



Australian Government

Department of Health

RATIFIED PICO

Application 1595:

**Closed-loop upper airway stimulation (UAS)
for moderate to severe obstructive sleep
apnoea (OSA), for patients who have failed
or are intolerant to continuous positive
airway pressure (CPAP)**

Summary of PICO/PPICO criteria to define the question(s) to be addressed in an Assessment Report to the Medical Services Advisory Committee (MSAC)

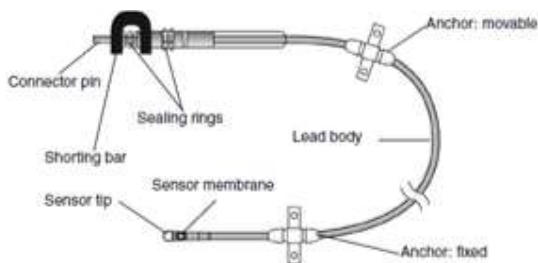
Component	Description
Patients	Patients aged ≥ 18 years with a BMI ≤ 32 kg/m ² and moderate to severe obstructive sleep apnoea (OSA), defined as having an Apnoea Hypopnea Index (AHI ^a) ≥ 15 and ≤ 65 , and who have been confirmed to have failed or cannot tolerate continuous positive airway pressure (CPAP) therapy or bi-level positive airway pressure (BIPAP) therapy. Patients with total concentric collapse at the soft palate level are not eligible.
Intervention	Implantation of an Upper Airway Stimulator System, including a respiratory sensing lead that senses breathing patterns, which is linked to an implantable pulse generator that delivers mild stimulation to the hypoglossal nerve via a stimulation lead.
Comparator	<p>Main comparator: Conservative medical management (e.g. weight and alcohol reduction; sleep hygiene).</p> <p>Supplementary comparator: Upper airway surgical procedures, such as uvulopalatopharyngoplasty (UPPP).</p> <p><i>Note: PASC determined that bariatric surgery^b is <u>not</u> adjunctive in the treatment of OSA in obese patients, given the restriction of the eligible population to those with a BMI ≤ 32 kg/m².</i></p>
Outcomes	<p>Efficacy/effectiveness</p> <ul style="list-style-type: none"> • Apnoea Hypopnoea Index (AHI) • Oxygen Desaturation Index (ODI) • Quality of Life <ul style="list-style-type: none"> ○ Epworth Sleepiness Scale (ESS) ○ Functional Outcomes of Sleep Questionnaire (FOSQ) <p>Safety</p> <ul style="list-style-type: none"> • Procedure related adverse events • Device related adverse events • Other adverse events <p>Healthcare resources</p> <ul style="list-style-type: none"> • Cost to deliver intervention <ul style="list-style-type: none"> ○ Subcutaneous placement of electrical pulse generator ○ Surgical placement of lead and connection to hypoglossal nerve ○ Surgical placement of respiratory sensing lead ○ Surgical repositioning or removal of electrical pulse generator <p>Total Australian Government Healthcare costs</p> <ul style="list-style-type: none"> • Total cost to the Medicare Benefits Schedule (MBS) • Total cost to other healthcare services

^a Apnoea Hypopnea Index measures the number of apnoea episodes per hour of sleep

^b Australian Guidelines for bariatric surgery suggest individuals with a BMI of 40kg/m², or with a BMI of 35kg/m² and one or more obesity-related complications should be eligible for surgery (1)

delivers stimulation to the hypoglossal nerve via a self-sizing cuff electrode that encircles the median division of the nerve (Figures 2 and 3).

Figure 2: Respiratory Sensing Lead



Source: Figure 2, p18 of the Application Form

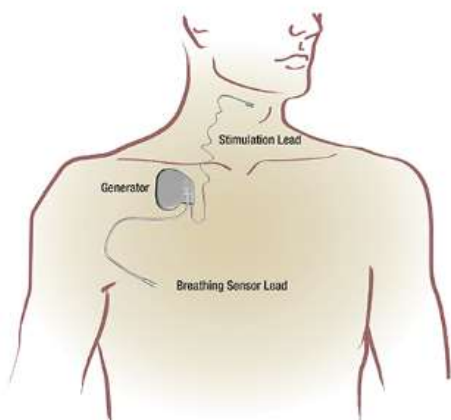
Figure 3: Stimulation Lead



Figure 3, p18 of the Application Form

The Inspire system is implanted under general anaesthetic via three small incisions. The stimulation electrode is placed on the median division of the hypoglossal nerve to recruit the tongue protrusion function. The sensing lead is placed via an incision in the fifth intercostal space and placed between the internal and external intercostal muscles to detect ventilatory effort. The IPG is placed in the right ipsilateral mid-infra-clavicular region (Figure 4).

Figure 4: Inspire System in situ



Comparator

PASC advised that 'conservative medical management' needs to be clearly defined in the assessment report. PASC recommended that (conservative intervention) oral devices should be considered, if appropriate (such as mandibular advancement splints).

The applicant has advised that oral devices are intended for use in patients with mild OSA, and are not in common use for moderate to severe OSA. The applicant therefore recommends that oral devices are not an appropriate comparator.

PASC is comfortable with this, as long as the applicant can justify it. PASC is still of the view that conservative medical management needs a clear definition.

PASC agrees that it might not be common in moderate and severe OSA, but the question is what happens to those who fail CPAP and do not receive surgery. PASC noted the American Academy of Dental Sleep Medicine 'Clinical Practice Guideline for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy' (2015 update) recommendations include:

"#3. We recommend that sleep physicians consider prescription of oral appliances, rather than no treatment, for adult patients with obstructive sleep apnea who are intolerant of CPAP therapy or prefer alternate therapy. (STANDARD)

"Quality of Evidence: Moderate"

(<http://dx.doi.org/10.5664/jcsm.4858>)

PASC noted that surgical measures may include one or more of a basket of surgeries, UPPP being one example. The supplementary comparator should therefore not be restricted to UPPP alone. The applicant has advised that UPPP is the most common surgery, adding that, as noted by PASC, UPPP is a reasonable and representative supplementary comparator.

The applicant recommends that, because of the diverse nature of surgeries other than UPPP, if PASC wishes another subset of surgeries be included as comparators, these should be specified. PASC recognises that the most common surgery is a basis for justification of the comparator. However, the justification and implications of this simplifying assumption should be explored and discussed in the assessment report.

PASC advised that bariatric surgery is not required as a comparator or adjunct, given the restriction of the population to patients with a BMI ≤ 32 kg/m².

PASC noted the applicant's estimated uptake of the intervention (153 services per year, after 3 years) was a small proportion of the eligible population (22,610 patients). The applicant stated this was primarily due to issues relating to patient access to ear, nose and throat surgeons, and appropriate facilities.

PASC considered that, if access is the main barrier, the comparator of conservative medical management is appropriate. However, PASC requested expert input to clarify whether access is the only issue, and whether this may affect the comparator for those patients who are not recommended for the intervention; that is, whether there are other differences between candidates for surgery and candidates for UAS (e.g. a different phenotype).

The applicant has advised that the UPPP population is not the same as the UAS population, but there is some crossover:

Current and Proposed Clinical Management Algorithms

PASC noted consultation feedback that DISE is not routinely used in Australia to select patients for OSA surgery. Confirmation (and justification) is needed if DISE will routinely be used to select patients for UAS, with associated reflection in the current and proposed algorithms.

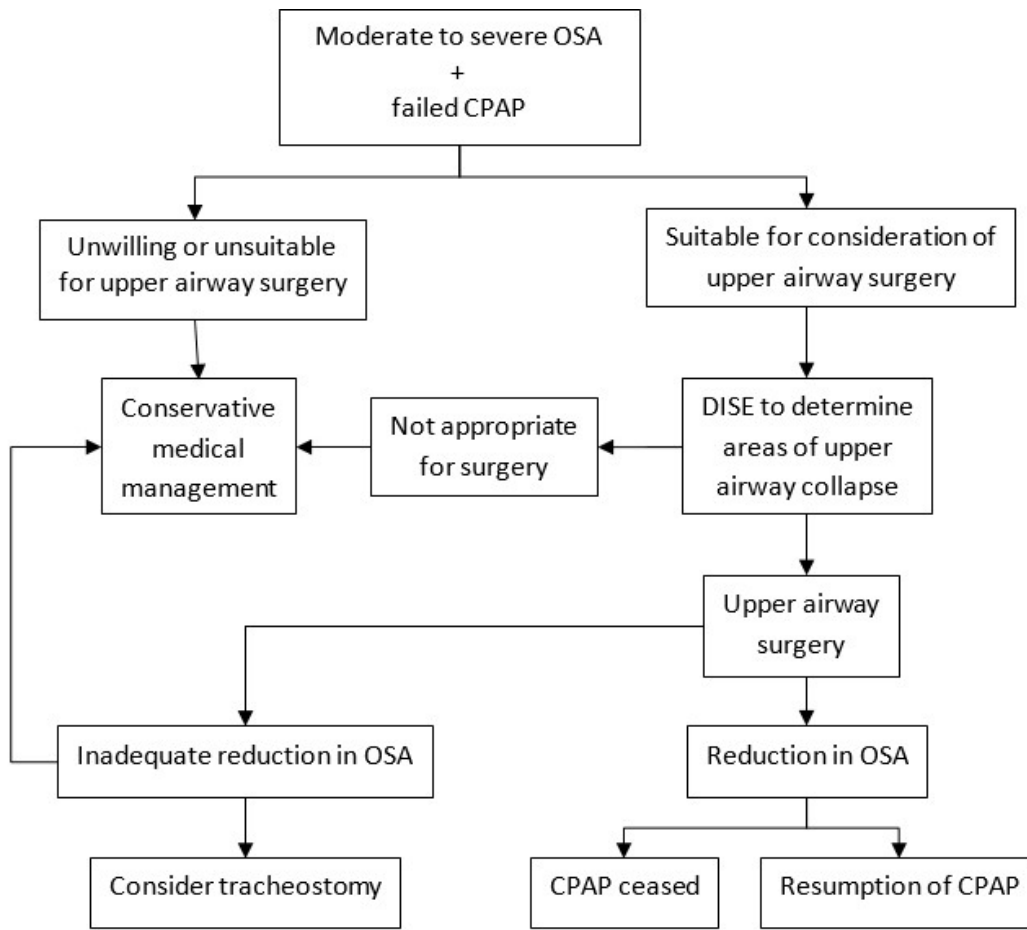
Current clinical management algorithm for identified population

The clinical pathway for patients who fail CPAP may be complex (Figure 5). Patients who are considered unsuitable or unwilling to have surgery may be managed conservatively by a sleep physician. Management may consist of lifestyle modifications such as weight loss, decrease in alcohol use and sleep position modification.

Some patients may be considered for upper airway surgery. A variety of upper airway surgeries exist, although only UPPP and maxillomandibular advancement (MMA) are specifically included on the MBS. MMA is rarely used to treat OSA although patients who have particular anatomic characteristics such as a receding chin may be suitable.(17)

Patients considered for UPPP must be carefully selected so surgery is targeted appropriately. Therefore, a DISE must be conducted prior to surgery. Patients may still use CPAP following surgery, as surgery may assist in increasing the tolerance and success of CPAP. Patients who fail surgery have limited options. Tracheostomy is rarely used but is a definitive treatment for OSA as the upper airway is bypassed, otherwise patients will continue to be conservatively managed.

Figure 5. Current clinical management algorithm



CPAP = continuous positive airway pressure treatment; DISE = drug induced sleep endoscopy; OSA = obstructive sleep apnoea

Note: (1) Bariatric surgery has been ruled out as adjunctive in the treatment of OSA in obese patients.

(2) The use of DISE needs to be confirmed and justified if it will routinely be used to select patients for UAS, with associated reflection in the current and proposed algorithms.

Proposed clinical management algorithm for identified population

The pathway following implementation of Inspire® therapy is similar to that following (UPPP) surgery or conservative management (Figure 6). However, it is unlikely that patients would use CPAP, as is the case with some patients following (UPPP) surgery. It is possible that some patients might proceed to surgery, although this is likely to be a smaller number than in the absence of closed-loop UAS, and in extreme cases, tracheostomy may be considered. Non-responders would likely be treated with conservative medical management.

Category 3 – Therapeutic Procedures	
YYYYY	<p>Proposed item descriptor: Unilateral closed-loop hypoglossal nerve stimulation therapy with Inspire® Upper Airway Stimulation System through stimulation of the hypoglossal nerve, surgical placement of lead, including connection of lead to the hypoglossal nerve and intra-operative test stimulation for management of moderate to severe obstructive sleep apnoea in a patient who:</p> <p>a) has an Apnoea Hypopnoea Index of greater than 15 and less than 65; and</p> <p>b) is aged 18 and over; and</p> <p>c) has failed or is intolerant to continuous positive airway pressure therapy; and</p> <p>d) has a BMI \leq 32 kg/m²; and</p> <p>e) does not have complete concentric collapse of the upper airway.</p> <p>Once only per patient</p> <p>Multiple Operation Rule (Anaes.)</p> <p>MBS Fee: \$684.95 Benefit: 75% = \$513.75 (in-hospital/admitted patient only)</p>

Category 3 – Therapeutic Procedures	
ZZZZZ	<p>Proposed item descriptor: Unilateral closed-loop hypoglossal nerve stimulation therapy with Inspire® Upper Airway Stimulation System through stimulation of the hypoglossal nerve, surgical placement of respiratory sensing lead and intra-operative test stimulation for management of moderate to severe obstructive sleep apnoea in a patient who:</p> <p>a) has an Apnoea Hypopnoea Index of greater than 15 and less than 65; and</p> <p>b) is aged 18 and over; and</p> <p>c) has failed or is intolerant to continuous positive airway pressure therapy; and</p> <p>d) has a BMI \leq 32 kg/m²; and</p> <p>e) does not have complete concentric collapse of the upper airway.</p> <p>Once only per patient</p> <p>Multiple Operation Rule (Anaes.)</p> <p>MBS Fee: \$684.95 Benefit: 75% = \$513.75 (in-hospital/admitted patient only)</p>

Category 3 – Therapeutic Procedures	
AAAAA	<p>Proposed item descriptor: Unilateral closed loop hypoglossal nerve stimulation therapy with Inspire Upper Airway Stimulation System through stimulation of the hypoglossal nerve, surgical repositioning or removal of electrical pulse generator, inserted for management of moderate to severe obstructive sleep apnoea in a patient who:</p> <p>a) has an Apnoea Hypopnoea Index of greater than 15 and less than 65; and</p> <p>b) is aged 18 and over; and</p> <p>c) has failed or is intolerant to continuous positive airway pressure therapy; and</p> <p>d) has a BMI \leq 32 kg/m², and</p> <p>e) does not have complete concentric collapse of the upper airway.</p>

Category 3 – Therapeutic Procedures	
Once only per patient	
Multiple Operation Rule (Anaes.)	
MBS Fee: \$161.95	Benefit: 75% = \$121.50 (in-hospital/admitted patient only)

In line with PASC’s advice, an MBS Explanatory Note should be considered, outlining the requirement for clinical expertise and patient management within a multidisciplinary environment.

Consultation feedback

PASC noted the consultation feedback, highlighting the importance of:

- BMI restriction in trials;
- importance of multi-disciplinary care; and
- importance of appropriate selection for type of surgery or UAS.

PASC also noted the feedback that early research was underway to investigate use of UAS in children, and those with complete collapse.

Next steps

Upon ratification of PICO 1595, the application can PROCEED to the pre-Evaluation Sub-Committee (ESC) stage.

The applicant has elected to prepare its own ADAR (applicant-developed assessment report).

References

1. Lee PC, Dixon J. Bariatric-metabolic surgery: A guide for the primary care physician. Australian family physician. 2017;46(7):465.
2. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med. 2002;162(8):893-900.
3. Marshall NS, Wong KK, Liu PY, Cullen SR, Knuiman MW, Grunstein RR. Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep. 2008;31(8):1079-85.
4. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005;365(9464):1046-53.
5. Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. J Clin Sleep Med. 2009;5(6):573-81.
6. Strollo Jr PJ, Soose RJ, Maurer JT, de Vries N, Cornelius J, Froymovich O, et al. Upper-airway stimulation for obstructive sleep apnea. New England Journal of Medicine. 2014;370(2):139-49.
7. Thaler E, Schwab R, Maurer J, Soose R, Larsen C, Stevens S, et al. Results of the ADHERE upper airway stimulation registry and predictors of therapy efficacy. The Laryngoscope. 2019.
8. Deloitte Access Economics. Re-awakening Australia. The economic cost of sleep disorders in Australia 2010 for the Sleep Health Foundation. 2011.
9. Adams R. Report to the Sleep Health Foundation 2016 Sleep Health Survey of Australian Adults. 2016.
10. Senaratna CV, English DR, Currier D, Perret JL, Lowe A, Lodge C, et al. Sleep apnoea in Australian men: disease burden, co-morbidities, and correlates from the Australian longitudinal study on male health. BMC Public Health. 2016;16(Suppl 3):1029.
11. Australian Institute of Health and Welfare. Procedure Data Cubes 2017-2018 2019 [Available from: <https://www.aihw.gov.au/reports/hospitals/procedures-data-cubes/contents/data-cubes>].
12. Smith DF, Cohen AP, Ishman SL. Surgical management of OSA in adults. Chest. 2015;147(6):1681-90.
13. Virk JS, Kotecha B. When continuous positive airway pressure (CPAP) fails. J Thorac Dis. 2016;8(10):E1112-E21.
14. Mohammadih A, Sutherland K, Cistulli PA. Sleep disordered breathing: management update. Internal medicine journal. 2017;47(11):1241-7.
15. Epstein LJ, Kristo D, Strollo PJ, Friedman N, Malhotra A, Patil SP, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. Journal of clinical sleep medicine. 2009;5(03):263-76.

16. Mechanick JI, Youdim A, Jones DB, Garvey WT, Hurley DL, McMahon MM, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient—2013 update: cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Obesity*. 2013;21(S1):S1-S27.
17. Virk JS, Kotecha B. Otorhinolaryngological aspects of sleep-related breathing disorders. *J Thorac Dis*. 2016;8(2):213-23.