Content of this Plain Language Summary

The objective of the Plain Language Summary is to help the general public understand EUnetHTA assessments. You can find the link to the full assessment report later in the summary.

What is included in this Plain Language Summary? First, this document explains what EUnetHTA is and what this network does. Second, you will find the summary of the assessment.

1 What is EUnetHTA?

EUnetHTA is the European Network for Health Technology Assessment (HTA). EUnetHTA was established to create an effective and sustainable network for HTA across Europe. Our partners work together to help develop information to contribute to HTA in European countries. For more information on our goals and how we work, please visit our website and our patient flyer.

EUnetHTA consists of over 80 partners that are all non-profit organisations. All partner organisations either produce or support the production of HTA reports. For more information on HTA, visit EUnetHTA's Frequently Asked Questions.

EUnetHTA does not give any advice on reimbursement of a specific health technology. The reimbursement decision is a national or regional decision. This means that reimbursement of health technologies can also differ between countries in Europe.

1.1 What does EUnetHTA do?

EUnetHTA supports national and regional research institutions and health ministries in their decision-making. For this task, EUnetHTA uses specific methods to assess health technologies. Health technologies that may be assessed by EUnetHTA include medicines and other health technologies such as specialist medical care, surgical interventions and diagnostic tests. The purpose of this plain language summary is to help the general public understand the findings from this assessment.

2 Summary of the assessment

This section provides a summary of the assessment and was published on 14/07/2020. To get a better understanding of commonly used HTA concepts, we advise you to look at the HTAi glossary.

2.1 Why did we conduct this assessment?

The purpose of this EUnetHTA assessment is to give national healthcare systems robust information about the Hypoglossal Nerve Stimulation (HGNS) Systems under assessment.

2.2 What is the context of this assessment?

Obstructive sleep apnea is a potentially serious sleep disorder in which breathing repeatedly stops (apneas) and starts during sleep. It occurs when the throat muscles intermittently relax and block the airway during sleep. Obesity, and in particular central adiposity, are the main risk factors for sleep apnea.

The current clinical management practice for obstructive sleep apnea is palliative. Continuous Positive Airway Pressure (CPAP) is considered the therapy of choice for moderate-to-severe obstructive sleep apnea. It is a device that uses positive pressure to keep the airway open while sleeping.

Hypoglossal Nerve Stimulation has emerged as an alternative approach, based on upper-airway stimulation for moderate-to-severe obstructive sleep apnea patients with intolerance or inadequate adherence to continuous positive airway pressure.

The hypoglossal nerve deals with the movement of the tongue. By stimulating the nerve, it manages to push forward the base of the tongue and the palate of the patient, preventing airway blockage and allowing air to enter during sleep.

There are three Hypoglossal nerve stimulation products available for use in Europe: the Inspire® Upper Airway Stimulation System (Inspire Medical Systems, Inc.), the aura6000™ System (ImThera Medical, Inc.) and Nyxoah's Genio™ system.

2.3 What did EUnetHTA review?

Through this assessment, EUnetHTA reviewed the clinical effectiveness and safety of Hypoglossal Nerve Stimulation for treatment of obstructive sleep apnea in eight studies.

What is the intervention under review?	Surgical implantation of Hypoglossal Nerve Stimulation
What is the study group?	Adults with moderate-to-severe Obstructive Sleep Apnea who presented inadequate adherence or failure to positive airway pressure systems or to other non-invasive procedures
What is the intervention compared to?	No treatment
What are the outcomes this review investigates?	Outcomes on effectiveness of the hypoglossal nerve stimulation: • Apnea-Hypopnea Index • Oxygen Desaturation Index • Percentage of sleep time with the oxygen saturation level below 90% • Epworth Sleepiness Scale • Quality of life • Technical and Procedural Success • Rate of cardiovascular events • Rate of cerebrovascular events • Overall mortality • Adherence to treatment Outcomes on safety: • Procedure-related complications • Device-related adverse events • Other serious adverse events

2.4 What are the main findings?

The assessment consists of 8 studies, 1 randomized controlled trial and 7 single arm trials. These were found through a systematic search of this topic. This search included all studies published up until January of 2020. A total of 1,353 people were included in these studies. Studies were multicentre, carried out mainly in centres in the USA and Europe. The people involved in these studies have moderate to severe obstructive sleep apnea with intolerance or inadequate adherence to Continuous Positive Airway Pressure.

Clinical effectiveness
The only comparative study selected was a randomized withdrawal study involving the Inspire® Upper Airway Stimulation System. In this study, 46 patients successfully treated with upper airway stimulation were randomized to have their device set to ON or OFF during a 1-week period. In this setting, an enrichment strategy was applied by including only responders to upper airway stimulation therapy.

The study found significant worsening in the Apnea Hypopnea Index Hyposemia Time (percentage of total sleep time with oxygen saturation <90%) and the Oxygen Desaturation Index (number of times per hour of sleep that the blood's oxygen levels drop by a certain degree from baseline) when the device was disconnected for one week. A significant worsening in the quality of life was also observed when the device was disconnected.

Neither the randomized controlled trial nor the observational single-arm studies reported any deaths related to the procedure or device.

No evidence was found regarding the following critical outcomes: cardio/cerebrovascular morbidity and long-term effects on quality of life.

Although no comparative evidence was found regarding adherence, the largest single-arm study found a median use of the device of 5.7 hours per night in 382 participants after 12 months of follow-up.

Safety

No comparative evidence allows for ascertaining whether Hypoglossal Nerve Stimulation Systems is safer than no treatment in the population of interest. However, information from prospective single-arm studies was retrieved and analysed.

A significant number of adverse events was reported, related both to the device and the procedure. An average of 1.02 adverse events per participant was reported and 3.45% of participants suffered a serious adverse event. The most frequent serious adverse events were surgical interventions due to replacement and repositioning or explantation of the device. The most frequent non-serious adverse event was discomfort/pain associated with device.

Quality of evidence

The quality of evidence was rated very low for both the comparative and non-comparative studies. The randomized controlled trial has a high risk of bias because of participants selection (only those who responded positively to the treatment), low number of participants, lack of blinding and no description of the randomization method.

2.5 Did EUnetHTA involve stakeholders?

EUnetHTA values involvement of stakeholders in the assessments. This ensures the assessments consider/include patient's experiences and improves applicability of the assessments. Individual patients were invited to provide input at various stages of this assessment. Their input was gathered via one-on-one conversation. Medical specialists were also invited to provide input on this assessment. Input from stakeholders was used to inform the selection of outcomes.

As patient input was deemed relevant for the scoping phase, their experiences living with the disease and even with the device under evaluation were collected and discussed during the scoping phase, including the scoping meeting, with the assessment team and the clinical experts.

A patient agreed to be interviewed about his experience with the device being evaluated. The initial treatment consisted of a CPAP device in conjunction with surgery to the nasal septum. In 2014 he received the new treatment with hypoglossal never stimulation. The patient reports being happy with it. He had no problems with the surgery and noticed positive effects from day one, including an improvement in sleep quality and an overall improvement in his quality of life..Futhermore, he indicates that the device is easy to use, and to carry when traveling. He also feels it lends him more autonomy

2.6 Additional information

This report was written by HTA organisations from Spain and Romania. Organizations from Romania, Spain and Switzerland have contributed in reviewing roles. The full scientific content is reported in EUnetHTA assessment OTCA 21, and can be found here. EUnetHTA has received funding from the European Union's Health Programme (2014-2020). The content of this summary reflects the views of the authoring team. This cannot be considered to reflect the views of the entire EUnetHTA or anybody of the European Union. Individuals involved in this assessment were cleared for any potential conflict of interests.

If you have further questions, please contact: eunethta@zinl.nl