Australian Government

Department of Health

Application Form

Closed loop upper airways stimulation for moderate to severe obstructive sleep apnoea, for patients who have failed or are intolerant to continuous positive airways pressure

(New and Amended Requests for Public Funding)

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires in order to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Phone: +61 2 6289 7550
Fax: +61 2 6289 5540
Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):
Corporation name: Inspire® Medical Systems Inc
ABN: REDACTED
Business trading name REDACTED

Primary contact name: REDACTED

Primary contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

Alternative contact name: REDACTED

Alternative contact numbers
Business: REDACTED
Mobile REDACTED
Email: REDACTED

2. (a) Are you a lobbyist acting on behalf of an Applicant?

☒ Yes
☐ No

(b) If yes, are you listed on the Register of Lobbyists?

☒ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Closed Loop Upper Airways Stimulation (UAS) for Moderate to Severe Obstructive Sleep Apnoea (OSA) for patients who have failed or are intolerant to Continuous Positive Airways Pressure (CPAP)

4. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Obstructive Sleep Apnoea (OSA) with Apnoea Hypopnoea Index (AHI) of greater than or equal to 15 in patients who have failed or are intolerant to CPAP therapy

5. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

Implantation of an Upper Airways Stimulator System. The system includes a respiratory sensing lead that senses breathing patterns. The respiratory sensing lead is linked to an implantable pulse generator that delivers mild stimulation to the hypoglossal nerve via a stimulation lead.

6. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☒ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

Not applicable

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

Not applicable

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☐ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

(g) If yes, please advise:

Not applicable

7. What is the type of service:

☒ Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☐ Co-dependent technology
☐ Hybrid health technology

8. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☐ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☐ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☐ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

☐ Pharmaceutical / Biological
☒ Prosthesis or device
☐ No

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

Not applicable

☐ Yes
☐ No

(b) If yes, please list the relevant PBS item code(s):

Not applicable

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

Not applicable

☐ Yes (please provide PBAC submission item number below)
☐ No

Not applicable

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Not applicable

Trade name: Not applicable
Generic name: Not applicable

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

☐ Yes
☒ No

(b) If yes, please provide the following information (where relevant):

Billing code(s): Not applicable
Trade name of prostheses: Not applicable
Clinical name of prostheses: Not applicable
Other device components delivered as part of the service: Not applicable

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

☐ Yes
☒ No

An application will be made at a later date following completion of the MSAC application process

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
☒ No

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

There have been devices manufactured in the past that stimulate the hypoglossal nerve, however none have included a respiratory sensing lead. To our knowledge, these devices are not available in Australia

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: A tunnelling tool is included in the Inspire® System.
Multi-use consumables: Not applicable

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good: Inspire® Upper Airway Stimulator
Manufacturer's name: Inspire® Medical Systems Inc
Sponsor's name: REDACTED

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☐ Class III
☒ AIMD
☐ N/A

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☒ No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

☐ Yes (if yes, please provide details below)
☒ No

ARTG listing, registration or inclusion number: Not applicable
TGA approved indication(s), if applicable: Not applicable
TGA approved purpose(s), if applicable: Not applicable

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

☒ Yes (please provide details below)
☐ No

Date of submission to TGA: REDACTED
Estimated date by which TGA approval can be expected: REDACTED
TGA Application ID: REDACTED
TGA approved indication(s), if applicable: Not applicable
TGA approved purpose(s), if applicable: Not applicable

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

Not applicable

☐ Yes (please provide details below)
☐ No

Estimated date of submission to TGA: Not applicable
Proposed indication(s), if applicable: Not applicable
Proposed purpose(s), if applicable: Not applicable

PART 4 – SUMMARY OF EVIDENCE

17. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
1.	Multicentre prospective, single-group, cohort design. Consecutive responsive participants were included in a randomised controlled therapy-withdrawal trial	Strollo PK, Soose RJ, Maurer JT, de Vries N, Cornelius J, Froymovich O, Hanson RD, Padhya TA, Steward DL, Gillespie B, Woodson T, Van de Heyning PH, Goetting MG, Vanderveken OM, Feldman N, Knaack L, Strohl KP *'Upper-Airway Stimulation for Obstructive Sleep Apnea'* N Engl J Med 2014; 370:139-49	126 patients were surgically implanted with an upper airway stimulation device. There were significant improvements in primary outcome measures that included apnea-hypopnea index (AHI), oxygen desaturation index (ODI). Secondary outcome measures also improved including the Epworth Sleepiness Scale (ESS), and the Functional Outcomes of Sleep Questionnaire (FOSQ) and % of sleep time with O^2 saturation < 90%	NEJM	January 9 2014

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
2.	**Multicentre prospective, single-group, cohort design. Consecutive responsive participants were included in a randomised controlled therapy-withdrawal trial**	**Woodson BT, Strohl KP, Soose RJ, Gillespie MB, Maurer JT, de Vries N, Padhya TA, Badr MS, Lin H, Vanderveken OM, Mickelson S, Strollo PJ *'Upper Airway Stimulation for Obstructive Sleep Apnea: 5-Year Outcomes'*** **Otalaryngology-Head and Neck Surgery 1-9 2019=8**	**5 year follow up of 126 patients who were surgically implanted with an upper airway stimulation device. (see above) Primary outcome measures were apnea-hypopnea index, oxygen desaturation index. Secondary outcome measures were the Epworth Sleepiness Scale, and the Functional Outcomes of Sleep Questionnaire and % of sleep time with O^2 saturation < 90%**	**Otolaryngology – Head and Neck Surgery**	**February 2018**
3.	**Multicentre, prospective and retrospective observational registry**	**Heiser C, Steffen A, Boon M, Hofauer B, Dofhramji K, Maurer JT, Sommer JU, Soose R, Strollo PJ, Schwab R, Thaler, E Withrow K, Kominsky A, Larsen C, Kezirian EJ, Hsia J, Chia S, Hareick J, Strohl K, Mehra R *'Post-Approval Upper Airway Stimulation Predictors of Treatment Efficacy in the Adhere Registry'*** **doi:10.1183/13993003.01405-2018**	**International multinational registry. 508 patients who had received upper airways stimulation were enrolled in 14 centres. Data collected included patient characteristics, AHI, ESS, objective adherence, adverse events and patient satisfaction measures**	**Euro Resp Journ**	**Nov 28 2018**

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
4.	**Meta-analysis of upper airways stimulation for the management of obstructive sleep Apnoea**	**Kompelli AR, Ni JS, Nguyen SA, Lentsch EJ, Neskey DM, Meyer TA *'The outcomes of hypoglossal nerve stimulation in the management of OSA: A systematic review and meta-analysis'* World J Otor. Head and Neck Surg. (2018) xx, 1-8**	**Meta-analysis and systematic review examining clinical trials of hypoglossal nerve stimulation (HNS) in adults.**	**World J Otor – Head and Neck Surg**	**2018**
5.	**Cost-Effectiveness Analysis of the Upper Airway Stimulation for the treatment of OSA**	**Pietzsch JB, Lui S, Garner AM, Kezirian EJ, Strollo PJ *'Long-Term Cost-Effectiveness of Upper Airway Stimulation for the Treatment of Obstructive Sleep Apnea: A Model-Based Projection Based on the STAR Trial'* SLEEP 2015:38(5): 735-744**	**5-State Markov model was used to predict cardiovascular endpoints (myocardial infarction, stroke, hypertension), motor vehicle collisions and QALYS and costs of UAS versus no treatment**	**SLEEP**	**May 1 2015**
6.	**Multicentre prospective single arm study of UAS for moderate to severe sleep apnoea**	**Steffen A, Sommer JU, Hofauer B, Maurer JT, Hasselbacher K, Heiser C, *'Outcomes After One Year of Upper Airway Stimulation for Obstructive Sleep Apnea in a Multicenter German Post-Market Study'* Laryngoscope, 00:000-00, 2017**	**60 patients were followed for 12 months measuring home sleep test results and patient-reported outcome measures.**	**https://onlinelibrary.wiley.com/doi/abs/10.1002/lary.26688**	**May 31 2017**

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

18. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). *Please do not attach full text articles, this is just intended to be a summary.*

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
1.	**Randomized, sham-controlled double-blinded, crossover trial**	**Cardiovascular Endpoints for Obstructive Sleep Apnea with Twelfth Nerve Stimulation (CARDIOSA-12): A Randomized, Sham-Controlled Double-Blinded, Crossover Trial**	**Patients will be randomized to sham UAS or therapeutic UAS for 28 days with sympathetic and vascular testing. Following a washout period the patients will be switched to the other intervention arm for 28 days**	**https://www.ncbi.nlm.nih.gov/pubmed/30194765**	**June 30 2020**

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
2.	**Prospective, multicentre, randomized, crossover assignment**	**Effect of Upper Airway Stimulation: A Randomized Controlled, Crossover Study**	**Subjects will be enrolled after they have been implanted using the Inspire device for at least 6 months. Participants will be randomised to either therapeutic stimulation or sham stimulation. During the second phase the therapy settings of the stimulation therapy will be adjusted for crossover**	**https://clinicaltrials.gov/ct2/show/NCT03760328?term=hypoglossal+nerve+stimulation&rank=13**	**June 30 2020**

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
3.	Observational Registry	**Adherence and Outcome of Upper Airway Stimulation (UAS) for OSA International Registry**	Observational Registry of 5000 participants with 12 month follow up.	**https://clinicaltrials.gov/ct2/show/NCT02907398?term=hypoglossal+nerve+stimulation&rank=19**	

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*

****Date of when results will be made available (to the best of your knowledge).*

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. **List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):**

    Australasian Sleep Association

20. **List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):**

    Royal Australian College of Physicians (Respiratory Medicine and Sleep Medicine)

21. **List the relevant consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):**

    Sleep Health Foundation was the only group that was identified. They are a charitable organisation and are not representative of consumers.

22. **List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:**

    Both Liva Nova and Apnex Medical supply hypoglossal nerve stimulators, however these are 'open loop' systems without a respiratory sensing lead.

23. **Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):**

    Name of expert 1: REDACTED

    Telephone number(s REDACTED

    Email address: REDACTED

    Justification of expertise:

    REDACTED.

    Name of expert 2: REDACTED

    Telephone number(s): REDACTED

    Email address: REDACTED

    Justification of expertise:

    REDACTED

    Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INDICATION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

The Inspire® Upper Airways Stimulation (UAS) System is intended to be used in adult patients who have been confirmed to have moderate to severe obstructive sleep apnoea (OSA) and who have also been confirmed to have failed or cannot tolerate continuous positive airways pressure (CPAP) therapy or bi-level positive airway pressure (BIPAP) therapy and who do not have concentric collapse at the soft palate level.

Moderate to severe OSA is defined as having an Apnoea Hypopnea Index (AHI) of greater than or equal to 15 and less than or equal to 65. AHI measures the number of apnoea episodes per hour of sleep. Failure of continuous positive airway pressure (CPAP) therapies is defined as an inability to eliminate OSA (AHI of greater than 20 despite CPAP usage) and CPAP intolerance is defined as

1. Inability to use CPAP (greater than 5 nights per week of usage: usage defined as greater than 4-hours of use per night), or

2. Unwillingness to use CPAP (for example, a patient returns the CPAP system after attempting to use it).

OSA is a disorder of sleep which is characterised by repeated upper airway obstructions during the night, with resultant oxygen desaturations and arousals. OSA occurs when breathing is repetitively interrupted during sleep due to collapse of the upper airway. An apnoea is defined as a complete cessation of breathing lasting 10 seconds or greater. Approximately 10% of middle-aged men and 5% of middle-aged women in the general population are likely to have OSA (defined as > 10 obstructed breathing events/hour of sleep)[1]. Deloitte Access Economics[2] estimated in 2011 the Australian prevalence of OSA with ≥ 15 AHI to be 2.2% for women, 7.2% for men with an overall prevalence of 4.7%. The Sleep Health Survey of Australian Adults in 2016[3] estimates that doctor diagnosed sleep apnoea is 8.3% overall (men-12.9% and women 3.7%).

Cross sectional and longitudinal studies have suggested that moderate to severe OSA is independently associated with greater risk of all-cause mortality after adjustment for age, gender, mean arterial pressure, total cholesterol, high density lipo-protein cholesterol, body mass, diabetes, angina and smoking status[4] and a higher incidence of fatal and non-fatal cardiovascular events in patients with severe disease[5]. OSA is also associated with daytime sleepiness and an increased incidence of road accidents[6]. Overall OSA that is unable to be treated by CPAP represents a significant societal burden.

25. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be

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[1] Young T et al *'Predictors of sleep-disordered breathing in community-dwelling adults: The Sleep Heart Health Study.'* Archives of internal medicine 2002; 162 (8): 893-900

[2] '*Re-awakening Australia. The economic cost of sleep disorders in Australia 2010*' for the Sleep Health Foundation October 2011. Deloitte Access Economics.

[3] Adams R et al *'Report to the Sleep Health Foundation 2016 Sleep Health Survey of Australian Adults'.*

[4] Mashall NS et al *'Sleep Apnea as an Independent Risk Factor for All-Cause Mortality: The Busselton Health Study'* Sleep 2008 Aug 1; 31(8): 1079-1085

[5] Marin JM *'Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study'* Lancet Vol 365, Iss 9464, P1046-1053, March 19, 2005

[6]Treager S et al *'Obstructive sleep apnea and risk of motor vehicle crash: systemic review and meta-analysis'* J Clin Sleep Med 2009 Dec 15;5 (6): 573-81.

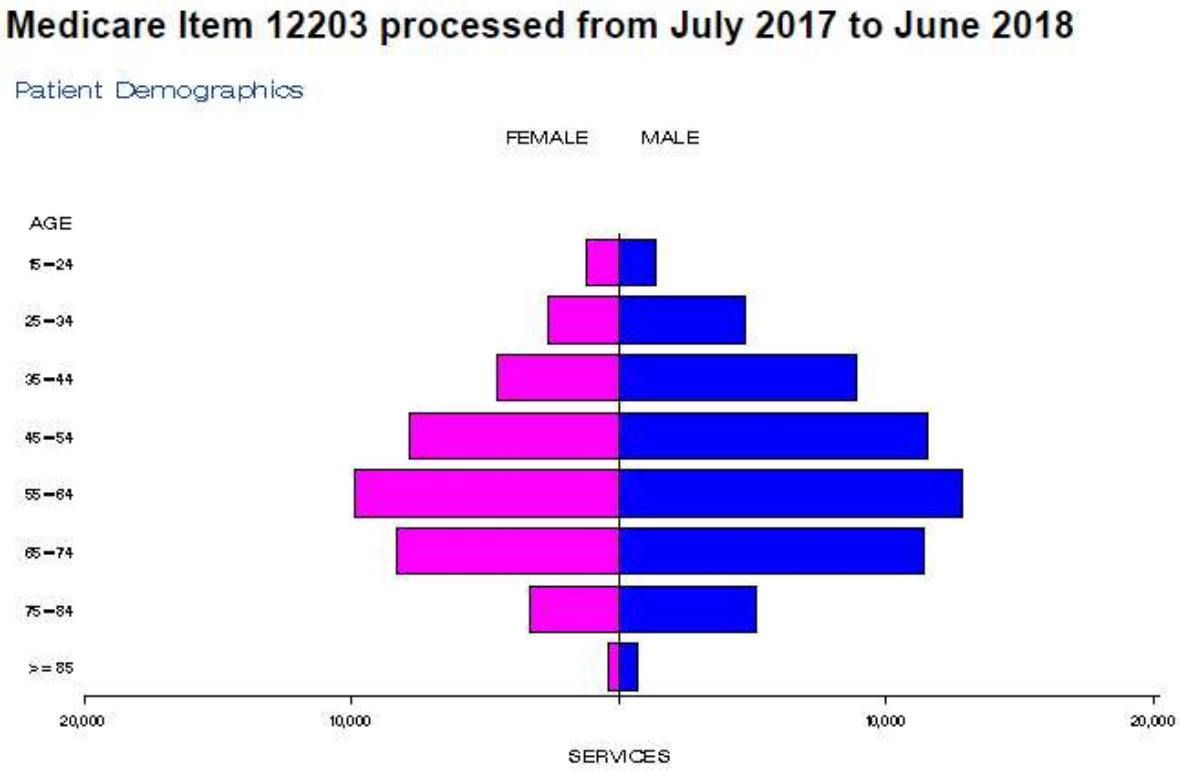
investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

OSA is more likely to occur in men than in women with a variety of prevalence studies consistently finding the disorder is more common in men. An Australian study, of men only, found that OSA was associated with older age, obesity, chronic obstructive airways disease, diabetes, asthma, hypercholesterolemia, and hypertension, and other lifestyle related disorders[7]. There are no specific item numbers on the Medical Benefits Schedule for the *treatment* of OSA. Therefore, it is difficult to accurately assess the demographic profile of Australians being treated for OSA. it is also likely that hospital admissions are for sleep investigations rather than treatment of OSA. It is therefore more useful to look at the demographics of those Australians undergoing sleep investigation for demographic detail.

There are two item numbers that relate to adult sleep investigations. Although it cannot be at all certain whether these people will receive a diagnosis of OSA, it is nevertheless a snapshot of those seeking treatment for sleep disorders.

MBS Item 12203 is a Level 1 Sleep Investigation. This item number was claimed 94,829 times in the 2017/2018 financial year. Please see the demographic distribution below in Figure 1.

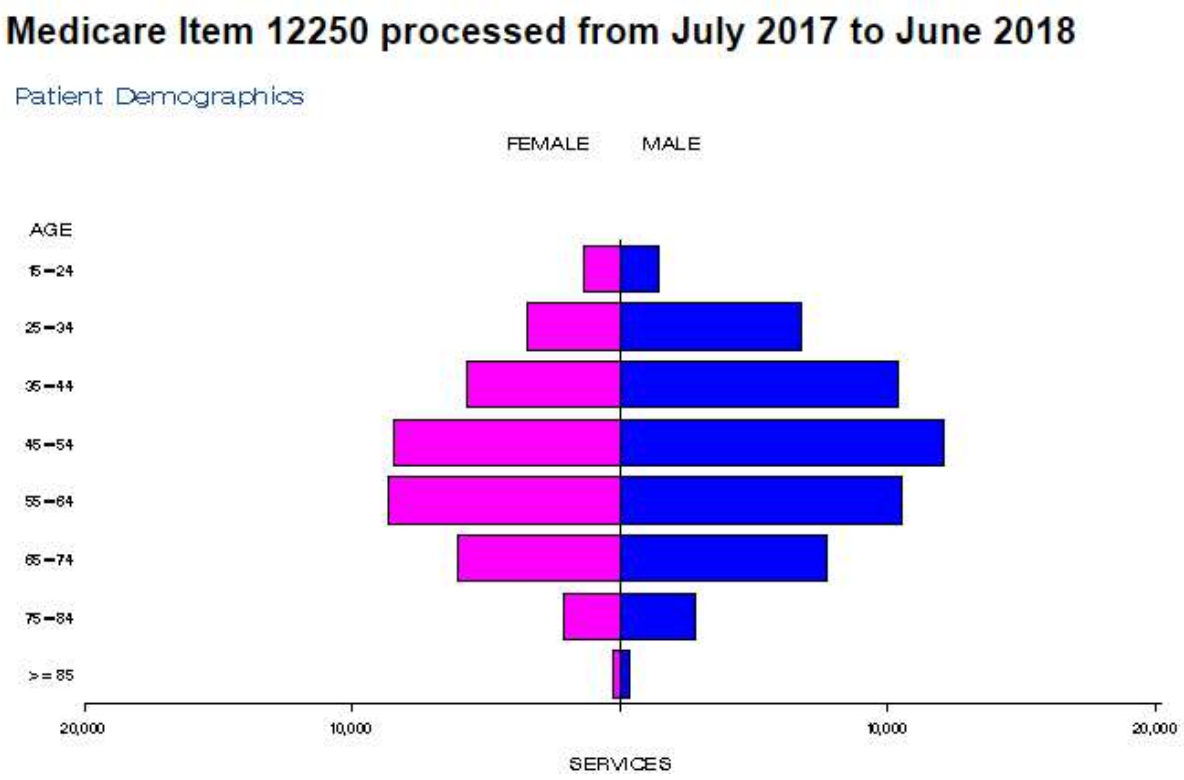
Figure 1



Medicare Item 12250 is a Level 2 Sleep Investigation. This item was claimed 88,136 times in the 2017/2018 financial year. Please see the demographic distribution below in Figure 2

[7] Senaratna CV 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): 10-29

Figure 2



Patients are likely to initially present to a general practitioner (GP) with one or more of a variety of symptoms. These may include excessive daytime sleepiness, loud snoring, observed episodes of stopped breathing during sleep, abrupt waking with gasping or choking, waking with a dry mouth or sore throat, morning headache, difficulty in concentration, mood changes or depression or irritability, night-time sweating or decreased libido. The patient may then be referred to a sleep specialist or otherwise a GP may make a referral directly for a diagnostic sleep study when validated screening questionnaires suggest a high pre-test probability for diagnosis of moderate to severe OSA.

The patient is then likely to undergo either a Level 1 sleep investigation (12203) or a Level 2 investigation (12250). Should the result of the investigation determine that the patient has OSA, then a trial of CPAP is instigated. Should the trial of CPAP be unsuccessful in eliminating OSA, or the patient is unable to tolerate CPAP, due to claustrophobia or similar reason, a patient may be considered for UAS.

Prior to surgery, an endoscopy under sedation must be performed so that the patient's upper airway anatomy may be observed in a sleep like state. The otalaryngologist is looking for the absence of a complete concentric collapse at the level of the soft palate. Patients with a complete collapse of the soft palate are not suitable for USA.

26. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):

As noted above patients who would be considered eligible for closed loop UAS with the Inspire® therapy would be likely to present to a General Practitioner. The patient may then be referred to a sleep physician or may proceed directly to a Level 1 or Level 2 sleep investigation. Following a diagnosis of moderate to severe sleep apnoea, a patient would undergo a trial of CPAP. Should CPAP be unsuccessful or not tolerated, a patient may be considered for Closed Loop UAS. A drug induced sleep endoscopy (DISE) is conducted to exclude patients who may have a complete concentric collapse of the soft palate. Once suitability for Closed Loop UAS is confirmed a patient may proceed to implant of the Inspire® device.

Please see the attached Clinical Pathway.

PART 6b – INFORMATION ABOUT THE INTERVENTION

27. Describe the key components and clinical steps involved in delivering the proposed medical service:

The Inspire® System consists of three components, an implantable pulse generator (IPG), a respiratory sensing lead and a stimulation lead. The leads connect to the IPG via two connection ports. Please see Figure 1

Figure 1: Inspire IPG and Connector Ports

The respiratory sensing lead detects respiratory effort. The lead has a pressure-sensitive membrane that converts the mechanical energy of respiration into an electronic signal. The stimulation lead delivers stimulation to the hypoglossal nerve via a self-sizing cuff electrode that encircles the median division of the nerve. Please see Figures 2 and 3

Figure 2: Respiratory Sensing Lead

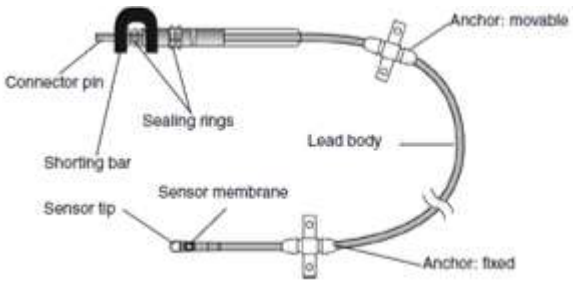
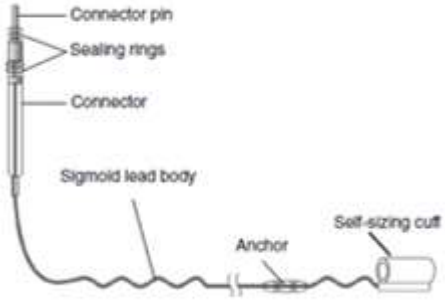
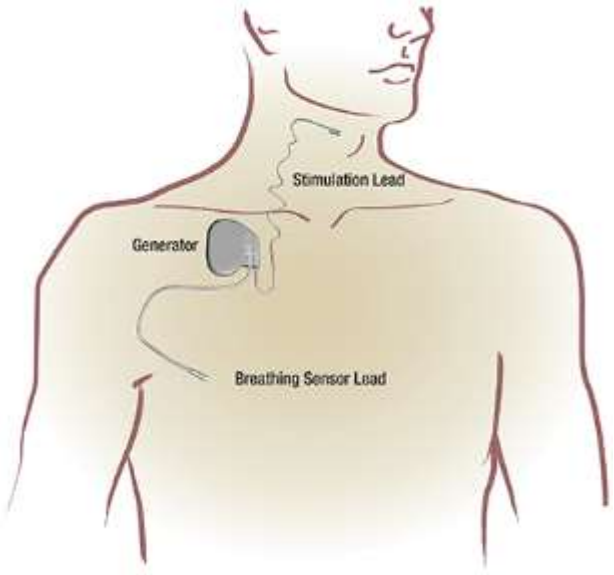


Figure 3: Stimulation Lead



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 place in the right ipsilateral mid-infra-clavicular region. Please see Figure 4

Figure 4: Inspire System in situ



To allow for healing, activating the device is delayed until approximately one month after surgery. The device is switched on and the patient begins therapy. The Inspire device continuously monitors the patient's breathing patterns and delivers mild hypoglossal nerve stimulation during inspiration to prevent airways collapse. The device is activated by the patient using a hand-held remote control. Therapy is adjusted by the specialist at a follow up monitoring visit(s). Patients are likely to have at least one sleep study following the procedure.

28. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

REDACTED.

29. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

Yes. The Inspire® Upper Airway Stimulation System is designed to treat patients with moderate to severe OSA who have failed or who are intolerant of CPAP. Patients indicated for the therapy are those with an AHI ≥ 15 and ≤ 65. Patients who have a complete concentric collapse at the soft palate level are not considered suitable. While OSA is associated with a high BMI, the majority of clinical evidence pertains to patients with a BMI < 32 kg/m².

30. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

Yes

There may be limitations in access to qualified specialists who have trained in the proper use and surgical procedure associated with Inspire® therapy. Should the new medical service be recommended, and the Inspire® System subsequently included on the Prostheses List, then it is more likely that the procedure would be carried out in private hospitals on those patients who have private health insurance. There may be budget constraints in the public hospital system.

A majority of ENTs practice in major cities so patients who live in rural or remote areas may have difficulty in accessing the service.

The device battery is conservatively estimated to last 10 years, so the initial procedure is likely to be carried out only once. Once the battery has depleted, the IPG may be removed and attached to the existing leads which would remain in situ.

31. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

Other than the procedure to implant the device and the services associated with the hospital admission, there are no other services required.

32. If applicable, advise which health professionals will primarily deliver the proposed service:

Ear, Nose and Throat Surgeon

33. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

The procedure should not be delegated.

34. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

It is not anticipated that there be any limitations on who might provide a referral for a service, although it is likely that GPs, specialist sleep physicians, or respiratory physicians may be the most likely referrers. Many ear nose and throat surgeons specialise in sleep disorders.

35. If applicable, advise what type of training or qualifications would be required to perform the proposed service as well as any accreditation requirements to support service delivery:

Nose and Throat surgeons will have fulfilled the requirements of the Australian Society of Otolaryngology Head and Neck Surgery (ASOHNS) or be otherwise qualified to practice this specialty in Australia.

Extensive training, provided by Inspire® Medical Systems, is required before ENTs may deliver this therapy. Training includes off-site classroom training and cadaver training. The first 3-5 cases conducted by an ENT are proctored and Inspire® Medical Systems is likely to provide continued theatre support for ENTs.

In addition to specific surgical training for ENTs, training is provided to operating room staff, sleep physicians and sleep laboratory staff. Additional training is provided to sleep physicians and other sleep or ENT clinic staff so that activation and programming of the device is appropriate.

36. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select all relevant settings):

- ☒ Inpatient private hospital
- ☒ Inpatient public hospital
- ☐ Outpatient clinic
- ☐ Emergency Department
- ☐ Consulting rooms
- ☐ Day surgery centre
- ☐ Residential aged care facility
- ☐ Patient's home
- ☐ Laboratory
- ☐ Other – please specify below

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

The service must be performed in an appropriate operating theatre under general anaesthetic. A proportion of patients may be appropriate for a same day discharge where others may have an overnight stay.

37. Is the proposed medical service intended to be entirely rendered in Australia?

- ☒ Yes
- ☐ No – please specify below

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

Patients who fail CPAP or who are intolerant of CPAP are usually managed by their GP or sleep physician with conservative measures. There are surgical treatment options for patients who fail CPAP. Surgical measures such as uvulopalatopharyngoplasty (UPPP) are implemented in a small proportion of patients who have been identified by DISE as being suitable for this type of intervention. These surgeries are designed to increase the volume of the airways. There was a total of 607 UPPP's and 1276 UPPP's with tonsillectomy performed in Australia in 2017-2018[8]. Surgical management of OSA has limited success[9] and CPAP may still necessary to reduce OSA[10]

The main comparator to closed loop UAS is conservative medical management.

39. Does the medical service that has been nominated as the comparator have an existing MBS item number(s)?

Medical management may consist of lifestyle changes such as weight and alcohol reduction and sleep hygiene. There is no pharmaceutical therapy available for OSA.

☒ Yes (please provide all relevant MBS item numbers below)
☐ No

41786

UVULOPALATOPHARYNGOPLASTY, with or without tonsillectomy, by any means

Multiple Operation Rule

(Anaes.) (Assist.)

Fee: $748.80 Benefit: 75% = $561.60

These would be included under GP and specialist attendance items (MBS 23, 24, 36, 37, 104, 105). UPPP is included on the MBS under MBS 41786

40. Define and summarise the current clinical management pathways that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards including health care resources):

The clinical pathway for patients who fail CPAP may be complex. 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 airways surgery.

A variety of upper airways 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.[11].

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[8] Australian Institute of Health and Welfare. Procedure Data Cubes 2017-2018. https://www.aihw.gov.au/reports/hospitals/procedures-data-cubes/contents/data-cubes

[9] Smith DF et al *'Surgical management of OSA in adults'* Chest 2015 Jun; 147 (6): 1681-1690

[10] Virk, JS and Kotecha B *'When continuous positive airways pressure (CPAP) fails'* J Thorac Dis. 2016 Oct 8 (10): E1112-E1121

[11] Virk JS and Kotecha B *'Otorhinolaryngological aspects of sleep-related breathing disorders'* J Thorac Dis 2016 Vol 8, No 2 (February 2016)

Patients who fail CPAP may be considered for UPPP. Patients must be carefully selected for appropriateness and surgery must be 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.

41. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

It is anticipated that closed loop UAS will be used instead of conservative management and some upper airways surgeries. Should the service be included on the MBS, there may initially be patients who have previously failed UPPP or other surgeries who may be eligible. It is, however, intended that closed loop UAS be used as a second line therapy following failed CPAP.

☐ Yes
☐ No

(b) If yes, please outline the extent of which the current service/comparator is expected to be substituted:

It is difficult to estimate the number of people in the community who are receiving conservative management following failed CPAP. Should closed loop UAS be included on the MBS, then it is anticipated that a proportion of patients who are currently being treated with UPPP will be treated with closed loop UAS instead. Only a proportion of patients receiving UPPP will be eligible for UAS. Patient with total concentric collapse, or who are aged less than 22 are not eligible. It is not anticipated that UPPP or conservative management will be displaced to a very large extent because of the narrower indications for closed loop UAS.

42. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service including variation in health care resources (Refer to Question 39 as baseline):

The pathway following implementation of Inspire® therapy is somewhat similar to that following surgery or conservative management. It is however unlikely that patients would use CPAP as is the case with some patients following surgery. Patients were classified as responders if there was a decrease in AHI > 50% and AHI < 20, however most patients who were not classified as responders still reported reductions in symptoms of OSA. It is possible that some patients might proceed to surgery, although this is likely to be a fewer number than in the absence of closed loop UAS and in extreme cases tracheostomy may be considered. but this is considered to be unlikely. Non-responders would be likely to treated with conservative medical management.

Should treatment with Inspire® therapy be successful, then the IPG will need to be replaced upon battery depletion. A conservative estimate of battery life is 10 years.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

Inspire® therapy is superior to medical management for patients with moderate to severe OSA and who have failed or unable to tolerate CPAP.

Inspire® therapy is superior to upper airways surgery (UPPP) for patients with moderate to severe OSA and who have failed or unable to tolerate CPAP

44. Please advise if the overall clinical claim is for:

☒ Superiority
☐ Non-inferiority

45. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes:

Device related adverse events

Other adverse events

Clinical Effectiveness Outcomes:

Apnoea Hypopnoea Index (AHI)

Oxygen Desaturation Index (ODI)

Quality of Life – Epworth Sleepiness Scale (ESS)

- Functional Outcomes of Sleep Questionnaire (FOSQ)

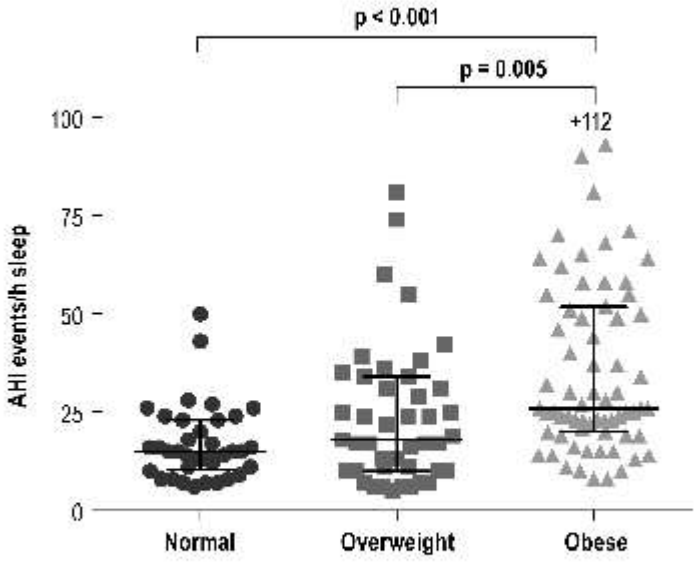
PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

46. Estimate the prevalence and/or incidence of the proposed population:

As noted above Deloitte Access Economics estimated in 2011 the Australian prevalence of OSA with ≥ 15 AHI to be 2.2% for women, 7.2% for men with an overall prevalence of 4.7%.[12] Many of these people may remain undiagnosed. As CPAP therapy does not have an MBS item number, or its use otherwise recorded in a publicly available source, it is very difficult to determine the number of patients in Australia currently being treated by CPAP and hence difficult to calculate how many may have failed CPAP therapy.

A useful alternative approach may be to look at the number of sleep studies conducted in Australia and use these numbers to estimate a population. A total of 182,965 primary diagnostic sleep studies (MBS items 12203 and 12250) were conducted in the 2017-2018 financial year. There is also no publicly available data that records how many sleep studies result in a diagnosis of moderate to severe OSA. Therefore, a 2016 Australian study[13] has been used to provide an estimate of what proportion of patients will be diagnosed with moderate to severe OSA. The relevant graph is reproduced below.

Figure 1—Distribution of obstructive sleep apnea severity by body mass index category.



AHI = apnea-hypopnea index measured via overnight in-laboratory polysomnography. Data are shown as individual participant values plus median and interquartile range. Note: "+112" refers to a single patient who had an AHI of 112 events/h of sleep.

While this study was focussed on obesity aspects of OSA, it nevertheless analysed 163 consecutive sleep studies of patients who did not previously have an OSA diagnosis in an Australian setting. Extrapolating the data in the graph, of the 163 participants, 91 (55.8%) fitted the criteria for moderate to severe OSA.

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[12] 'Re-awakening Australia. The economic cost of sleep disorders in Australia 2010' for the Sleep Health Foundation October 2011. Deloitte Access Economics

[13] Gray et al *'Obstructive Sleep Apnea without Obesity Is Common and Difficult to Treat: Evidence for a Distinct Pathophysiological Phenotype'* J Clin Sleep Med. 2017; 13 (1): 81-88.

Assuming that 55.8% of patients receiving a primary sleep study in Australia are diagnosed with moderate to severe OSA, then there are likely to be **102,094** new cases each year.

The Australasian Sleep Association[14] estimates that approximately 50% of patients are likely to fail or be non-adherent to CPAP. Therefore, there are likely to be **51,047** who may be considered for UAS.

Closed loop UAS is only indicated for patients 22 and older. Medicare statistics are reported in age ranges. The relevant age range in this instance is 15-24. It is assumed that 50% of this age range is over 22 as the item number is restricted to those aged 18 and over. 98.5% of those who may be considered for UAS with Inspire are likely to be 22 and over. Therefore **49,542** are likely to be eligible.

The majority of clinical evidence for closed loop UAS with Inspire® is in those patients who have a BMI < 32 kg/m². Again, extrapolating from the graph included above, 41 (45.1%) of the 91 patients diagnosed with moderate to severe OSA had a BMI < 30 kg/m². Therefore **22,343** patients are likely to be eligible. To account for the discrepancy between a BMI < 32 and the study classification of BMI < 30, it is assumed that an additional 10% of patients will be eligible resulting in an eligible population of **24,577**.

Not all patients who are referred receive closed loop UAS, 8% are likely to be excluded due to complete concentric collapse identified at DISE[15] leaving an eligible population of **22,610.**

These calculations are summarised in the Table 1.

Table 1

Description	Source	Estimated Population
Annual Sleep Studies	**MBS items 12203 and 12250**	**182,965**
55.8% with diagnosis of moderate to severe OSA	**Gray et al 2017**	**102,094**
50% failure of CPAP	**Australasian Sleep Association**	**51,047**
98.5% > 22 years	**Medicare Australia Statistics**	**49,542**
45.1% BMI < 30	**Gray et al 2017**	**22,343**
10% adjustment for patients with BMI ≥ 30 < 32	**Assumption**	**24,577**
Exclude 8% of patients with complete concentric collapse	**Strollo et al 2014**	**22,610**

47. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

Once

48. How many years would the proposed medical service(s) be required for the patient?

One. It is anticipated that the IPG would be replaced after 10 years.

49. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

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[14] Australasian Sleep Association *'Australasian Sleep Association submission re: Adult Sleep Apnea Surgery'* 2013.
https://sleep.org.au/common/Uploaded%20files/Public%20Files/Professional%20resources/Sleep%20Documents/ENT%20MSAC.pdf

[15] Strollo PK et al 'Upper-Airway Stimulation for Obstructive Sleep Apnea' N Engl J Med 2014; 370:139-49

1883 patients received UPPP with and without tonsillectomy in the 2017/2018 financial year.[16] This is an indication of the number of patients who may seek a surgical intervention for their OSA. It is likely that UAS with Inspire therapy will be accessed primarily by patients with private health insurance. As of March 2019, 44.5% of the Australian population had private hospital insurance[17]. 1263 patients accessed UPPP MBS item number 41786 in 2017/218 which indicates that UPPP is carried out 67% in the private sector. It is unknown how many of these patients would have been eligible for UAS with Inspire® therapy.

As there is significant unmet clinical need for patients who have failed CPAP and who may not wish to undergo or who are unsuitable for UPPP, it is anticipated that UAS with Inspire® therapy may be a suitable option for many patients, however there are considerable systemic restraints to delivering the service and uptake will be dependent upon physician referral patterns and whether patients who have failed CPAP are actively being managed by a sleep physician. Closed loop UAS requires excellent integration between the sleep medicine team and the surgical team. Therefore, the service is only suitable for delivery in hospitals that meet this requirement. The applicant's experience in western Europe and the United States has been that tertiary teaching hospitals are the most suitable for delivering the service.

Due to the intensive training requirements before the service can be delivered, it is anticipated that three centres would be likely to satisfactorily meet the training requirements and deliver the service in the first year. From previous experience it is likely that these centres would carry out 10-15 procedures in the first year.

50. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

While the eligible population for UAS with Inspire therapy is large, it is unlikely that the Australian healthcare system would have the capacity to provide this therapy to all eligible patients. The main constraints to uptake of the procedure are those listed in Question 49. Other constraints include

- Capacity of ENTs to meet demand. In 2016 there were 460 ENTs in Australia[18]. 81.5% of these work in the private sector. There is unlikely to be capacity in this relatively small group of practitioners to treat all eligible patients.
- The ability of the hospital system to absorb this number of additional procedures
- The rate of diffusion of the technology

It is anticipated that the number of UAS Inspire therapy procedures will increase by 50% each year

Year	Estimated Utilisation
2021	45
2022	68
2023	102
2023	153

It should be noted that the applicant considers that maximum utilisation in Australia will be limited by the number of appropriate centres. From previous experience, most centres who are operating at capacity will carry out between 20 and 30 procedures per year. It is anticipated that at full capacity, the Australian health system will have the ability to accommodate procedures in up to 20 centres.

[16] Australian Institute of Health and Welfare. Procedure Data Cubes 2017-2018

[17] Quarterly Private Health Insurance Statistics, Australian Prudential Regulation Authority. March 2019 (released 21 May 2019)

[18] Australian Department of Health, Otolaryngology 2016 Fact Sheet

PART 8 – COST INFORMATION

51. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

Service	Source	Fee/Cost	Benefit	Frequency	Cost
Presurgical services					
DISE	MBS Item 41764	$124.80	$93.60	1	$106.10
	MBS Item 41889	$180.90	$135.70	1	$135.70
Surgical Services					
Subcutaneous Placement of IPG	Proposed Fee	$346.05	$259.55	1	$259.55
Implantation of hypoglossal nerve lead	Proposed Fee	$684.95	$513.75	1	$513.75
Implantation of respiratory sensing lead	Proposed Fee	$684.95	$513.65	1	$513.65
Surgical repositioning or removal of IPG	Proposed Fee	$161.95	$121.50	0.016	$1.95
Anaesthesia	MBS Item 20320	$120.60	$90.45	1	$90.45
	MBS Item 23091	$180.90	$135.70	1	$135.70
Post-op Chest x-ray	MBS Item 58500	$35.35	$26.55	1	$26.55
Post-op neck x-ray	MBS 57945	$43.40	$32.85	1	$32.85
Hospitalisation	AR-DRG D12B	$4,778	$4,778	1	$4,778
Follow up					
Programming Inspire Device	MBS 105	$44.35	$37.70	2	$75.40

Service	Source	Fee/Cost	Benefit	Frequency	Cost
DISE	MBS Item 41764	$124.80	$93.60	1	$106.10

The Inspire Upper Airways Stimulation System including IPG, stimulation lead, respiratory sensing lead and sleep remote is $33,500.

52. Specify how long the proposed medical service typically takes to perform:

The surgery takes approximately 2 hours to perform.

53. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Category 3 – Therapeutic Procedures
XXXXX **Proposed item descriptor**: Closed Loop hypoglossal nerve stimulation therapy with Inspire® Upper Airways Stimulation System through stimulation of the hypoglossal nerve, subcutaneous placement of electrical pulse generator for management of moderate to severe obstructive sleep apnoea in a patient who: a) has an Apnoea Hypopnoea Index of greater than 15 and less than 65 b) is aged 22 and over c) has failed or is intolerant to continuous positive airways pressure therapy d) does not have complete concentric collapse of the upper airway Fee: $346.05

Category 3 – Therapeutic Procedures
XXXXX **Proposed item descriptor**: Closed loop hypoglossal nerve stimulation therapy with Inspire® Upper Airways 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: a) has an Apnoea Hypopnoea Index of greater than 15 and less than 65 b) is aged 22 and over c) has failed or is intolerant to continuous positive airways pressure therapy d) does not have complete concentric collapse of the upper airway Fee: $684.95

Category 3 – Therapeutic Procedures
XXXXX **Proposed item descriptor**: Closed loop hypoglossal nerve stimulation therapy with Inspire® Upper Airways Stimulation System through stimulation of the hypoglossal nerve, surgical placement of respiratory sensing

Category 3 – Therapeutic Procedures
lead and intra-operative test stimulation for management of moderate to severe obstructive sleep apnoea in a patient who: a) has an Apnoea Hypopnoea Index of greater than 15 and less than 65 b) is aged 22 and over c) has failed or is intolerant to continuous positive airways pressure therapy d) does not have complete concentric collapse of the upper airway Fee: $684.95

Category 3 – Therapeutic Procedures
XXXXX **Proposed item descriptor**: Closed loop hypoglossal nerve stimulation therapy with Inspire Upper Airways 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: a) has an Apnoea Hypopnoea Index of greater than 15 and less than 65 c) is aged 22 and over d) has failed or is intolerant to continuous positive airways pressure therapy e) does not have complete concentric collapse of the upper airway Fee: $161.95

The proposed fees have been based on the current MBS item numbers 40701, 40702, and 40704 for vagus nerve stimulation as these item numbers are very similar procedures both in time and complexity.