National Institute for Health and Care Excellence

IP1470 – Hypoglossal nerve stimulation for moderate to severe obstructive sleep apnoea

IPAC date: Thursday 14th September 2017

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Overseas health care professional	**General**	To whom it may concern, with regards to the consultation document about Hypoglossal nerve stimulation, as an expert in the field, I would like to add the following comments: As mentioned in the comprehensive reviews (1,2 see below) by our group, the invasive approach (hypoglossal nerve stimulation) when compared with the non-invasive (transcutaneous) approach, requires an adequate screening of patients. In the STAR trial (Strollo P et al, NEJM 2014) the total screened patients was 929 whilst the device was implanted in only 126 (13.6%) of the screened patients. This can be explained by the different phenotypes of patients with OSA (multiple obstructions/concentric obstruction), some of which do not benefit from the approach, while an anterior wall collapse in upper airway seems to be favourable. In the US, patients are pre-assessed using DISE to identify responders to this technology whilst this is not current practice in the UK. Furthermore, the tested severity of OSA in the original STAR trial (Strollo et al NEJM 2014) excluded the following patients	Thank you for your comment. The Strollo (2014) study is included in the main extraction table (table 2) in the overview and the following statement is already written in the patient exclusion criteria for this study: ‘*’Participants were excluded if the AHI score from the screening polysomnography was less than 20 or more than 50 events per hour, if central or mixed sleep- disordered breathing events accounted for more than 25% of all apnea and hypopnea episodes, or if the AHI score while the person was not in a supine position was less than 10 events per hour.* ‘’ The committee has decided to add the following committee comment to the guidance in section 6.2: ‘’ Drug-induced sedated endoscopy was used for patient screening in the studies, but this assessment

			and I think that this needs to be mentioned in the context of moderate-severe OSA: "Participants were excluded if the AHI score from the screening polysomnography was less than 20 or more than 50 events per hour, if central or mixed sleep- disordered breathing events accounted for more than 25% of all apnea and hypopnea episodes, or if the AHI score while the person was not in a supine position was less than 10 events per hour".	technique is not commonly used in the UK .''
2	Consultee 1 Overseas health care professional	**2.2 or 6**	The current consultation does not mention the transcutaneous approach. Although the non-invasive electrical stimulation seems to be slightly less effective, it certainly warrants consideration giving that the magnitude of the effect in terms of AHI drop on treatment in responders is similar to the effect seen in the STAR trial. This should be al least included as a field of interest in future research, as it is less costly and could be widely available to many patients who suffer from a highly prevalent condition. The TESLA trial (3) has already confirmed that in responders the expected effect size is not unsimilar that one observed with the hypoglossal nerve stimulation.	Thank you for your comment. NICE considers the transcutaneous approach as a different interventional procedure. It is being monitored and will soon be reviewed by the IP programme to decide on whether to produce guidance on this procedure or not. The committee has decided to add the following committee comment to the guidance in section 6.3: '' A transcutaneous approach can be used for hypoglossal nerve stimulation but this is not covered by this guidance.''
3	Consultee 1 Overseas health care professional	**4**	As NICE is committed to try to involve as wide a range of people and interest groups as possible in the development of interventional procedures guidance, patients' preference should be considered. We have conducted a pilot study (4)	Thank you for your comment. The Campbell (2015) paper was retrieved by our original literature search. It is a survey of patient

			on patients preference with regards to the treatment of OSA and we found that patients are more keen to consider alternative treatments for OSA with the non-invasive (transcutaneous) approach being the more requested. I think this paper should be added in the current consultation as a proof of the need to consider treatments alternative to CPAP in OSA.	preferences for different treatments of obstructive sleep apnoea (including hypoglossal nerve stimulation). Patients expressed their interest in trying emerging technologies but did not actually have the procedure done to them. This paper has been included in Appendix A.
4	Consultee 1 Overseas health care professional	**2.2**	the section about non CPAP treatments for OSA does not mention mandibular advancement devices (e.g. Quinnell T et al, TOMADO trial Thorax),	Thank you for your comment. The committee considered your comment and decided not to change section 2.2 of the guidance because the use of mandibular advancement devices is usually used for snoring rather than OSA.
5	Consultee 1 Overseas health care professional	**Overview**	nor does it mention that the evidence for surgical procedures has been reviewed and assessed by the European Respiratory Task Force on Non-CPAP Therapy in OSA (Eur Respir J 2011) with cautious recommendations.	Thank you for your comment. The conclusions of the assessment of training of the upper airway muscles and hypoglossus nerve stimulation for OSA published by the European Respiratory Society task force on non-CPAP therapies in sleep apnoea will be added to the overview (with attribution) as follows: ‘’*Apnoea triggered muscle stimulation cannot be recommended as an effective treatment of OSAS at the moment. Although oropharyngeal exercise has shown limited effects on snoring and respiratory disturbances, its role is not*

				clear at the moment and, therefore, it cannot be recommended."
6	Consultee 1 Overseas health care professional	**References**	References: Expert Rev Respir Med. 2017 Jul 21. doi: 10.1080/17476348.2017.1358619. [Epub ahead of print] 1. Electrical stimulation for the treatment of obstructive sleep apnoea: a review of the evidence. Bisogni V1, Pengo MF2, De Vito A3, Maiolino G1, Rossi GP1, Moxham J4, Steier J4,5 J Thorac Dis. 2015 Aug;7(8):1286-97. doi: 10.3978/j.issn.2072-1439.2014.04.04. 2. Emerging technology: electrical stimulation in obstructive sleep apnoea. Pengo MF1, Steier J1. TESLA trial: 3. Randomised sham-controlled trial of transcutaneous electrical stimulation in obstructive sleep apnoea. Pengo MF, Xiao S, Ratneswaran C, Reed K, Shah N, Chen T, Douiri A, Hart N, Luo Y, Rafferty GF, Rossi GP, Williams A, Polkey MI, Moxham J, Steier J. Thorax. 2016 Oct;71(10):923-31. doi: 10.1136/thoraxjnl-2016-208691. Epub 2016 Jul 19. PMID: 27435610	Thank you for your comment. The Bisogni (2017) study was retrieved by our update literature search. It is a narrative review on electrical stimulation for obstructive sleep apnoea. It has been added to Appendix A. The Pengo (2015) study was found in our original literature search. We did not select this paper for inclusion because more recent reviews are included in Appendix A. The Pengo (2016) study (TESLA trial) and the Steier (2011) study are about transcutaneous electrical stimulation in OSA. The Cambell (2015) study has been included in Appendix A (please refer to comment 3). The Randerath (2011) paper is the assessment of non-CPAP therapy in OSA by the European Respiratory Task Force. This has been included in the overview (please refer to comment 5).

			4. Patients' preference of established and emerging treatment options for obstructive sleep apnoea. Campbell T, Pengo MF, Steier J. J Thorac Dis. 2015 May;7(5):938-42. doi: 10.3978/j.issn.2072-1439.2015.04.53. PMID: 26101652 5. Continuous transcutaneous submental electrical stimulation in obstructive sleep apnea: a feasibility study. Steier J, Seymour J, Rafferty GF, Jolley CJ, Solomon E, Luo Y, Man WD, Polkey MI, Moxham J. Chest. 2011 Oct;140(4):998-1007. doi: 10.1378/chest.10-2614. Epub 2011 Mar 31. PMID: 21454399 Eur Respir J. 2011 May;37(5):1000-28. doi: 10.1183/09031936.00099710. Epub 2011 Mar 15. 6. Non-CPAP therapies in obstructive sleep apnoea. Randerath WJ1, Verbraecken J, Andreas S, Bettega G, Boudewyns A, Hamans E, Jalbert F, Paoli JR, Sanner B, Smith I, Stuck BA, Lacassagne L, Marklund M, Maurer JT, Pepin JL, Valipour A, Verse T, Fietze I; European Respiratory Society task force on non-CPAP therapies in sleep apnoea.	

			I hope that this is helpful to you, but please let me know if you have any further questions. Kind regards, [redacted]	
7	Consultee 2 Professional Organisation British Thoracic Society	**1.3**	"The British Thoracic Society is grateful for the opportunity to comment on the Interventional procedure consultation document for Hypoglossal nerve stimulation for moderate to severe obstructive sleep apnoea. We wish to record the following points: " "Recommendation 1.3 Patient selection and the procedure should be done by clinicians with special expertise in the management of obstructive sleep apnoea. We note that the STAR trial (Strollo P et al, NEJM 2014) screened and selected patients using drug-induced sleep endoscopy (DISE). Certain phenotypes of patients with OSA (multiple obstructions/concentric obstruction) do not benefit from the approach, while an anterior wall collapse in upper airway seems to be favourable. In the US, patients are still pre-assessed using DISE to identify responders to this technology. An expert in this area, Prof Meir Kryger from Yale University has confirmed that it is current practice to exclude many patients from the interventional approach if found unsuitable (in the US). Strollo et al (NEJM 2014) mentioned the following exclusion criteria in the STAR trial: â€œParticipants were also excluded if pronounced anatomical abnormalities preventing the effective use or assessment of upper-airway stimulation were identified during the surgical consultation (e.g., tonsil	Thank you for your comment. The Strollo (2014) study is included in the main extraction table (table 2) in the overview and the following exclusion criteria are written in the table: ‘’*Pronounced anatomical abnormalities preventing the effective use or assessment of upper-airway stimulation or complete concentric collapse at the retropalatal airway*.’’ The committee has decided to add the following committee comment to the guidance in section 6.2: ‘’ Drug-induced sedated endoscopy was used for patient screening in the studies, but this assessment technique is not commonly used in the UK .’’

			size of 3 or 4 [tonsils visible beyond the pillars or extending to midline]) or if complete concentric collapse at the retropalatal airway was observed on endoscopy performed during drug-induced sleep.â€	
8	Consultee 2 Professional Organisation British Thoracic Society	**1.4**	" "Recommendation 1.4 Further research including the use of observational data from registries should provide information on patient selection, safety outcomes, quality of life, long-term outcomes and the position of the procedure in the treatment pathway. NICE may update the guidance on publication of further evidence. The current consultation does not mention the transcutaneous approach in this point or any patient and public involvement (PPI). Although the non-invasive electrical stimulation seems to be less effective, this should be included as a field of interest in future research, as it is less costly and could be widely available to many patients who suffer from a highly prevalent condition. The TESLA trial has already confirmed that in responders the expected effect size is not unsimilar that one observed with the hypoglossal nerve stimulation: TESLA trial: Randomised sham-controlled trial of transcutaneous electrical stimulation in obstructive sleep apnoea. Pengo MF, Xiao S, Ratneswaran C, Reed K, Shah N, Chen T, Douiri A, Hart N, Luo Y, Rafferty GF, Rossi GP, Williams A, Polkey MI, Moxham J, Steier J. Thorax. 2016 Oct;71(10):923-31. doi: 10.1136/thoraxjnl-2016-208691. Epub 2016 Jul 19. PMID: 27435610	Thank you for your comment. NICE considered the transcutaneous approach as a different interventional procedure. It is being monitored and will soon be reviewed by the IP programme to decide on whether to produce guidance on this procedure or not. The committee has decided to add the following committee comment to the guidance in section 6.3: ‘’ A transcutaneous approach can be used for hypoglossal nerve stimulation but this is not covered by this guidance.’’

9	Consultee 2 Professional Organisation British Thoracic Society	**2.2**	" "Section 2.2 OSA may be improved by lifestyle changes such as weight loss, avoiding alcohol or sedative medication, and change of sleeping position. The most common treatment for severe OSA is continuous positive airway pressure, applied through a face mask during sleep. Surgical interventions include tonsillectomy, adenoidectomy, uvulopalatopharyngoplasty and, rarely, tracheostomy and bariatric surgery. This section does not mention mandibular advancement devices for OSA (e.g. Quinnell T et al, TOMADO trial Thorax),	Thank you for your comment. The committee considered your comment and decided not to change section 2.2 of the guidance because the use of mandibular advancement devices is usually used for snoring rather than OSA.
10	Consultee 2 Professional Organisation British Thoracic Society	**Overview**	nor does it mention that the evidence for surgical procedures has been reviewed and assessed by the European Respiratory Task Force on Non-CPAP Therapy in OSA (Eur Respir J 2011) with cautious recommendations: Eur Respir J. 2011 May;37(5):1000-28. doi: 10.1183/09031936.00099710. Epub 2011 Mar 15. Non-CPAP therapies in obstructive sleep apnoea. Randerath WJ1, Verbraecken J, Andreas S, Bettega G, Boudewyns A, Hamans E, Jalbert F, Paoli JR, Sanner B, Smith I, Stuck BA, Lacassagne L, Marklund M, Maurer JT, Pepin JL, Valipour A, Verse T, Fietze I; European Respiratory Society task force on non-CPAP therapies in sleep apnoea.	Thank you for your comment. The conclusions of the assessment of training of the upper airway muscles and hypoglossus nerve stimulation for OSA published by the European Respiratory Society task force on non-CPAP therapies in sleep apnoea has been added to the overview (with attribution) as follows: *''Apnoea triggered muscle stimulation cannot be recommended as an effective treatment of OSAS at the moment. Although oropharyngeal exercise has shown limited effects on snoring and respiratory disturbances, its role is not clear at the moment and, therefore, it cannot be recommended.''*
11	Consultee 2 Professional Organisation	**Overview**	The tested severity of OSA in the original STAR trial (Strollo et al NEJM 2014) excluded the following	Thank you for your comment.

	British Thoracic Society		patients this could be mentioned in the context of moderate-severe OSA: â€œParticipants were excluded if the AHI score from the screening polysomnography was less than 20 or more than 50 events per hour, if central or mixed sleep- disordered breathing events accounted for more than 25% of all apnea and hypopnea episodes, or if the AHI score while the person was not in a supine position was less than 10 events per hour. â€œ	The Strollo (2014) study is included in the main extraction table (table 2) in the overview and the following statement is already written in the patient exclusion criteria for this study: ‘*’Participants were excluded if the AHI score from the screening polysomnography was less than 20 or more than 50 events per hour, if central or mixed sleep-disordered breathing events accounted for more than 25% of all apnea and hypopnea episodes, or if the AHI score while the person was not in a supine position was less than 10 events per hour.* ‘’
12	Consultee 2 Professional Organisation British Thoracic Society	**7.2**	" "Section 7.2 No patient commentary was sought because the procedure is not currently done in the UK) The following two papers may be of interest: Patients' preference of established and emerging treatment options for obstructive sleep apnoea. Campbell T, Pengo MF, Steier J. J Thorac Dis. 2015 May;7(5):938-42. doi: 10.3978/j.issn.2072-1439.2015.04.53. PMID: 26101652 Continuous transcutaneous submental electrical stimulation in obstructive sleep apnea: a feasibility study. Steier J, Seymour J, Rafferty GF, Jolley CJ, Solomon E, Luo Y, Man WD, Polkey MI, Moxham J.	Thank you for your comment. The Campbell (2015) paper was retrieved by our original literature search. It is a survey of patient preferences for different treatments of obstructive sleep apnoea (including hypoglossal nerve stimulation). Patients expressed their interest in trying emerging technologies but did not actually have the procedure done to them. This paper has been included in Appendix A.

			Chest. 2011 Oct;140(4):998-1007. doi: 10.1378/chest.10-2614. Epub 2011 Mar 31. PMID: 21454399	The Steier (2011) study is about transcutaneous electrical stimulation in OSA.
13	Consultee 3 Professional Organisation Royal College of Physicians	**General**	Dear Hawra The RCP is grateful for the opportunity to respond to the above consultation. We would like to endorse the response submitted by the British Thoracic Society (BTS). I would be grateful if you could confirm receipt. Best wishes	Thank you for your comment.
14	Consultee 4 Company Inspire Medical Systems, Inc.	**4 and 5**	**ONLY THE EXECUTIVE SUMMARY WAS INCLUDED BECAUSE THE DOCUMENT CONTAINS MORE THAN 10 PAGES** EXECUTIVE SUMMARY RE: IPCD: Hypoglossal nerve stimulation for moderate to severe obstructive sleep apnoea Dear Dr. Clutton-Brock and Interventional Procedures Advisory Committee members: Inspire Medical Systems, Inc. welcomes the opportunity to provide comments to your draft Interventional Procedures Guidance (IP1450) regarding Hypoglossal Nerve Stimulation for OSA. We have provided several clinical studies that were published during your review period, and several	Thank you for your comment and for sending us a list of 64 papers and abstracts on hypoglossal nerve stimulation using the Inspire system for the treatment of OSA. Conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview, unless they contain important safety data. Studies that do not contain clinical information on efficacy and safety outcomes (for example, narrative review articles, animal studies or studies reporting only on physiological

			abstracts/oral presentations made during several society conferences in 2017 for your consideration.	outcomes) are not included in the overview, and are therefore not considered by the committee. The papers eligible for inclusion in the overview that had not already been identified by the original literature search or by the post-consultation updated literature search were included in the post consultation literature search table for presentation to the committee.
15	Consultee 4 Company Inspire Medical Systems, Inc.	**General**	Positioning of the technology: Inspire wishes to reinforce the comments provided by Prof. Bhik Kotecha regarding the patient population which is most appropriate for this technology. Inspire is approved in the United States and in Europe for patients with an Apnea-Hypopnea Index (AHI) between 15-65 events per hour, without an airway susceptible to lateral wall collapse, and for those patients who may not be positively treated with CPAP (Continuous Positive Airway Pressure). Many of the publications cited in the review do not reflect this patient population, and evaluated broader inclusion criteria. As an example, the Certal meta-analysis does not factor into account this patient selection criteria, but was rather a combination of three different technologies. The Strollo paper was the phase III pivotal study and the first clinical study to fully evaluated the safety and efficacy of the technology using the approved patient selection criteria.	Thank you for your comment. The IP programme issues guidance on procedures rather than individual devices. The Certal (2014) systematic review and meta-analysis and the Strollo (2014) study are both included in table 2. The committee has decided to add the following committee comments to the guidance: Section 6.2: ‘’ Drug-induced sedated endoscopy was used for patient screening in the studies, but this assessment technique is not commonly used in the UK .’’ Section 6.4: ‘’In the studies reviewed, the procedure was used in patients intolerant to continuous positive airway pressure.’’

16	Consultee 4 Company Inspire Medical Systems, Inc.	**General**	Inspire wishes to highlight that in August of 2017, the new German guidelines for the treatment of sleep disorders was published. The publication is in German, but a translated pdf of the guidelines is provided as Attachment I to this document. The new German guidelines recommends the use of Hypoglossal Nerve Stimulation for properly diagnosed patient who cannot tolerate CPAP. Therefore, Hypoglossal Nerve Stimulation for OSA is included as an approved therapy in Germany and not subject to consent.	Thank you for your comment. The new German guidelines for the treatment of sleep disorders has been referenced in the overview. It states: *''Neural stimulation of the hypoglossal nerve can be used in patients who do not have any anatomical abnormalities and who have moderate to severe OSA if positive pressure therapy cannot be used under the above-mentioned conditions. It should only be used in patients with CPAP intolerance or ineffectiveness with an AHI of 15–50/h and an obesity severity level of ≤ I if no concentric obstruction has been documented in the sleep endoscopy .''* The committee decided not to change the main recommendations but decided to add the following committee comments to the guidance: Section 6.2: ''Drug-induced sedated endoscopy was used for patient screening in the studies, but this assessment technique is not commonly used in the UK .'' Section 6.4: '' In the studies reviewed, the procedure was used in patients intolerant to continuous positive airway pressure .''
17	Consultee 4 Company	**1.1**	In summary, Inspire does not feel it is a true reflection to state in the draft guidelines that the evidence is "limited in quantity and quality" when hypoglossal nerve stimulation has 1) been recommended as an	Thank you for your comment.

	Inspire Medical Systems, Inc.		approved therapy in national guidelines in Germany and 2) has undergone FDA approval which is a rigorous review process regarding the safety and efficacy of a therapy.	The Committee considered this comment but decided not to change the main recommendations.
18	Consultee 4 Company Inspire Medical Systems, Inc.	**General**	Inspire requests that the IPCD review be conducted on the technologies independent of each other as each have very different systems, mechanisms of action, patient selection, device implantation techniques and programming algorithms. Thank you and please do not hesitate to call me at [redacted] with any questions. Inspire Medical Systems, Inc. [redacted]	Thank you for your comment. The IP programme issues guidance on procedures rather than individual devices.