</sup> Thresholds for the interpretation of  $I^2$  can be misleading, since the importance of inconsistency depends on several factors. A rough guide to interpretation is as follows:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity\*;
- 50% to 90%: may represent substantial heterogeneity\*;
- 75% to 100%: considerable heterogeneity\*.

\*The importance of the observed value of  $I^2$  depends on (i) magnitude and direction of effects and (ii) strength of evidence for heterogeneity (e.g. P value from the chi-squared test, or a confidence interval for  $I^2$ ). [Reference: Cochrane 9.5.2 Identifying and measuring heterogeneity [https://handbook-5-1.cochrane.org/chapter\\_9/9\\_5\\_2\\_identifying\\_and\\_measuring\\_heterogeneity.htm](https://handbook-5-1.cochrane.org/chapter_9/9_5_2_identifying_and_measuring_heterogeneity.htm)]

>45). Therefore, the commentary concluded that the evidence presented in the ADAR did not clearly demonstrate a benefit for LATERA for all patients who would be eligible for LATERA in the proposed MBS item descriptor (i.e., moderate population NOSE score >45-55). Further, the commentary highlighted that the results of the naïve indirect comparison should be interpreted with caution, given differences in the trial populations and differences in the timing of assessments, and therefore the claim of non-inferior effectiveness for LATERA compared to functional rhinoplasty is of low certainty.

Table 10 Naïve indirect comparison of change in NOSE scores at 1 to 24 months follow-up

FU post procedure, months	LATERA NOSE score, mean (SD)				Functional rhinoplasty NOSE score, mean (SD)							
	Trial ID	Baseline	Post procedure	Change	Trial ID	Baseline	Post operation	Change				
1	LATERA-RCT (N=69)	76.2 (13.1)	40 (21.9)	-36.2 (25.8)	NR	NR	NR	NR				
	LATERA-OFFICE (N=103)	77.8 (13.5) <sup>b</sup>	37.1 (NR) <sup>c</sup>	-40.7 (24.5)								
	Trial 4350-001 (N=30)	76.7 (14.8) <sup>b</sup>	27 (NR) <sup>c</sup>	-49.7 (25.6)								
	MA (95% CI)	<b>-41.54 (-48.87, -34.21), I<sup>2</sup>=66%, p=0.06</b>										
3	LATERA-RCT (N=70)	76.2 (13.3)	40 (21.9)	-41.7 (24.2)	Most 2006 – external valve suspension (N=7)	66.3 (7.3)	20 (20.1)	<b>-46.3 (NR); p&lt;0.01</b>				
	LATERA-OFFICE (N=100)	77.8 (13.5) <sup>b</sup>	33.9 (NR) <sup>c</sup>	-43.9 (25.7)								
	Trial 4350-001 (N=29)	76.7 (14.8) <sup>b</sup>	28.3 (NR) <sup>c</sup>	-48.4 (27.8)	Sainio 2022 (N=17)	70.0 (range: 30, 95)	39.4 (range: 5, 80)	<b>-30.6 (NR)</b>				
	MA (95% CI)	<b>-43.59 (-47.12, -40.07), I<sup>2</sup>=0%, p=0.52</b>							MA	NE		
6	LATERA-RCT (N=65)	76.2 (13.1)	28.9 (22.5)	-47.3 (24)	Palesy 2015 (N=19)	60.53 (21.9)	30 (22.24)	<b>-30.53 (26.14); p&lt;0.01</b>				
	LATERA-OFFICE (N=95)	77.8 (13.5) <sup>b</sup>	32.6 (NR) <sup>c</sup>	-45.2 (25.3)								
	Trial 4350-001 (N=30)	76.7 (14.8) <sup>b</sup>	33.4 (NR) <sup>c</sup>	-43.3 (31.3)	Sainio 2022 (N=18)	70.3 (range: 30, 95)	41.7 (range: 10, 90)	<b>-28.6 (NR)</b>				
	MA (95% CI)	<b>-45.81 (-49.44, -42.18), I<sup>2</sup>=0%, p=0.78</b>							MA	NE		
12	LATERA-RCT (N=58)	76.8 (13)	31.8 (23.4)	-45 (25.2)	Taha 2021 – primary (N=10)	80.1 (5.79)	37.3 (NR)	-42.8 (6.49); NR				
	LATERA-OFFICE (N=90)	77.8 (13.5) <sup>b</sup>	34.2 (NR) <sup>c</sup>	-43.6 (26.4)	Taha 2021 – revision (N=16)	70 (19.05)	38.75 (NR)	-31.25 (25.33); NR				
	Trial 4350-001 (N=30)	76.7 (14.8) <sup>b</sup>	36.5 (NR) <sup>c</sup>	-40.2 (30.9)	Tan 2012 (N=15) <sup>a</sup>	86.5 (8)	26.5 (11.5)	-60 (NR); p<0.001				
	MA (95% CI)	<b>-43.68 (-47.59, -39.78), I<sup>2</sup>=0%, p=0.76</b>							Rao 2016 (N=50) <sup>a</sup>	55 (NR)	23 (NR)	-32 (NR); p<0.0005
									Most 2006 – spreading grafting	62.3 (12)	24.3 (17.8)	-38 (NR); p<0.01

FU post procedure, months	LATERA NOSE score, mean (SD)				Functional rhinoplasty NOSE score, mean (SD)			
	Trial ID	Baseline	Post procedure	Change	Trial ID	Baseline	Post operation	Change
					without turbinate reduction (n=7)			
					Sainio 2022 (N=18)	70.3 (range: 30, 95)	42.5 (range: 5, 100)	-27.8 (NR)
					MA	<b>-38.58 (-49.48, -27.68), I<sup>2</sup>=67%, p=0.08</b>		
18	LATERA-RCT (N=48)	78.4 (12.1)	31.8 (21.7)	-46.7 (24.6)	NR	NR	NR	NR
	LATERA-OFFICE (N=69)	77.8 (13.5) <sup>b</sup>	30.6 (NR) <sup>c</sup>	-47.2 (24.6)				
	Trial 4350-001 (N=26)	76.7 (14.8) <sup>b</sup>	35.5 (NR) <sup>c</sup>	-41.2 (32.8)				
	MA (95% CI)	<b>-46.35 (-50.55, -42.15), I<sup>2</sup>=0%, p=0.69</b>						
24	LATERA-RCT (N=43)	78.8 (12.1)	35 (25.5)	-43.8 (26.4)	NR	NR	NR	NR
	LATERA-OFFICE (N=65)	77.8 (13.5) <sup>b</sup>	30.4 (NR) <sup>c</sup>	-47.4 (27.8)				
	Trial 4350-001 (N=25)	76.7 (14.8) <sup>b</sup>	32.7 (NR) <sup>c</sup>	-44.0 (31.1)				
	MA (95% CI)	<b>-45.59 (-50.32, -40.86), I<sup>2</sup>=0%, p=0.76</b>						
Baseline to last FU	LATERA-RCT and LATERA-OFFICE at 24 months FU	MA of mean change in NOSE score (95% CI): <b>-45.59 (-50.32, -40.86), I<sup>2</sup>=0%, p=0.76</b>			All studies of functional rhinoplasty	MA of mean change in NOSE score (95% CI): <b>- 36.74 (-45.00, -28.74), I<sup>2</sup>=67%, p=0.05</b>		

Source: Table 36, pg 113-114 of MSAC 1719 ADAR; LATERA-RCT CSR Table 10, LATERA-OFFICE CSR Table 6, Trial 4350-001 Table 7, Most 2006, Palesy 2015, Taha 2021, Tan 2012, Rao 2016, Sainio 2022.

Abbreviations: CI= confidence interval; FU= follow-up; MA= meta-analysis; NA= not applicable; NE= not estimable; NOSE= Nasal Obstruction Symptom Evaluation; NR= not reported.

Note:

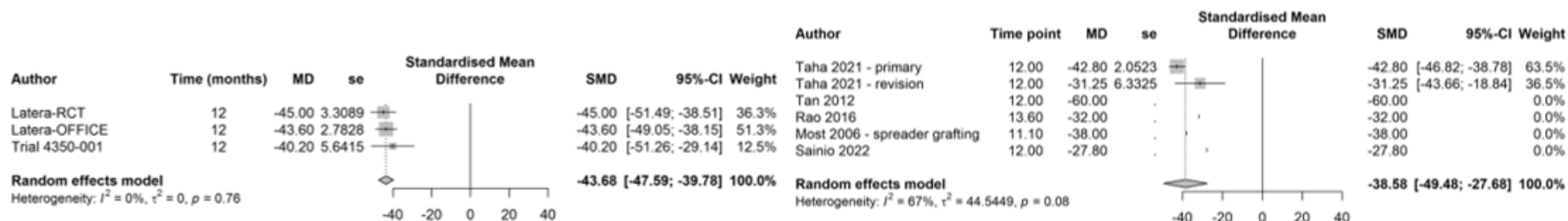
a NOSE score calculated from raw scores reported in publications.

b Baseline NOSE scores in LATERA-OFFICE based on the LATERA only arm (N=105) at enrolment and in Trial 4350-001 based on N=30 at enrolment.

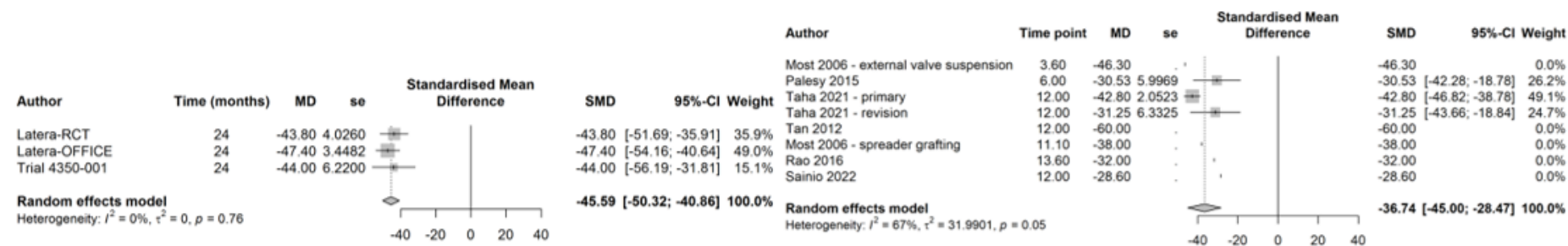
c NOSE scores post procedure were calculated by subtracting change in NOSE scores from the baseline NOSE scores, as they were not reported in the CSRs for LATERA-OFFICE and Trial 4350-001.

Figure 2 Meta-analysis of LATERA vs functional rhinoplasty at 12 months and last follow-up (NOSE score)

NOSE: LATERA vs functional rhinoplasty at 12 months post procedure



NOSE: LATERA at 24 months post procedure vs functional rhinoplasty at last follow-up



Source: Figure 21, pg 115 of MSAC 1719 ADAR

Abbreviations: CI= confidence interval; MD= mean difference; SE= standard error; SMD= standard mean difference

Based on the evidence presented and summarised in Table 11, the ADAR claimed that LATERA was non-inferior to functional rhinoplasty.

**Table 11 Summary of evidence table: LATERA versus functional rhinoplasty**

Outcomes	Anticipated absolute effects		№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	MD with LATERA	MD with rhinoplasty			
LATERA vs functional rhinoplasty alone					
Change in NOSE score at 3 months	The pooled mean change in NOSE score was -43.59	Range in mean change in NOSE was -30.6 to -46.3	223 (LATERA: 3; rhinoplasty: 2)	⊕○○○ Very low	LATERA likely to be non-inferior to functional rhinoplasty.
Change in NOSE score at 6 months	The pooled mean change in NOSE score was -45.81	Range in mean change in NOSE was -28.6 to -30.53	227 (LATERA: 3; rhinoplasty: 2)	⊕○○○ Very low	Potentially greater NOSE score reduction with LATERA compared to functional rhinoplasty.
Change in NOSE score at 12 months	The pooled mean change in NOSE score was -43.68	The pooled mean change in NOSE score was -38.58 (range:-27.8 to -60) <sup>a</sup>	276 (LATERA: 3; rhinoplasty: 5 <sup>a</sup> )	⊕○○○ Very low	Potentially greater NOSE score reduction with LATERA compared to functional rhinoplasty.
Change in NOSE score at last follow-up	The pooled mean change in NOSE score was -45.59	The pooled mean change in NOSE score was -36.74	257 (LATERA: 3; rhinoplasty: 7 <sup>a</sup> )	⊕○○○ Very low	Potentially greater NOSE score reduction with LATERA compared to functional rhinoplasty.
LATERA vs functional rhinoplasty with adjunct procedures					
Change in NOSE score at follow-up (3.1-4.8 mts)	Mean change in NOSE score was -40.5	Mean change in NOSE score was -40.3	90 (1 study)	⊕○○○ Very low	LATERA likely produces similar improvement in the NOSE score to rhinoplasty when used with adjunct procedures.

Source: Table E3, pg12 of MSAC 1719 ADAR+inline commentary  
 Abbreviations: MD= mean difference, NOSE= nasal obstruction symptom evaluation.  
 a All studies reporting mean changes.

***Transitivity/exchangeability issues with the naïve indirect comparison of LATERA versus functional rhinoplasty***

The commentary noted the following transitivity issues for the naïve indirect comparison of LATERA versus functional rhinoplasty:

- Patients in the rhinoplasty arm were not well defined given that rhinoplasty is used for a broader range of aetiologies.
- The indication being sought 'NAO due to LWI' is confounded by collapse caused by a multitude of anatomical structures: static such as septum and turbinates (not relevant to this ADAR), or dynamic such as the lateral wall with the upper cartilage in it (relevant to this ADAR) in rhinoplasty studies.

- Rhinoplasty studies had a wider range of pre-treatment mean NOSE scores (55-86) compared with LATERA studies (mean NOSE score, 76-78) albeit rhinoplasty studies included the proposed MBS descriptor population.
- The rhinoplasty study by Most 2006 included a broader population than the population in the LATERA studies (and for whom listing for LATERA is sought); that is patients with NAO due to 'identifiable anatomical cause' such as septal deviation, turbinate hypertrophy, internal valve collapse (IVC), or external nasal valve collapse. Of these aetiologies, external nasal valve collapse and potentially IVC (if due to LWI) are relevant aetiologies.
- In some of the LATERA studies participants had received prior nasal surgery (59% in LATERA-RCT, 70% in LATERA-OFFICE, 66% Trial 4350-001), and may be considered to have received LATERA as 'revision'. Data was not stratified by primary or revision treatment.
- Taha (2021) reports that 60% of participants had functional rhinoplasty in the revision setting. Other rhinoplasty studies did not report proportion of primary and revision procedures. The rates of revision were somewhat similar between LATERA and the rhinoplasty study population. The proportion of treatment experienced population being ~60-70%.

Overall, the commentary considered that the results comparing the effectiveness of LATERA with functional rhinoplasty should be interpreted with caution as the comparison was naïve therefore of low certainty, due to the transitivity issues discussed above and the statistically high heterogeneity in the rhinoplasty studies not significant at 12 months ( $I^2=67%$ ,  $p=0.08$ ) and significant at 24 months ( $I^2=67%$ ,  $p=0.05$ ).

### **LATERA vs. conservative management**

The results of the primary endpoint, NOSE score, from the LATERA-RCT comparing LATERA versus sham procedure, are presented in Table 12. At one-month post procedure, patients in the LATERA arm experienced a greater reduction in NOSE score than the sham arm, albeit the mean difference was not statistically different  $p=0.29$ . The ADAR suggested that the 'placebo effect' at 1 month, observed in the sham arm, is likely explained by minor scarring tissue as a consequence of the cannula insertion, resulting in temporary support and hence improvement, rather than the regression to the mean phenomenon.

At three-months post procedure, on average, subjects in the LATERA arm had statistically greater improvement in NOSE scores than the sham arm, with a mean difference of  $-19.7$  points (95% CI:  $-28.65$ ,  $-10.75$ ;  $p<0.0001$ ).

The results of the primary endpoint, NOSE response, based on per protocol and an indicative intention-to-treat analysis constructed for the ADAR, based on individual patient level data are displayed in Table 13.

The commentary considered the applicability of results from the LATERA-RCT to the population for whom listing is sought is highly uncertain because (i) no patient recruited to the LATERA-RCT trial would be considered representative of the moderate population of patients for whom LATERA is being sought (i.e. patients who are moderate NOSE score of 45-54 were not recruited) (ii) the Sham procedure is not reflective of conservative management, although the incremental treatment effect between LATERA and conservative management is biased against LATERA with demonstrated treatment effect at one month MD  $-4.80$  (95% CI  $-13.76$ ,  $4.16$ );  $p=0.29$  although not significant. It is understood that the insertion of the canula triggered temporary mechanical support caused by the scar tissue within the lateral wall, resulting in the observed sham benefits.



**Table 12 Change from baseline in NOSE score**

Follow-up / analysis set	LATERA-RCT												LATERA vs Sham MD (95% CI); p value <sup>a</sup>
	LATERA						Sham						
	Baseline		Follow-up		Change		Baseline		Follow-up		Change		
	n	Mean ±SD	N	Mean ±SD	n	Mean ±SD	n	Mean ±SD	n	Mean ±SD	n	Mean change ±SD	
1 months – PP	61	77.5±12.9	61	40.9±21.0	61	-36.6±24.8	60	77.4±15.0	60	45.6±24.2	60	-31.8±25.5	-4.80 (-13.76, 4.16); p=0.29
3 months – PP	63	77.4±13.1	63	35.0±22.6	63	-42.4±23.4	64	77.7±15.1	64	55.0±25.2	64	-22.7±27.9	-19.70 (-28.65, -10.75); <0.0001
3 months – TS	70	76.2±13.3	70	34.5±22.5	63	-41.7±24.2	NR						NR

Source: Table 18, pg 86 of MSAC 1719 ADAR; LATERA-RCT CSR 5254-001 Table 9 pg 22, Table 10 pg. 23.

Abbreviations: CI= confidence interval; MD= mean difference; NOSE= nasal obstruction symptom evaluation; PP= per protocol; SD= standard deviation; TS= treated set.

Note: Risk of bias was rated moderate by the commentary

<sup>a</sup> Calculated using Review Manager 5.4

**Table 13 Response\* based on the NOSE score in the LATERA-RCT: LATERA vs sham at 3 months**

Outcome	LATERA-RCT					
	Bias	LATERA n/N (%)	Sham n/N (%)	OR [95% CI] <sup>a</sup> ; p value	RR [95% CI] <sup>a</sup> ; p value	RD [95% CI] <sup>a</sup> ; p value
Response at 3 months - PP	Moderate	52/63 (82.5)	35/64 (54.7)	3.92 [1.73, 8.85]; p=0.001	1.51 [1.18, 1.94]; p=0.001	0.28 [0.12, 0.43]; p=0.0004 NNT=4
Response at 3 months – ITT <sup>b, c</sup>	Moderate	61/71 (85.9)	43/66 (65.2)	3.26 [1.41, 7.55]; p=0.006	1.32 [1.08, 1.61]; p=0.007	0.21 [0.07, 0.35]; p=0.004 NNT=5

Source: Table 21, pg 111 of MSAC 1719 ADAR+inline commentary

Abbreviations: CI= confidence interval; ITT= intention to treat; NNT= number needed to treat; OR= odds ratio; PP= per protocol; RD= risk difference; RR= relative risk.

<sup>a</sup> Calculated using Review Manager 5.4

<sup>b</sup> Calculated based on individual patient data as per Table 23 of Section 12.4 Listing of NOSE Scores by Participant at Follow-ups pg 53 of the LATERA-RCT CSR. Responders and non-responders were tallied up; data for response at 1 month was carried forward to 3 months for patients with missing response category data at 3 months (N=5 patients). Patients were analysed according to randomised treatment groups, hence, as stipulated elsewhere in the CSR, it is known that one sham patient was accidentally implanted with LATERA (it is not clear from the listing which patient this was). (Refer to Attachment 3 - NOSE response\_IPD for ITT analysis.xls for extracted data).

<sup>c</sup> The 'Response at 3 months – ITT' results presented in Table 13 are derived from ad-hoc/ post-hoc analyses provided specifically for the purposes of informing the MSAC consideration. These analyses were not part of the pre-specified statistical plan for the LATERA-RCT trial. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the MSAC outcome and should not be used for any other purpose.

\* Response was defined as a participant who has at least one NOSE class improvement (5-25=mild; 30-50=moderate; 55-75=severe; 80-100=extreme) or at least 20% NOSE score reduction from baseline.

In the LATERA-RCT, patients assigned to the sham control arm had the option to crossover to receive the implant after 3-month follow-up. While the trial was uncontrolled beyond 3 months, the mean NOSE scores and response rate in the LATERA arm is available over 24 months (Table 14 and Table 15). Table 14 indicates the treatment benefit was maintained in the LATERA arm over 24 months, which the ADAR suggested demonstrated the durability of effect although the

implant is reabsorbed over 18 months. Figure 3 shows the mean NOSE score for the LATERA and cross-over arms over 24 months. Data for the cross-over arm indicated that, similar to the LATERA arm, there is a drop in the mean NOSE score from 70 (baseline) to ~45 at 1 month and then ~40 at 3 months. The commentary noted that it was not clear if the baseline, 1 month and 3 month NOSE score for the cross-over patients was from when these patients entered the study as sham patients or from when the patients crossed over and received the LATERA. The LATERA-RCT final clinical study report did not present 1 and 3 month individual patient level data for the cross-over study arm (i.e. the tables in CSR only presented the individual patient NOSE scores for cross-over study arm at 6, 12, 18 and 24 month follow up).

**Table 14 Change in NOSE score over time for patients randomised to LATERA in the LATERA-RCT**

Follow-up	Participant randomised to LATERA				
	n	Baseline Mean ± SD	Visit	Change	P value
1 month	69	76.2 ± 13.1	40.0 ± 21.9	-36.2 ± 25.8	<0.001
3 months	70	76.2 ± 13.3	34.5 ± 22.5	-41.7 ± 24.2	<0.001
6 months	65	76.2 ± 13.1	28.9 ± 22.5	-47.3 ± 24.0	<0.001
12 months	58	76.8 ± 13.0	31.8 ± 23.4	-45.0 ± 25.2	<0.001
18 months	48	78.4 ± 12.1	31.8 ± 21.7	-46.7 ± 24.6	<0.001
24 months	43	78.8 ± 12.1	35.0 ± 25.5	-43.8 ± 26.4	<0.001

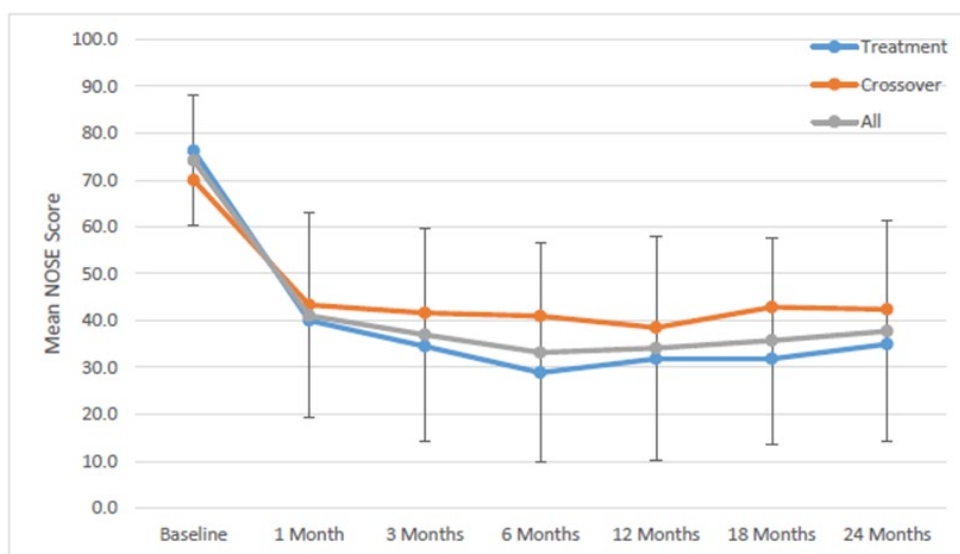
Source: Table 20, pg 109 of MSAC 1719 ADAR+inline commentary  
Abbreviations: SD= standard deviation.

**Table 15 Response rate over time for patients randomised to LATERA in the LATERA-RCT**

Follow-up	LATERA Randomised subjects		
	Risk of bias	n/N	Response rate (95% CI)
1 month	Moderate	59/69	85.5% (75.0%, 92.8%)
3 months	Moderate	62/70	88.6% (78.7%, 94.9%)
6 months	Moderate	61/65	93.8% (85.0%, 98.3%)
12 months	Moderate	53/58	91.4% (81.0%, 97.1%)
18 months	Moderate	46/48	95.8% (85.7%, 99.5%)
24 months	Moderate	39/43	90.7% (77.9%, 97.4%)

Source: Table 22, p111 of MSAC 1719 ADAR+inline commentary  
Abbreviations: CI= confidence interval.

**Figure 3 Mean NOSE scores over time with LATERA**



Source: Figure 14, pg 108 of MSAC 1719 ADAR+inline commentary.

Abbreviations: NOSE= nasal obstruction symptom evaluation.

Error bars represent standard deviation (SD).

Based on the evidence presented and summarised in Table 16, the ADAR claimed that LATERA had superior effectiveness and inferior safety compared to conservative management.

**Table 16 Summary of evidence table: LATERA versus sham (as a proxy for conservative management)**

Outcomes	Anticipated absolute effects (95% CI)		RR (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with sham	Risk with LATERA				
Change in NOSE score at 3 months	Mean change: -22.7	MD 19.7 lower (28.65 lower to 10.75 lower)	-	127 (1 RCT)	⊕⊕⊕○ Moderate	LATERA likely reduces change in NOSE score at 3 months.
Responders at 3 months	547 per 1,000	826 per 1,000 (645 to 1,000)	1.51 (1.18 to 1.94)	127 (1 RCT)	⊕⊕⊕○ Moderate	LATERA likely increases responders at 3 months.
Change in VAS score at 3 months	Mean change -13.3	MD 25.7 lower (36.08 lower to 15.32 lower)	-	127 (1 RCT)	⊕⊕⊕○ Moderate	LATERA likely reduces change in VAS score at 3 months.

Source: Table E.4, pg 14 of MSAC 1719 ADAR+inline commentary

Abbreviations: CI= confidence interval; MD= mean difference; NOSE= nasal obstruction symptom evaluation; RR= relative risk, RCT= randomised controlled trial; VAS= visual analogue scale.

Moderate certainty: 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.

## Minimal clinically important difference (MCID)

The ADAR presented three studies attempting to inform the MCID in the NOSE score. None of the MCID studies were conducted in patients with NAO due to LWI. Stewart 2004<sup>17</sup> and Lodder<sup>18</sup> 2018 used the anchored approach to patients who underwent septoplasty alone or with adjunct turbinectomy and proposed an MCID of 19.4 and 39.2 points respectively. Patients undergoing rhinoplasty were excluded in these studies. Kandathil 2019<sup>19</sup> proposed an MCID of 24.4 points, which was anchored to a survey and the Standardised Cosmesis and Health Nasal Outcomes Survey (SCHNOS) questionnaire in patients who underwent cosmetic, functional or combined cosmetic/functional rhinoplasty.

Based on the Stewart 2004 study, the ADAR nominated 19.4 points as the MCID in the NOSE score.

The commentary noted that given that the change in the NOSE score in the sham arm of the LATERA-RCT at 1 month (mean change  $\pm$ SD  $-31.8 \pm 25.5$ ) and at 3 months ( $-22.7 \pm 27.9$ ) exceeds the MCID, the MCID may not be applicable. Further while the mean difference in the NOSE score at 3 months for LATERA vs. Sham is  $-19.70$  ( $-28.65, -10.75$ ) just exceeds the nominated MCID, it is within the upper 95% CI.

## Additional LATERA evidence

The ADAR also presented additional evidence for LATERA, i.e., the data from the other arms of the LATERA studies that assessed effectiveness of LATERA when used with septoplasty  $\pm$  turbinate reduction (i.e., the relevant cohort from LATERA-OFFICE, the LATERA-OR study and Saadat 2018). This was presented to support the effectiveness of LATERA when used with adjunct procedures.

At baseline all participants were in the severe or extreme NOSE score range. None were in the broader population of patients for whom LATERA is being sought (i.e., moderate). At 24 months, the improvement in NOSE score was between 44 to 49.5 in most studies, with LATERA-OR reporting a larger reduction of 61 points improvement. LATERA-OR was the only study that included septoplasty with or without turbinate reduction, suggesting septoplasty may have contributed to the improvement in NOSE score.

The ADAR reported that the response rate results in the additional LATERA studies were similar to those observed with LATERA in the LATERA-RCT study, where a response rate of 90.7% was reported at 24 months in participants randomised to LATERA except in Trial 4350-001 where response was not a primary endpoint and LATERA was used alone.

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<sup>17</sup> Stewart MG, Witsell DL, Smith TL, et al. (2004) Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. *Otolaryngol Head Neck Surg.* 130:157-63

<sup>18</sup> Lodder WL, & Leong SC (2018) What are the clinically important outcome measures in the surgical management of nasal obstruction? *Clinical otolaryngology:* 43(2):567–571

<sup>19</sup> Kandathil CK, Saltychev M, Abdelwahab M, et al. (2019) Minimal Clinically Important Difference of the Standardized Cosmesis and Health Nasal Outcomes Survey. *Aesthetic surgery journal.* 39(8):837–8400

**Table 17 Response rate at 24 months across LATERA studies**

LATERA study	Subgroup	n/N	Response rate (95% CI)
LATERA-RCT -24 months	All participants	60/68	88.2% (78.1%, 94.8%)
	Treatment	21/25	90.7% (77.9%, 97.4%)
	Crossover	39/43	84.0% (63.9%, 95.5%)
LATERA-OFFICE - 24 months	All participants	93/102	91.2% (83.9%, 95.9%)
	LATERA only	58/65	89.2% (79.1%, 95.6%)
	LATERA + ITR	35/37	94.6% (81.8%, 99.3%)
LATERA-OR (all participants: LATERA ± septoplasty/ITR) - 24 months	N/A	72/75	96.0% (NR)
Trial 4350-001 (LATERA only) - 24 months	N/A	20/25	80.0% (NR)

Source: Compiled from Table 22, 33, 34 and 35 of MSAC ADAR 1719+inline commentary  
 Abbreviations: CI= confidence interval; ITR= inferior turbinate reduction; NA= not applicable; NR= not reported.

## Clinical claim

### ***LATERA versus functional rhinoplasty***

The ADAR claimed that LATERA (i.e., insertion of bioabsorbable implants) had non-inferior clinical effectiveness and safety compared with rhinoplasty based on the primary outcome of: % of treated patients with at least 1 NOSE class improvement; or  $\geq 20\%$  reduction in NOSE score from baseline.

The commentary noted that claim of non-inferior clinical efficacy of LATERA was supported by the available evidence albeit in the severe and extreme LATERA population not in the moderate population based on NOSE score. At 12 months, reductions in the NOSE score were greater with LATERA than functional rhinoplasty (-43.68 vs -38.58) respectively, however confidence intervals crossed over demonstrating non-inferiority. These results should be interpreted with caution. At 24 months, reductions in the NOSE score were greater with LATERA than functional rhinoplasty (-45.59 vs -36.74).

### ***LATERA versus conservative management***

The ADAR claimed that LATERA (i.e., insertion of bioabsorbable implants) had superior clinical effectiveness and inferior safety compared with conservative management based on the primary outcome of: % with at least 1 NOSE class improvement; or  $\geq 20\%$  reduction in NOSE score from baseline, at three months.

The commentary noted that the claim of superior clinical efficacy of LATERA was reasonably supported by the available evidence. Although clinical evidence aligned to the proposed MBS item description (i.e., a moderate population NOSE score  $>45$ ) at baseline was not presented. However, it should be noted that analysis in the severe to extreme population showed a higher proportion of patients treated with LATERA achieve a reduction in NOSE score at 3 months compared to patients in the sham arm (-19.70 [-28.65, -10.75];  $p < 0.0001$ ) in the PP population.

The claim of a comparable safety profile with conservative management is supported by the available evidence. Moreover, the sham treatment (given via canula insertion) in the clinical trials is not a true reflection of conservative management (no insertion) in clinical practice.

The commentary highlighted the following limitations with the clinical claims:

- The applicability of the clinical evidence for LATERA to the proposed MBS population is uncertain. That is, the patient population included in the LATERA evidence base had a NOSE score of  $\geq 55$  (i.e., severe to extreme NOSE score) which is narrower than the proposed MBS population which includes patients with a moderate NOSE score (i.e., NOSE score of  $>45$ ).
- A positive Cottle manoeuvre is a non-discriminatory test (input from a healthcare professional in the PASC ratified PICO confirmation). In most people it is positive, and if it's negative, the obstruction is likely static and will not be affected by the device, hence affecting the reliability of the test.
- The transitivity/exchangeability issues with the naïve indirect comparison of LATERA versus functional rhinoplasty. Of note, the mean NOSE score at baseline in the LATERA studies was 77-78 (range 55 to 100) compared to the functional rhinoplasty studies mean NOSE score 55-86 (range 38 to 94).
- The claim of non-inferiority of LATERA versus functional rhinoplasty is based on a naïve indirect comparison of low certainty which should be interpreted with caution.
- The long-term safety and effectiveness of LATERA (i.e., after 24 months) is unknown.
- There is insufficient data on whether the procedure could be delivered once per lifetime or over multiple occasions.

### 13. Economic evaluation

The ADAR claimed that LATERA had non-inferior safety and effectiveness compared to functional rhinoplasty (primary comparator) and therefore, presented a cost-minimisation analysis (CMA) for LATERA versus rhinoplasty. In addition, based on the clinical claim that LATERA had inferior safety and superior effectiveness compared the conservative management (secondary comparator), the ADAR also presented a cost-utility analysis (CUA) comparing LATERA and extended conservative management (ECM).

#### CMA – LATERA versus functional rhinoplasty

The CMA compared total cost of LATERA (performed in a same-day hospital setting) versus total cost of a functional rhinoplasty (the cost comprises of partial rhinoplasty and full-rhinoplasty procedures). Based on the results of the CMA, the ADAR claimed that LATERA provided a cost-saving of ~\$**redacted** compared to functional rhinoplasty (Table 18). The main cost components for the CMA are shown in Table 19. As LATERA provides a less-invasive procedure, the procedure allows for local anaesthesia and technically can be performed in-office rather in hospital setting. Other costs that may be incurred include prior consultations to confirm eligibility. This would also be true for rhinoplasty. As both would incur a consultation fee for assessing eligibility, it was assumed that these costs would have been incurred regardless of the intervention as a result of standard healthcare services – whereby the patient is exploring options to resolve a presenting complaint. On that basis, the costs for prior consultations would be the same for both arms and have not been included. If, however, there was a bespoke work-up of the patient for the LATERA procedure then these costs would need to be included. However, no information was presented to suggest this.

**Table 18 ADAR Cost-minimisation analysis of LATERA vs functional rhinoplasty for the treatment of NAO due to LWI**

Treatment strategy	LATERA#	Rhinoplasty				
		Partial rhinoplasty	Total rhinoplasty, local graft	Total rhinoplasty, distant graft	Weighted average*	Weighted average, total rhinoplasty only*
Total cost, per procedure	\$redacted	\$2,783.17	\$3,828.56	\$4,474.45	\$3,829.03	\$3,935.35
Cost saving for LATERA	Reference	-\$redacted	-\$redacted	-\$redacted	-\$redacted	-\$redacted

Source: Table 63, pg 173 of MSAC 1719 ADAR+inline commentary

\* Weighting across the three rhinoplasty surgery types was based on the 2021 MBS statistics; 9% for partial rhinoplasty (MBS item 45632), 75% for total rhinoplasty local graft (MBS item 45641) and 11% for total rhinoplasty distant graft (MBS item 45644).

# Total cost for LATERA is a weighted cost based on the assumption that 16% unilateral and 84% bilateral LATERA procedures (based on Clark 2018)

**Table 19 Summary of cost components for LATERA and functional rhinoplasty used in the ADAR cost-minimisation analysis**

Resource item	LATERA	Functional Rhinoplasty	Source / notes
<b>Prosthesis (implant)</b>	\$redacted	N/A	Costing based on the proposed price of LATERA. No implant use assumed for conventional surgery.
<b>Professional services</b>			
<b>Anaesthetist</b>	N/A (local only)	\$309 \$432 \$432	Costing based on the current MBS fees for MBS items. LATERA implantation is performed with local anaesthesia (given by the same surgeon performing the implantation).
<b>ENT surgeon / rhinologist</b>	\$198.95 \$282.51	\$541 \$1126 \$1623	Costing based on the proposed fee for LATERA (unilateral and bilateral) Costing for rhinoplasty based on the current MBS fees (45632, 45641 and 45644, respectively) and assistant for total rhinoplasty distant graft.
<b>Other hospital resource use</b>			
<b>Hospital stay (ie, hotel cost)</b>	N/A	\$435 \$522 \$671	Costing based on the SIRA 2019 Private Hospital Fee Schedule and adjusted for proportion of overnight stay according to ACHI data. LATERA does not require an overnight stay.
<b>Other consumables / theatre time / overheads</b>	\$630.90	\$1534 \$1760 \$1760	Costing based on the SIRA 2019 Private Hospital Fee Schedule.

Source: Compiled from Table 56 and 58 of MSAC 1719 ADAR+inline commentary

The commentary highlighted that functional rhinoplasty is always performed in hospital and therefore includes hospital admission and theatre time for the procedure. Although LATERA could be performed in a consulting room, the ADAR states it has costed the LATERA procedure as a same-day hospital procedure. The pre-ESC response clarified that the applicant considered that the use of LATERA as an outpatient consultation room procedure in Australia would be rare and that the applicant considered that the decision to perform the LATERA procedure as a same-day hospital procedure is not a clinical decision / requirement but more a financial decision for patients (and doctors) as the prosthesis subsidisation (i.e. if LATERA implant is included on the Prostheses List) would not be provided for the LATERA implant if the service is delivered in a consultation room. Sensitivity analyses requested by ESC and additional sensitivity analyses presented in the pre-MSAC response are shown in Table 20 and Table 21, respectively.

**Table 20 Sensitivity analyses requested by ESC**

	Total cost, per procedure		Difference
	Latera	Rhinoplasty	
<b>Base case</b>	<b>\$redacted</b>	<b>\$3,829.03</b>	<b>\$redacted</b>
Weighted average across Rhinoplasty procedures (base case: across all 3 procedures)			
#1 - Latera only compared against partial rhinoplasty	<b>\$redacted</b>	\$2,783.17	<b>-\$redacted</b>
Rhinoplasty overnight stay (base case: 46% same day)			
#2 - 100% same day - Partial rhinoplasty	<b>\$redacted</b>	\$1,534.50	<b>\$redacted</b>
#3 - 100% same day - weighted rhinoplasty across all 3 procedures	<b>\$redacted</b>	\$3,292.47	<b>-\$redacted</b>
Rhinoplasty theatre time & costs (base case: partial rhinoplasty - 1.5hr/band 5, total rhinoplasty - 3 hours/Band 6)			
#4 - All three rhinoplasty procedures 1.5hr/band 5	<b>\$redacted</b>	\$3,490.77	
Weight average across unilateral and bilateral LATERA procedures (base case: 16% unilateral, 84% bilateral)			
#5 - 100% bilateral LATERA procedures, weighted rhinoplasty across all 3 procedures	<b>\$redacted</b>	\$3,829.03	<b>-\$redacted</b>
#6 - 100% bilateral LATERA procedures, partial rhinoplasty only	<b>\$redacted</b>	\$2,783.17	<b>-\$redacted</b>
No response to LATERA subsequent rhino/ revision of rhino (base case: did not include)			
#7 - 4.5% LATERA reintervention, base case rhinoplasty costs	<b>\$redacted</b>	\$3,829.03	<b>-\$redacted</b>
#8 - 4.5% LATERA reintervention, partial rhinoplasty costs	<b>\$redacted</b>	\$2,783.17	<b>-\$redacted</b>
#9 - 3.6% LATERA undergo subsequent rhinoplasty revision and 5.6% rhinoplasty procedures undergo revision	<b>\$redacted</b>	\$3,984.13	<b>-\$redacted</b>
#10 - 3.6% LATERA undergo subsequent rhinoplasty revision and 5.6% partial rhinoplasty procedures undergo revision	<b>\$redacted</b>	\$2,938.27	<b>-\$redacted</b>
#11 - 20% no response to LATERA have subsequent rhinoplasty and 5.6% rhinoplasty procedures undergo revision	<b>\$redacted</b>	\$2,938.27	<b>\$redacted</b>
#12 - 20% no response to LATERA have subsequent rhinoplasty and 5.6% partial rhinoplasty procedures undergo revision	<b>\$redacted</b>	\$2,938.27	<b>\$redacted</b>
Multiway sensitivity analyses			
#13 - Partial rhinoplasty only - 100% same day, both LATERA and partial rhinoplasty - 100% bilateral LATERA procedures - 4.5% LATERA reintervention	<b>\$redacted</b>	\$1,534.50	<b>\$redacted</b>
#14 - Partial rhinoplasty only - 100% same day, both LATERA and partial rhinoplasty - 100% bilateral LATERA procedures - 3.6% of LATERA procedures have subsequent rhinoplasty - 5.6% partial rhinoplasty undergo revision	<b>\$redacted</b>	\$1,689.59	<b>\$redacted</b>
#15 - Partial rhinoplasty only - 100% same day, both LATERA and partial rhinoplasty - 100% bilateral LATERA procedures - 20% no response to LATERA have subsequent rhinoplasty - 5.6% partial rhinoplasty undergo revision	<b>\$redacted</b>	\$1,689.59	<b>\$redacted</b>



**Table 21 Pre-MSAC response: Additional cost-minimisation analyses with 2-year time horizon, discounted at 5% pa**

Scenario	Total cost, two years		Incremental cost
	LATERA	Rhinoplasty	
vs all rhinoplasty items (weighted; as per the ADAR) Reintervention rate (annual) =4.5%/5.6% for LATERA/rhinoplasty (as per ESC) Reintervention cost = <b>\$redacted</b> /\$3,829.03 for LATERA/rhinoplasty (as per the ADAR)	<b>\$redacted</b>	\$4,248	<b>-\$redacted</b>
vs partial rhinoplasty (as per ESC) Reintervention rate (annual) =4.5%/5.6% for LATERA/rhinoplasty (as per ESC) Reintervention cost = <b>\$redacted</b> /\$2,783.17 for LATERA/rhinoplasty	<b>\$redacted</b>	\$3,087	<b>-\$redacted</b>
vs partial rhinoplasty (as per ESC) Reintervention rate (annual) =3.6%/5.6% for LATERA/rhinoplasty (as per ESC; any rhinoplasty provided as reintervention) Reintervention cost = <b>\$redacted</b> /\$3,829.03 for LATERA/rhinoplasty	<b>\$redacted</b>	\$3,202	<b>-\$redacted</b>
vs partial rhinoplasty (as per ESC) Reintervention rate (annual) =3.6%/5.6% for LATERA/rhinoplasty (as per ESC; partial rhinoplasty provided as reintervention) Reintervention cost = <b>\$redacted</b> /\$2,783.17 for LATERA/rhinoplasty	<b>\$redacted</b>	\$3,087	<b>-\$redacted</b>
vs partial rhinoplasty (as per ESC) Reintervention rate (annual) =10%*/5.6% for LATERA/rhinoplasty (as per ESC; any rhinoplasty provided as reintervention) Reintervention cost = <b>\$redacted</b> /\$3,829.03 for LATERA/rhinoplasty	<b>\$redacted</b>	\$3,202	<b>-\$redacted</b>
vs partial rhinoplasty (as per ESC) Reintervention rate (annual) =10%*/5.6% for LATERA/rhinoplasty (as per ESC; partial rhinoplasty provided as reintervention) Reintervention cost = <b>\$redacted</b> /\$2,783.17 for LATERA/rhinoplasty	<b>\$redacted</b>	\$3,087	<b>-\$redacted</b>

Source: Table 2 of MSAC 1719 Pre-MSAC response

\*Based on the 20% reintervention rate mentioned by ESC, annualised

Abbreviations: ADAR = Applicant Developed Assessment Report; ESC = Evaluation Sub-Committee

## CUA – LATERA versus extended conservative management

The ADAR presented a cost-utility analysis to examine the cost-effectiveness of LATERA compared to extended conservative management (ECM). The population for this economic analysis was defined as a sub-group of patients with NAO due to LWI who are eligible for functional rhinoplasty but for clinical and personal reasons these patients remain on conservative management such as nasal steroids, antihistamines, and temporary external supports. Table 22 summarise the structure of the economic evaluation for LATERA versus conservative management.

The commentary noted the following limitations for the CUA presented in the ADAR:

- As no cost-effectiveness studies of LATERA have been reported to inform the model, the analysis applied a given mean of QALYs from a reference study (Tjahjono et al. 2019). There is a potential bias with the approach as cohorts in the reference study have different patient’s characteristics and different clinical results (see the in-line commentary section 3B.2 for details).
- There is insufficient data in the LATERA-RCT study to inform the benefit of LATERA nor the granularity of QALYs gain between pre- and post-LATERA treatment in the literature (or other bioabsorbable nasal implants studies).
- There is no evidence in the literature for the time-horizon used in the CUA. The base-case time horizon was set at five years with no evidence to justify the approach.

On that basis, the ADAR CUA applied an exploratory approach by using parameters and assumptions based on key reference studies.<sup>20</sup> However, the commentary cautioned that the outcomes of CUA should be interpreted in the context of those limitations and assumptions applied in the analysis.

**Table 22 Summary of the economic evaluation for LATERA versus conservative management**

Component	Description
Perspective	Health care system perspective
Population	The population is patients with NAO due to LWI confirmed by positive modified Cottle manoeuvre and the patient has a self-reported NOSE scale score of greater than 45. The modelled population is a subgroup of patients consisting of those who are contraindicated or not suitable for conventional functional rhinoplasty (thus stay on conservative management, despite meeting the current rhinoplasty eligibility otherwise).
Comparator	Extended conservative management (ECM)
Type(s) of analysis	Cost-utility analysis (CUA)
Outcomes	Quality-adjusted life years
Time horizon	Five years (base-case result)
Computational method	Markov analysis
Generation of the base case	Modelled analysis with extrapolation to 5 years (background mortality captured according to the Australian life table). Minimal “modelling” components exist (primarily for extrapolation and background mortality)
Health states	Alive and death (but mortality does not influence the calculation of ICER)
Cycle length	Annual
Transition probabilities	Not involving specific transition probabilities.
Discount rate	5% for both costs and outcomes
Software	Excel

Source: Section 3B in ADAR.

Abbreviations: NOSE= Nasal Obstruction Symptom Evaluation; NAO= nasal airway obstruction; LWI= lateral wall insufficiency; QALY= quality-adjusted life year, CEA= cost-effectiveness analysis, CUA= cost-utility analysis, ICER= incremental cost-effectiveness ratio.

Table 23 summarises parameters used in ADAR for the economic evaluation. The commentary highlighted that there is a high degree of uncertainty in parameters used in the CUA. These include:

- The ADAR stated it took a conservative approach by assuming zero cost for the comparator group however the commentary considered that this does not represent the true economic cost (but this may bias against LATERA). Further, there is no information of clinical outcomes in the CUA for the comparator group.
- The baseline utility values applied in the CUA were based on a reference study of septorhinoplasty in Australia (Tjahjono et al. 2019). The analysis assumed a utility value of 0.72 to be applied for both the treatment and alternative groups. Patient demographics and characteristics at the baseline are different between the cohort in LATERA-RCT study and the septorhinoplasty study (Tjahjono et al. 2019). The mean age of patients in the LATERA-RCT study was 51 years old, while in the septorhinoplasty study was 38 years old, thus, there are potential different effects associated with patient’s age after the treatment. Moreover, there are also significant differences in NOSE scores between LATERA cohort and septorhinoplasty cohort at baseline (77.4 versus 48.2

<sup>20</sup> These include a study case in Germany of septorhinoplasty (Oladokun et al. 2018), LATERA-RCT studies (Stolovitzky et al. 2018 and 2019), and a study case in Australia of septorhinoplasty (Tjahjono et al. 2019).

respectively). On that basis, the assumption that patients in the LATERA-RCT have the same baseline utility as the baseline utility observed in Tjahjono et al. (2019) is potentially overestimated.

- The utility value post-surgery for LATERA was assumed to be the same as the 0.78 utility value post-surgery reported for the treatment group in the septorhinoplasty study (Tjahjono et al. 2019). This assumption is potentially biased due to a different period of assessment. The CUA follows the LATERA-RCT study of three-month treatment effect. Meanwhile, the reference study showed that QALY of 0.78 was observed six months after the procedure of septorhinoplasty. With standard deviation of 0.12, QALYs at follow-up overlap the average QALYs at baseline (0.72) and QALYs for the Australian norm (0.81).
- The utility value post-treatment for the comparator (ECM) was assumed to be constant at 0.72. With no patients' data available in the analysis to inform detail of the ECM group, the assumption of constant QALYs is biased in favour of LATERA.
- The CUA did not specify QALY's threshold to determine the effectiveness of LATERA treatment. It is noted that the estimated ICERs does not differentiate unilateral and bilateral procedures and that revision rates costs and safety costs have not been provided and included in the ICER.

Based on these uncertainties, the commentary considered the CUA was not suitable to measure cost-effectiveness of LATERA compared to ECM.

**Table 23 Summary of parameters for the CUA presented in the ADAR**

Parameters	Treatment group (LATERA)	Comparator group (ECM)	Source / note
Modelled population (sample)	n=70	n/a	Stolovitzky et al. (2019) for LATERA, no specification for the ECM.
Cost per treatment	\$redacted	\$0	Estimated (LATERA) and model assumption (ECM)
QALY at baseline (QoL)	0.72	0.72	Tjahjono et al. (2019)
QALY at follow-up (3-month)	0.78	0.72	Tjahjono et al. (2019) for the LATERA and the ECM.
QALYs gain (3-month)	0.06	0.00	
Time horizon for base case result	5 years	5 years	Model assumption.
Health state disposition	As per general population using life tables	As per general population using life tables	Australian Bureau of Statistics (ABS) life tables data.

Source: Table 23, p 38 of MSAC 1719 Commentary Executive Summary

Abbreviations: ECM= extended conservative management, QALY= quality adjusted life year, NOSE= nasal obstruction symptom evaluation.

The results of the CUA as presented in the ADAR with ongoing benefits overtime are shown in Table 24. This approach is subject to a zero-cost in the comparator group (ECM) and no revision rates for LATERA. Using extrapolated QALYs gain, the ICERs were estimated from one to 10 years, including a five-year base case result. The base-case 5-year ICER was estimated \$8,952 per QALY gain.

**Table 24 Stepped economic evaluation – extrapolation to 5 years, 5% discount (results in the ADAR)**

Model duration	Incremental cost	Incremental QALYs	ICER
1 year analysis (trial data available)	\$redacted	0.059	\$redacted
2-year analysis (trial data available)	\$redacted	0.116	\$redacted
3-year analysis	\$redacted	0.170	\$redacted
5-year analysis (base-case)	\$redacted	0.270	\$redacted
10-year analysis	\$redacted	0.478	\$redacted

Source: Table 75, pg 189 of MSAC 1719 ADAR+inline commentary.

Abbreviations: QALYs= quality-adjusted life years; ICER= incremental cost-effectiveness ratio.

## 14. Financial/budgetary impacts

The ADAR used a mixed epidemiological and market share approach to estimate the financial impact of the proposed MBS and PL listing of LATERA. The ADAR presented utilisation analyses of MBS items for partial and total rhinoplasty (MBS items 45632, 45641 and 45644), estimating the proportion (72%) of these patients who underwent the rhinoplasty procedure for correction of NAO due to LWI and then estimated the market share for LATERA by assuming redacted% (Year 1) to redacted% (Year 6) of patients would receive LATERA instead of rhinoplasty. The ADAR also assumed an additional redacted % use of LATERA for the subgroup of patients who are eligible for rhinoplasty, but who are contraindicated or elect not to undergo rhinoplasty procedure. The ADAR also claimed an additional healthcare utilisation advantage of reduced length of hospital stay relative to functional rhinoplasty.

The commentary noted the following limitations with the financial estimates for LATERA:

- There is no evidence for the estimated uptake of LATERA, redacted% in Year 1 increasing to redacted% in Year 6, and is likely to be underestimated.
- Local expert advice expects the proposed procedure would be performed as day surgery, with few patients requiring overnight stay. Those that choose not to undergo a GA could potentially be treated in private consulting rooms with LA. It is uncertain what proportion of LATERA patients would not elect to have insertion as a day patient with a GA.

The financial implications to the MBS resulting from the proposed listing of LATERA are summarised in Table 25. In Year 6, the estimated number of patients who receive LATERA would be redacted costing the MBS \$redacted but with estimated cost-offsets from substituting rhinoplasty procedures the ADAR estimated LATERA would save the MBS \$redacted in Year 6. When considering all costs and cost-offsets, the ADAR estimated a net saving to the Australian Healthcare System of -\$1,185,386 in Year 6.

**Table 25 Net financial implications of LATERA (84% bilateral)**

Year	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Number of rhinoplasty surgeries (LWI correction), derived	3,546	3,645	3,745	3,844	3,943	4,043
Uptake, market share vs conventional surgery	redacted	redacted	redacted	redacted	redacted	redacted

Year	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated LATERA implantation procedures due to rhinoplasty substitution	redacted	redacted	redacted	redacted	redacted	redacted
% of LATERA use in the "rhinoplasty-contraindicated" group	redacted	redacted	redacted	redacted	redacted	redacted
Estimated LATERA implantation procedures in the "rhinoplasty-contraindicated" subgroup	redacted	redacted	redacted	redacted	redacted	redacted
Total LATERA implantation procedures	redacted	redacted	redacted	redacted	redacted	redacted
Unilateral (16%) <sup>^</sup>	redacted	redacted	redacted	redacted	redacted	redacted
Bilateral (84%) <sup>^a</sup>	redacted	redacted	redacted	redacted	redacted	redacted
<b>Cost to MBS</b>						
Total MBS costs of LATERA, 75% benefit	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted
Changes in the MBS costs for rhinoplasty	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted
Net changes to the MBS	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted
<b>Other hospital resource use</b>						
Other hospital costs with LATERA, total	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted
Changes in other hospital costs, total	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted
Net changes	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted
<b>Cost to Prostheses List</b>						
Prosthesis costs with LATERA, total	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted
Changes in prosthesis	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted
Net financial implications, total	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted
<b>Total cost to Australian Healthcare</b>						

Year	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
LATERA costs, all resource items	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted
Changes in overall healthcare costs, all resource items	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted	-\$ redacted
Net financial implications	-\$298,079	-\$548,679	-\$780,716	-\$933,518	-\$1,054,452	-\$1,185,386

Source: Compiled from Table 83, 86, 88, 89, 90 and 91 applying the 75% MBS rebate

Abbreviations: LWI= lateral wall insufficiency; MBS= Medicare Benefits Schedule

<sup>a</sup> ADAR % of unilateral and bilateral procedures based on Clark (2018)

a Commentary note that 99-100% of LATERA patients had bilateral implants therefore the percentage could be 100% bilateral

The commentary considered the estimates provided in the ADAR to be uncertain and likely to be underestimated as:

- The estimates do not include any revision or subsequent rhinoplasty procedures following LATERA procedure. In the LATERA studies, up to 20% of patients did not respond to LATERA (these patients may end up seeking further intervention) and ~9% of patients experienced migration/extrusion/retrieval adverse events which could lead to reintervention/revision.
- The uptake of LATERA is potentially underestimated. The ADAR reports the proportion of rhinoplasty surgery in patients with LWI as 72% although only accounts for an uptake of **redacted** increasing to **redacted**% in Year 6. The ADAR uptake is based on LATERA being a less invasive alternative affected by doctor awareness/familiarity and patient acceptance. This approach may not be reasonable. No other market uptakes were provided as a proxy, such as uptake rates of LATERA in USA, Medtronic ALAR nasal valve stent or uptake rates of other uptake rates of implantable novel technologies.
- The estimates do not consider the potential for use beyond the evidence (i.e., in those with moderate NAO due to LWI, those electing for cosmetic device insertion over invasive rhinoplasty) although these would be captured in the 72% suggested by Clarke 2018. Importantly the MBS does not fund cosmetic procedures. Previous reviews of rhinoplasty have led to the refinement of item descriptors to clarify the clinical circumstances where MBS payments may be appropriate.<sup>21</sup>
- The estimates do not specifically consider NOSE score severity, Clarke 2018 found that 64% of the patients had severe/extreme NOSE scores ( $\geq 55$ ), representing the most likely nasal obstruction candidates for intervention.
- Bilateral LATERA implantation was conducted more frequently in the LATERA trials (87-99%) then estimated in Section 4 (84%) based on Clark 2018. Underestimated bilateral implantation increases the impact to the MBS.

<sup>21</sup> Medicare Benefits Schedule Review Taskforce. Interim Report to the Minister for Health 2016

<https://www.health.gov.au/sites/default/files/documents/2021/05/medicare-benefits-schedule-review-taskforce-interim-report.pdf>

**Table 26 Sensitivity analyses requested by ESC**

<b>Year</b>	<b>Year 1</b>	<b>Year 6</b>
<b>Base case</b>		
Total LATERA implantation procedures	redacted	redacted
Net change to the MBS	-\$ redacted	-\$ redacted
Net changes to other hospital resource use	-\$ redacted	-\$ redacted
Net change to the PL	\$ redacted	\$ redacted
Net financial implications to the Australian Healthcare system	-\$298,079	-\$1,185,386
<b>SA1 - compared to partial rhinoplasty only</b>		
Total LATERA implantation procedures	redacted	redacted
Net change to the MBS	-\$ redacted	-\$ redacted
Net changes to other hospital resource use	-\$ redacted	-\$ redacted
Net change to the PL	\$ redacted	\$ redacted
Net financial implications to the Australian Healthcare system	\$1,258	\$6,084
<b>SA2 - partial rhinoplasty only, all as same day procedure</b>		
Total LATERA implantation procedures	redacted	redacted
Net change to the MBS	-\$ redacted	-\$ redacted
Net changes to other hospital resource use	-\$ redacted	-\$ redacted
Net change to the PL	\$ redacted	\$ redacted
Net financial implications to the Australian Healthcare system	\$29,106	\$115,300
<b>SA3 - partial rhinoplasty only, all as same day procedure, all LATERA procedures bilateral</b>		
Total LATERA implantation procedures	redacted	redacted
Net change to the MBS	-\$ redacted	-\$ redacted
Net changes to other hospital resource use	-\$ redacted	-\$ redacted
Net change to the PL	\$ redacted	\$ redacted
Net financial implications to the Australian Healthcare system	\$29,927	\$118,657
<b>SA4 – partial rhinoplasty only, all as same day procedure, all LATERA procedures bilateral, 4.5% of LATERA procedures require reintervention</b>		
Total LATERA implantation procedures	redacted	redacted
Net change to the MBS	-\$ redacted	-\$ redacted
Net changes to other hospital resource use	-\$ redacted	-\$ redacted
Net change to the PL	\$ redacted	\$ redacted
Net financial implications to the Australian Healthcare system	\$35,435	\$140,300

## **15. Other relevant information**

Nil

## 16. Key issues from ESC to MSAC

### Main issues for MSAC consideration

#### Clinical issues:

- ESC considered that the primary comparator, functional rhinoplasty, for LATERA should be restricted to comparison with the partial rhinoplasty MBS items only, because the other rhinoplasty MBS items included in the application involve correction of bony
- ESC considered that the secondary comparator, conservative management, was not an appropriate comparator, as the clinical algorithm depicted that patients would be eligible for LATERA only after they had failed conservative management.
- The clinical claim that LATERA has non-inferior safety and effectiveness compared to functional rhinoplasty is uncertain as it is based on naïve comparisons of low certainty using low quality evidence with a moderate to high risk of bias.
- Given the lack of data on long-term effectiveness, ESC considered that it was uncertain whether patients would require either a repeat procedure or subsequent rhinoplasty at a later time.

#### Economic issues:

- As a consequence of the clinical issues, ESC considered that the cost-effectiveness analysis comparing LATERA with conservative management was not relevant to decision making, as conservative management was not an appropriate comparator.
- ESC considered that the cost-minimisation analysis comparing LATERA with functional rhinoplasty required substantial revision to include only partial rhinoplasty as the appropriate comparator.
- The overall cost savings relied on assumed hospital cost savings that may not be realistic if rhinoplasty is performed as a day procedure.
- The potential number of patients who require revision or removal of the device was not considered in the ADAR. ESC considered the cost-minimisation model should be extended to 2 years to account for reintervention and subsequent rhinoplasty procedures.
- Sensitivity analyses requested by ESC, testing the above parameters indicate the cost-savings of LATERA compared to rhinoplasty reported in the ADAR is highly uncertain.

#### Financial issues:

- ESC considered that the financial estimates required substantial revision in line with the economics to account for the appropriate comparator only, and to revise the prevalent population and projected rate of uptake.
- Sensitivity analyses requested by ESC indicated that the overall savings to the Australian Healthcare System reported in the ADAR may not be realised.
- The cost of the LATERA device appeared to be higher than other comparable bioabsorbable implants on the PL.
- Overall, ESC considered the financial estimates to be highly uncertain

#### Other relevant information:

- If the procedure is categorised as type C, consumers will face out-of-pocket costs if the procedure is performed in a consulting room, as the device (if included on the Prostheses List) would not be covered by Private Health Insurers.



## ESC discussion

ESC noted that the application sought Medicare Benefits Schedule (MBS) listing of services for the insertion of a bioabsorbable implant (LATERA) for the treatment of nasal airway obstruction (NAO) due to lateral wall insufficiency (LWI). ESC also noted that the applicant had also submitted an application to the Prostheses List Advisory Committee seeking listing of the LATERA implant on the Prostheses List (PL).

ESC noted the consultation feedback raised concern that consumers would face out-of-pocket costs if the LATERA device was not listed on the PL. Feedback also noted that the intervention may provide considerable cost savings compared with rhinoplasty, and may also save time for consumers and carers who rely on temporary relief through conservative management. ESC also noted feedback had queried whether the item could be claimed only once per lifetime or whether revision would be included. Feedback also highlighted that the procedure should not be provided by cosmetic surgeons, as the MBS cannot be used for cosmetic procedures.

ESC noted the commentary proposed MBS item descriptor and considered the descriptor should not specify “in patients contraindicated to general anaesthetic”, as the procedure can be done under either local or general anaesthetic. ESC noted the applicant’s pre-ESC response agreed with the commentary that the MBS item descriptor should specify a Nasal Obstruction Symptom Evaluation (NOSE) score of  $\geq 55$  (rather than  $>45$ ) to match the eligibility criteria and NOSE score of patients included in the clinical studies for the LATERA implant. ESC noted that the commentary had also posed a suggestion to increase the NOSE score to 70 based on the mean NOSE score in the LATERA studies. However, ESC did not consider this suggestion appropriate as it was not supported by the available evidence (i.e., the patients included in the LATERA clinical evidence had a NOSE score range of 55-100). ESC noted that MBS items for revision or removal had not been covered in the Applicant Developed Assessment Report (ADAR).

ESC noted the NOSE score is determined using an instrument<sup>22</sup> that is completed by patients and asks how much of a problem each of five conditions has been in the past month. ESC considered that several of the questions appeared to be overlapping and non-discriminatory – for example, the difference between “nasal blockage or obstruction” and “trouble breathing through my nose” was unclear. ESC queried whether an objective measure of nasal flow would be more appropriate. However, it was noted that objective measures are often not reproducible or concordant, and the NOSE score is consistently more sensitive and specific than objective measures in this field<sup>1</sup>.

ESC noted the clinical management algorithm (Figure 1), in which patients with NAO due to LWI with a NOSE score of 45 or more despite conservative management (that is, who have failed conservative management) could either continue conservative management, have insertion of a bioabsorbable implant or have functional rhinoplasty. Therefore, the nominated comparators are functional rhinoplasty (primary) and conservative management (secondary). ESC noted that patients with NAO have a very mixed aetiology, and while ~73% may have LWI it is often in conjunction with other causes of NAO such as inferior turbinate hypertrophy. As such, ESC considered only a small percentage of patients (~7%) would have isolated LWI causing NAO. ESC noted that functional rhinoplasty is covered by three existing MBS items. Partial rhinoplasty (MBS item 45632) involves correction of cartilage only and accounts for ~9% of utilisation of rhinoplasty items. The other two rhinoplasty MBS items are for total rhinoplasty that involves correction of all bony and cartilaginous elements of the external nose. MBS item 45641 (total rhinoplasty with or without autogenous cartilage or bone graft from a local site [nose]) accounts

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<sup>22</sup> Stewart MG, Witsell DL, Smith TL et al. (2004) Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. *Otolaryngol Head Neck Surgery*.130(2):157-63.

for 75% of utilisation of rhinoplasty items, and item 45644 (total rhinoplasty with autogenous bone or cartilage graft obtained from distant donor site) accounts for 16% of utilisation. ESC considered that the two total rhinoplasty MBS items involving correction to bony elements of the nose were not relevant to the proposed population with NAO due to LWI, as the implant only addresses the soft tissue component of obstruction. Therefore, the only relevant comparator for this population was partial rhinoplasty (MBS item 45632). ESC also did not consider the secondary comparison with conservative management to be useful for decision making noting that, as described in the clinical management algorithm, patients would be eligible for LATERA only after they had failed conservative management.

ESC noted the clinical evidence presented to support the comparison of LATERA versus functional rhinoplasty was highly uncertain. ESC noted that only naïve comparisons between LATERA and functional rhinoplasty were presented. The studies had variable follow-up periods and the rhinoplasty studies had variable surgical interventions. ESC noted that around 85% of patients in the LATERA studies received bilateral insertion of the device. Regarding comparative safety, ESC noted the most common adverse event for LATERA was implant retrieval/ exclusion/ migration, which was ~9% in the extended LATERA-RCT study. Regarding comparative effectiveness, ESC noted the ADAR reported that NOSE score reductions were potentially greater following LATERA compared with functional rhinoplasty at 6 months, 12 months and last follow-up. However, ESC noted that these conclusions were based on naïve comparisons of low certainty using low quality evidence with a moderate to high risk of bias.

ESC also noted a study comparing NOSE scores after autologous cartilage grafts compared with LATERA, which indicated that autologous grafting may be superior to LATERA<sup>23</sup>. ESC also noted data on the response rate over time from the LATERA studies indicated that >80% of patients who received LATERA achieved a response after 24 months (Table 17). ESC queried whether this meant that up to 20% of patients would go on to have either a repeat LATERA procedure or subsequent functional rhinoplasty procedure. In addition, ESC noted that long-term data on the longevity of the clinical effectiveness for LATERA were lacking. ESC considered that the applicant's assertion that the remaining scar tissue after the device had been bioabsorbed would be sufficient to maintain the effect was speculative. ESC noted that the applicant's claim that the device is bioabsorbed was based on a single animal study<sup>24</sup>. Given the lack of available data on the long-term effectiveness, for all patients, ESC queried whether LATERA would simply act as a bridge to functional rhinoplasty and would therefore only delay rhinoplasty and increase costs. ESC noted that there may be safety (and utilisation) data from the United States on LATERA which may be helpful in MSAC's decision making. However, based on the presented evidence, ESC considered that the ADAR's claim that LATERA has non-inferior effectiveness and at least non-inferior safety compared to functional rhinoplasty was uncertain.

ESC noted for the comparison of LATERA versus conservative management, a randomised controlled trial (RCT) comparing LATERA with sham treatment (as a proxy for conservative management) was presented. ESC noted the evidence indicated that compared to the sham procedure, LATERA likely reduces NOSE score at 3 months, likely increases the proportion of responders at 3 months, and likely reduces Visual Analog Scale score at 3 months. Most patients in the LATERA arm were of older age and had higher NOSE scores than patients in the sham arm (which may overestimate effectiveness of LATERA). The trial results reported the median change in score, not the proportion of patients with change in NOSE severity category. The study had a

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<sup>23</sup> Clark CM, Hakimi AA, Parsa KM, et al. Comparison of Nasal Obstruction Symptom Evaluation Score Outcomes After Autologous Cartilage Grafts and Latera Nasal Implants. *Annals of Otology, Rhinology & Laryngology*. 2022;0(0)

<sup>24</sup> Rippey MK, Baron S, Rosenthal M, Senior BA. Evaluation of absorbable PLA nasal implants in an ovine model. *Laryngoscope Invest Otolaryngol*. 2018 May 25;3(3):156-161.

moderate risk of bias and ESC noted the conflicts of interest of the study authors. ESC queried whether sham treatment was an appropriate proxy for conservative management, and considered the ADAR's claim that LATERA has superior effectiveness and superior safety compared to conservative management was uncertain. Although ESC considered these issues were less relevant if conservative management was excluded as a comparator altogether.

ESC noted the ADAR presented a cost-minimisation analysis comparing LATERA with functional rhinoplasty (primary comparator). ESC noted the main cost components for rhinoplasty were anaesthetist, ENT (ear, nose & throat) surgeon/rhinologist, and hospital stay costs, calculated based on the distribution of rhinoplasty surgeries across Australia. ESC considered that these costs should be revised to only include those for partial rhinoplasty as the appropriate comparator. ESC noted this would reduce the anaesthesia and theatre hospital costs for rhinoplasty. ESC also noted that the analysis did not list all of the costs associated with the intervention and the comparator, for example the analysis did not include follow-up costs for revisions or removals. ESC considered that the cost-minimisation model should be extended to 2 years to account for reintervention and subsequent rhinoplasty procedures. ESC requested sensitivity analyses (which were developed by the department) testing the above parameters (Table 20). ESC noted these sensitivity analyses suggested that the proposed cost savings are uncertain and in some circumstances, LATERA may be more costly than the comparator of partial rhinoplasty.

ESC noted the ADAR presented a cost-utility analysis comparing LATERA with conservative management (secondary). ESC noted the commentary raised a number of issues including assuming the comparator had zero cost, using utility values from septorhinoplasty with a different population to the LATERA studies, and did not include revision rates or safety costs. Overall, ESC considered that the cost-utility analysis comparing LATERA with conservative management was not useful for decision making.

ESC noted the issues identified with the comparator and inputs to the economic analyses flow on to impact the financial analysis. ESC noted the ADAR used a mixed epidemiological and market share approach, using the current MBS utilisation rates for rhinoplasty and assumed 72% of these procedures were patients who underwent rhinoplasty for LWI. The ADAR then assumed **redacted**% (Year 1) to **redacted**% (Year 6) of these patients would take up LATERA instead. The ADAR proposed there would be a net saving to the MBS of around **\$redacted** by Year 6. However, as noted earlier, ESC considered partial rhinoplasty involving cartilage only to be the appropriate comparator. ESC also agreed with the commentary that the rate of uptake was likely to be underestimated, and the revision rate was also not included. ESC requested sensitivity analyses (which were developed by the department) to test these parameters (Table 26). ESC noted that these additional analyses indicate that the ADAR proposed cost savings may not be realised in practice. Overall, ESC considered that the financial estimates were highly uncertain.

### Other discussion

ESC noted that the cost of the LATERA device is higher than other comparable bioabsorbable implants on the PL. ESC noted that if the application seeking listing of the LATERA implant on the PL was successful, that the location of the procedure will impact whether Private Health Insurers will pay a benefit for the implant (i.e., along with other requirements the patient must receive the product as part of hospital treatment or hospital substitute treatment). ESC considered it would be appropriate to categorise the LATERA procedure as a type C<sup>25</sup>. However, if the LATERA

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<sup>25</sup> Type C procedure – Under the Private Health Insurance (Benefits Requirements) Rules 2001, Type C procedures are procedures that do not normally require hospital treatment or accommodation. If a medical practitioner certifies that the

procedure is performed in a consulting room then consumers may face out-of-pocket costs for the cost of the LATERA implant that may not be covered by Private Health Insurers. ESC noted the applicant's pre-ESC response clarified that the applicant considered that the procedure will be mostly provided as a same-day hospital procedure and its use in outpatient consulting rooms will be rare. However, ESC noted that the procedure was designed to be used in consulting rooms, and that while PL listing may provide incentives to perform the procedure in hospitals, that clinical factors, not financial incentives, should be used to determine the appropriate setting for the procedure.

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

Stryker welcome MSAC's recommendation to create new MBS items for the insertion and removal of a bioabsorbable implant for nasal airway obstruction (NAO) due to lateral wall insufficiency (LWI). Stryker believes that the findings of this application are an important step forward in addressing an unmet clinical need and improving the clinical outcomes for patients suffering from NAO due to LWI.

## **18. Further information on MSAC**

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

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patient requires hospital treatment for a clinical reason, health insurers can pay hospital accommodation benefits (and associated PL costs). The majority of LATERA procedures could be undertaken in consulting rooms with a local anaesthetic, with a minority or more complex cases requiring a day surgery settings or overnight hospital treatment for clinical reasons.