# Effects of the Inspire(tm) Implantable Nerve Stimulation System on Obstructive Sleep Apnea (Inspire 4)

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The purpose of this pivotal study is to demonstrate long-term safety and efficacy of hypoglossal nerve stimulation to treat obstructive sleep apnea (OSA) using the Inspire II system and to support market release in the United States, Europe and...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Upper respiratory tract disorders (excl infections) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON36821

**Source**
ToetsingOnline

**Brief title**
Inspire IV

### Condition

- Upper respiratory tract disorders (excl infections)

**Synonym**
obstructive sleep apneu syndrome (OSAS)

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Inspire Medical Systems Inc.
**Source(s) of monetary or material Support:** Inspire medical Systems;Inc

## Intervention

**Keyword:** apnea, hypoglossal nerve, OSAS

## Outcome measures

### Primary outcome

1st Efficacy Endpoint: The primary endpoint is the responder rate at the 12-Month follow-up visit. A responder to the Inspire therapy is defined as a subject with at least a 50% reduction of apnea and hypopnea events per hour (AHI) compared to the 1-Month visit, and AHI less than 20 events per hour.

Co-primary Endpoint is the percentage of study subjects with a 25% reduction in ODI at the 12-Month visit compared to the 1-Month visit.

1st Safety Endpoint: Safety of the Inspire system will be assessed via two primary safety objectives that will assess the acute safety of the device system and implant procedure and the long-term safety of the systemquantitative assessment of all adverse events identified in the first 12 months.

### Secondary outcome

2o Endpoints: Evaluate the following

· Randomized therapy withdrawal study

· Modified intent-to-treat analysis of Inspire effect on AHI

· Functional Outcomes of Sleep Questionnaire (FOSQ)

· Epworth Sleepiness Scale (ESS)

· Percentage of time SaO2 below 90%

In addition to the primary and secondary endpoint analyses, other supplementary data will be collected as part of the study protocol to ensure patient safety and for further examination of the effect of the therapy.

# Study description

**Background summary**

Over the last several years, obstructive sleep apnea (OSA) has received increased attention in the medical community as well as in the media. Despite this increased awareness, the majority of the 20 million people afflicted with this disorder in the United States remain undiagnosed. Of those who are treated, less than half remain effectively treated due to poor compliance or inadequate therapeutic effect. While numerous alternatives to current therapies have been proposed, none have been shown to be effective long term and broadly accepted by the clinical community. The proposed treatment delineated in this protocol offers a unique approach to treat OSA.

**Study objective**

The purpose of this pivotal study is to demonstrate long-term safety and efficacy of hypoglossal nerve stimulation to treat obstructive sleep apnea (OSA) using the Inspire II system and to support market release in the United States, Europe and other geographies.
Study objectives include demonstrating that the Inspire system reduces the AHI and ODI in a pre-specified percentage of patients, at 12 months.

**Study design**

1. prospective, nonrandomized, multicenter clinical investigation
2. sub-study (13th month-serial control): prospective, randomized, multicenter clinical investigation

**Intervention**

The Inspire II system is intended for the treatment of obstructive sleep apnea. The system is comprised of the following components with additional details about each component described in the protocol.

* Inspire II Upper Airway Stimulator, Model 3024 (Implantable Pulse Generator, IPG)
* Inspire Stimulation Lead, Model 4063 (stimulation lead)
* Inspire Sensing Lead, Model 4323 (sensing lead)
* External programmers used with the system are:
o Inspire Programmer, Model 2740 (physician programmer)
o Inspire Patient Programmer, Model 3032 (patient programmer

The Inspire II system, as shown in the protocol, works in concert to sense the patterns of respiration and in synchrony with those respiratory events, generate electrical signals, that stimulate the hypoglossal nerve, contracting a patient*s upper airway muscles with the intent to open the airway and maintain airway patency.

**Study burden and risks**

All patients enrolled will participate in pre-implant testing, including overnight PSG, prior to undergoing a surgical procedure to implant the Inspire II system. The surgeon will conduct a post-implant follow-up visit to ensure the patient is properly recovering from the procedure. At the one month follow-up visit, the system will be activated by the principle investigator, and the patient will be provided a patient programmer with instructions for using the system on a daily basis for sleep. Following activation of the Inspire II system, patients will have scheduled follow-up visits including overnight PSG at one month, two months, four months, and six months post-implant, and every six months thereafter until study closure (5 year follow-up). Each of these visits will include an interview of the patient including interrogation of Inspire II system with the use of the physician programmer (either the Medtronic Model 7432AE or the Inspire II Programmer Model 2740). At each visit, months 1, 2, 4, and 6, the physician will review the performance of the stimulation parameters including synchronization of the respiratory signal, and titrate the system as appropriate. All titration/optimization of the system must occur prior to the patient having the 6-month overnight PSG. After the 6-month follow-up visit, the patient will continue to be followed long term at 6 month intervals to have the system interrogated/titrated as appropriate, and to conduct overnight PSG. Patients participating in this study are subject to the same risks shared by all patients undergoing implantation of a neuro-stimulation system. The protocol

testing uses standard techniques that are routinely used for the management of OSA patients. There are risks to patients in the Inspire 2 study associated with surgical implantation of the Inspire II system, biostability and therapy effectiveness as well as the impact to patient*s future medical care. The surgical risks are minimized in this study by including OSA patients who do not have significant co-morbidities, utilizing surgeons who have previous clinical experience and through protocol related training prior to initiation of the clinical trial. There may be potential benefits to the patient for participating in this clinical trial, but it is not guaranteed. One benefit is the collection of data that will assist with the development of future OSA therapies, another would be by providing a major contribution to improvement of current treatment methods.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Suffer from moederate to severe OSA (AHI * 20) 2. Have failed or have not tolerated CPAP treatment 3. Age 22 or above 4. Willing and capable of providing informed consent and to return for all follow*up visits and sleep studies, including the evaluation procedures and filling out the questionnaires.

## Exclusion criteria

1. Body Mass Index (BMI) of > 32
2. Surgical resection or radiation therapy for cancer or congenital malformations in the larynx, tongue, or throat (Note that some prior surgeries to remove obstructions related to obstructive sleep apnea are allowed; such as uvulopalatopharyngoplasty, tonsillectomy, or adenoidectomy)
3. Hypoglossal nerve palsy (obvious limited tongue movement, such as inability to protrude tongue, or unintended lateral deviation of the tongue when protruding).
4. Previous surgery within 12 weeks of scheduled implant performed on the soft tissue of the upper airway (e.g., uvula, soft palate or tonsils).
5. Obvious fixed upper airway obstructions (tumors, polyps, nasal obstruction)
6. Intrinsic neuromuscular disease, or other neurologic deficits (for examplee.g., multiple sclerosis, muscular dystrophy, Parkinson*s disease, amyotrophic lateral sclerosis, epilepsy, transient ischemic attack, or cerebrovascular accident)
7. Clinical evidence of severe chronic obstructive or restrictive pulmonary disease (for example chronic bronchitis, emphysema, pulmonary fibrosis), which may be) such as a normal or high FEV1/FVC with an FEV1 less than 50% of predicted, or severe chronic obstructive pulmonary disease (COPD) indicated by FEV1 (forced expiratory volume) < 50% predicted or FEV1/ FVC (forced vital capacity) ratio < 50%
8. Active, severe pulmonary vascular disease (0.7 as defined by the Global Initiative for example pulmonary arterial hypertension or pulmonary embolism)Chronic Obstructive Lung Disease (GOLD); Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease updated 2009
9. Moderate to severe pulmonary arterial hypertension as defined as Class III or higher as defined by the World Health Organization functional class, WHO FC) or documented by direct measurements of mean pulmonary arterial pressure by heart catheterization (PAPmean * 30 mmHg) or estimates of systolic pulmonary arterial pressure by echocardiogram (PAsys * 40 mmHg) [Barst RJ, McGoon M, Torbicki A, et al. Diagnosis and differential assessment of pulmonary arterial hypertension. J Am Coll Cardiol 2004;43:40S-47S]
10. Need for chronic supplemental oxygen therapy for any other reason, pO2 (partial pressure of oxygen) < 55 mm Hg
11. Currently receiving treatment for severe cardiac valvular dysfunction, NYHA Class III or IV heart failure, unstable angina or recent (< 6 month) myocardial infarction or severe cardiac arrhythmias
12. Clinical evidence of severe renal failure (Stage 4 or 5) undergoing dialysis or expected to institute dialysis within 6 months

13. Persistent uncontrolled hypertension (defined as systolic pressure *160 mm Hg or a diastolic pressure of * 100 mm Hg) despite medications
14. Active psychiatric disease (psychotic illness, major depression, or acute anxiety attacks) which prevents patient compliance with the requirements of the investigational study testing
15. Other sleep disorders that confound functional assessments of sleepiness such as narcolepsy with cataplexy, insomnia, or sleep movement disorders such as restless leg syndrome or periodic limb movement producing sleep disturbances unrelated to obstructive sleep apnea
16. Taking medications that in the opinion of the consulting physician may alter consciousness, the pattern of respiration, or sleep architecture. Medications not given explicitly to impact nighttime sleep may be allowed (e.g. SSRI*s) as long as the dose is stable and is anticipated to remain stable for the next 12 months. Patients with any history of chemical substance abuse within the previous 3 years should also be excluded.
17. Taking blood thinning medications, such as warfarin, aspirin, plavix, or other blood thinning agents which cannot be safely stopped or bridged (by using low molecular weight heparins such as Lovenox) temporarily to allow surgery to take place. This decision should be made in consultation with patient*s cardiologist and/or primary physician managing his/her anticoagulation therapy
18. Diagnosis of coagulopathy
19. Pregnant or plan to become pregnant within the next year
20. Has an implanted electrical stimulation device (for example pacemaker, defibrillator, peripheral nerve stimulator) and/or implanted drug infusion pumps
21. Any chronic medical illness or condition that contraindicates a surgical procedure under general anesthesia, as judged by the investigatorsInvestigators
22. Has a terminal illness with life expectancy < 12 months
23. Participation in another clinical study (enrolled in any concurrent study) whose investigational plan is judged to interfere or affect any of the measures of this study

# Study design

## Design

**Study type:** Interventional

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 10-11-2010 |

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| Enrollment: | 10 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Generic name: | implantable pulse generator;a pulmonary pressure sensor and a stimulation lead |
| Registration: | Yes - CE intended use |

## Ethics review

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| Approved WMO Date: | 22-10-2010 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 01-02-2011 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-05-2011 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 21-12-2011 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 04-05-2012 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

## Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| CCMO | NL33571.029.10 |

# Study results

Date completed: 25-01-2017

Actual enrolment: 25