inspire®
UPPER AIRWAY STIMULATION

Inspire Therapy for Obstructive Sleep Apnea

For OSA patients unable to tolerate or get consistent benefit from CPAP

Clinical Data Update

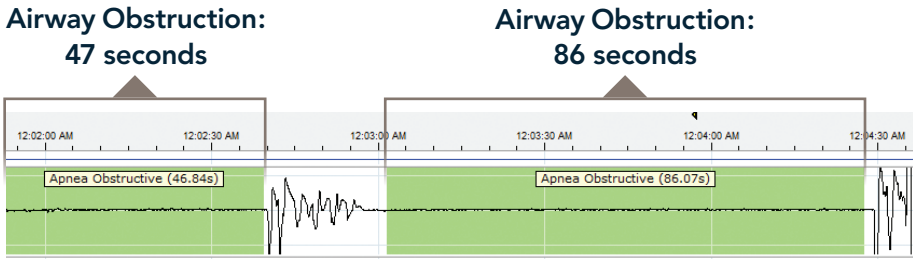
Summary of published long-term 3-year outcomes data

Treatment Goals for OSA Patients

- Reduce Symptoms
- Improve Quality of Life
- Reduce Accident Risk
- Minimize Cardiovascular and Other Health Risks

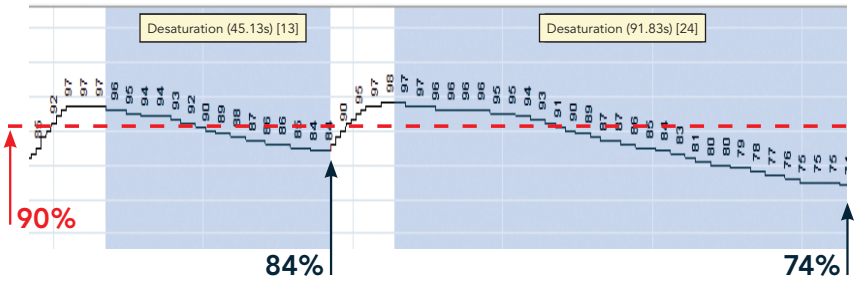
Consequences of Untreated Obstructive Sleep Apnea (OSA)

AIRFLOW



- During sleep, OSA patients experience repetitive airway obstructions followed by oxygen desaturations

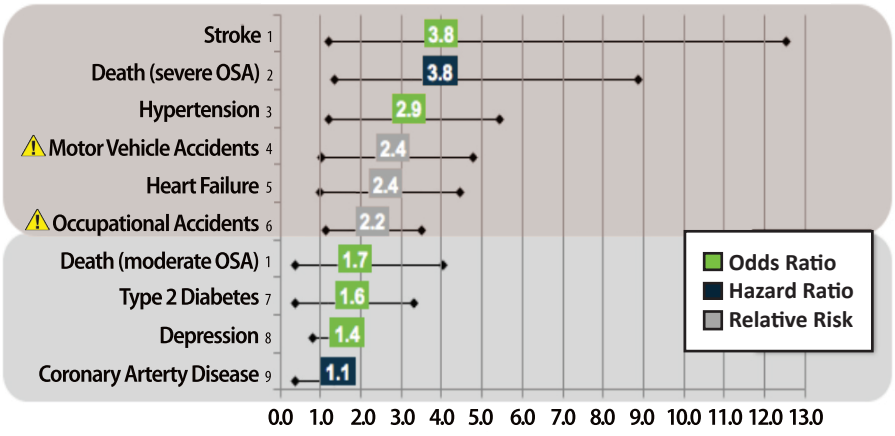
OXYGEN SATURATION LEVEL



- Moderate to severe OSA patients can experience hundreds of obstructions and desaturations each night

*Excerpt from a sleep study of an Inspire therapy candidate

INCREASED RISK DUE TO UNTREATED OSA

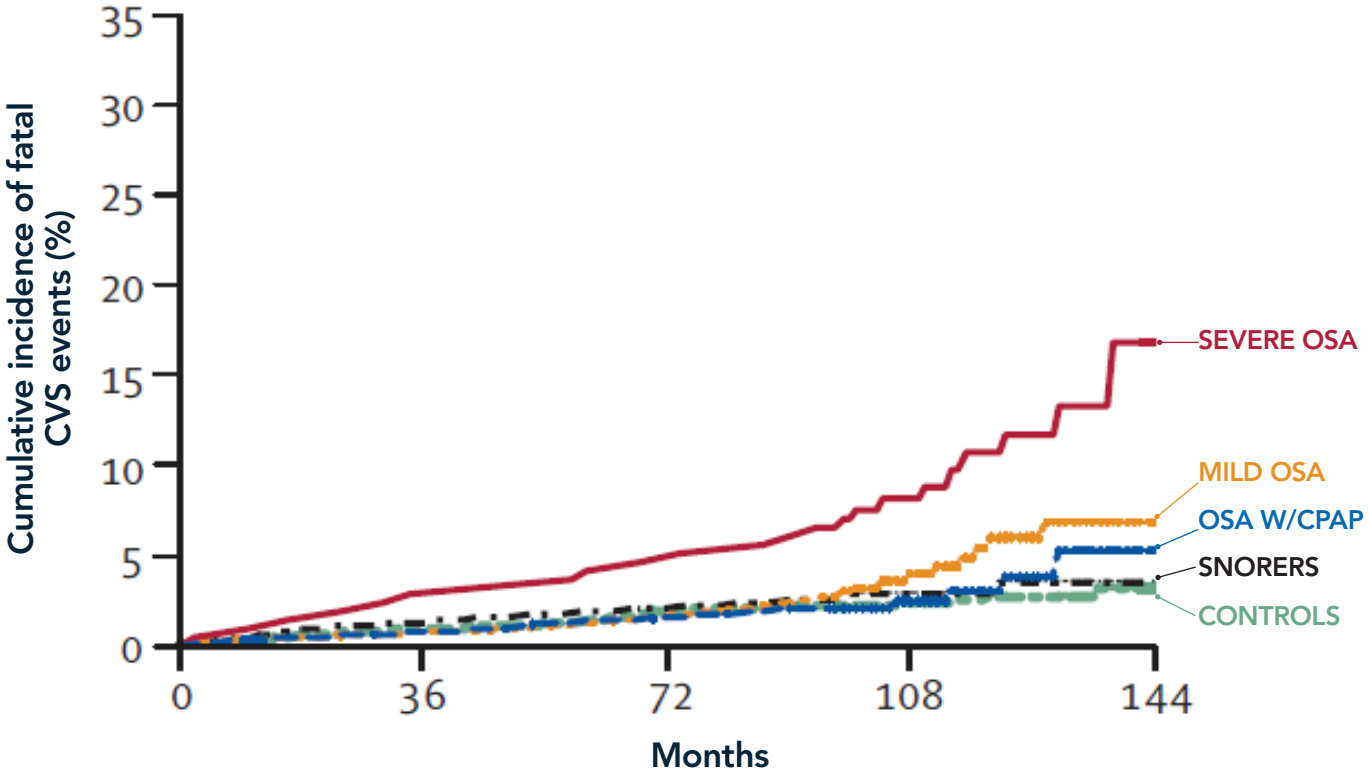


- Untreated OSA can have devastating effects on heart and brain health, impair quality of life and increase motor vehicle and occupational accident risk

1. Artz et al., Am J Respir Crit Care Med 2005 2. Young et al., Sleep 2008 3. Peppard et al., N Engl J Med 2000 4. Tregear et al., J Clin Sleep 2009 5. Shahar et al., Am J Respir Crit Care Med 2001 6. Lindberg et al., Am J Respir Crit Care Med 2001 7. Reichmuth et al., Am J Respir Crit Care Med 2005 8. Smith et al., CHEST 2002 9. Gottlieb et al., S Circulation. 2010

OSA Treatment Shown to Reduce Cardiovascular Events

- Untreated severe OSA (AHI of 30+) is associated with an increased risk of both fatal and non-fatal cardiovascular events
- Consistent treatment with Continuous Positive Airway Pressure[1] (CPAP) or an AHI <15 reduces risk

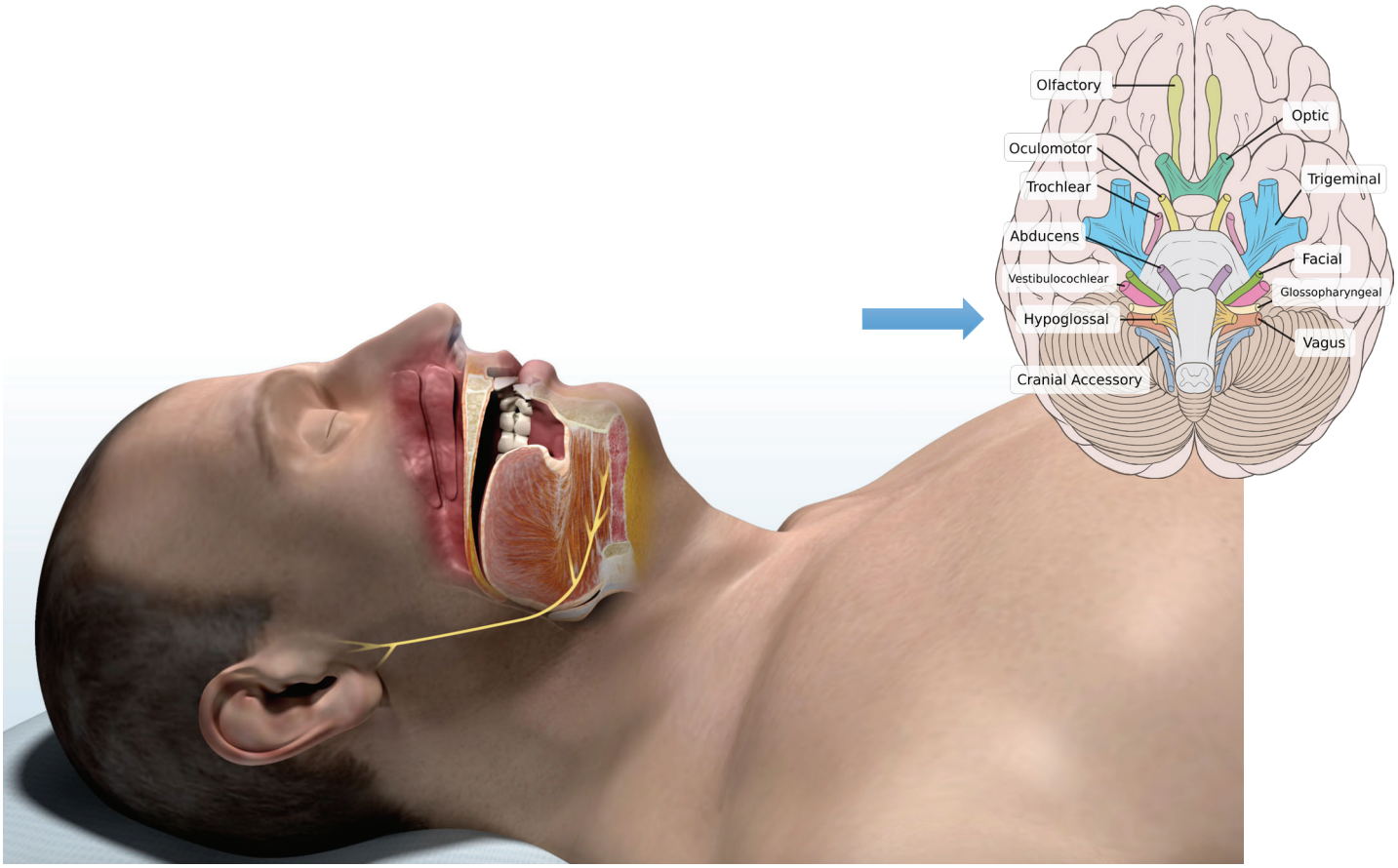


Adapted from Spanish Sleep Cohort (n=1,651, mean follow-up of 10 yrs; age ~ 50 yr)

[1] Consistent use - Average daily use more than 4 hours; Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea w/ or w/o treatment with CPAP: an observational study; Marin et al., Lancet 2005

The Hypoglossal Nerve (Cranial Nerve XII)

The Basis for Inspire Upper Airway Stimulation Therapy



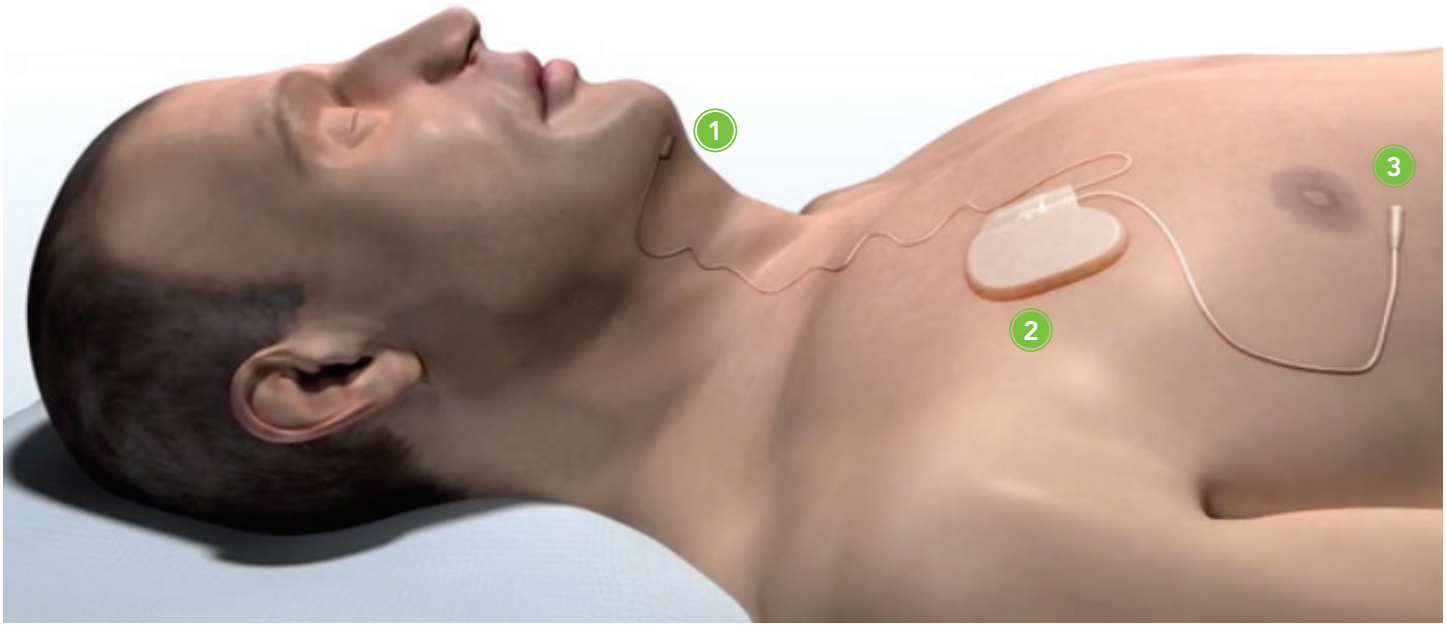
Adapted from IVLine.org

- Motor nerve
- Controls the muscles and movements of the tongue
- Mild stimulation of the distal hypoglossal nerve restores upper airway muscle tone
- Increase in muscle tone can prevent the tongue and other soft tissues from collapsing and obstructing the airway during sleep

Stimulation Synched with Breathing

The Inspire System Delivers Therapy When Airway is Most Vulnerable to Collapse

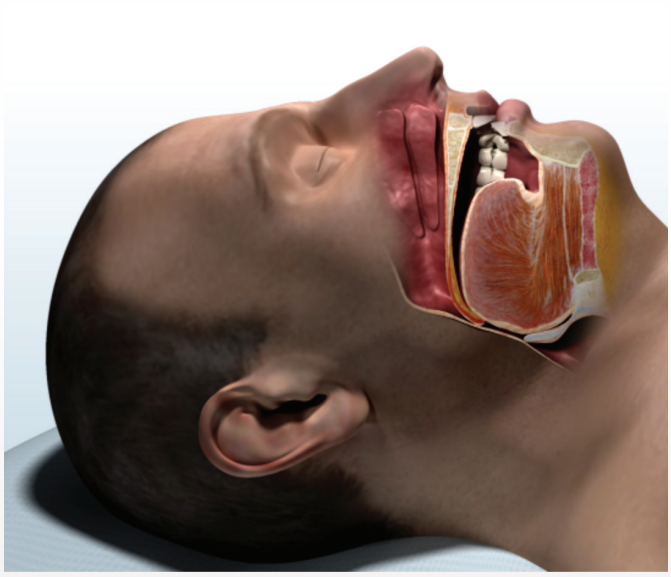
1) **Stimulation Cuff**
2) **Generator**
3) **Breathing Sensor**

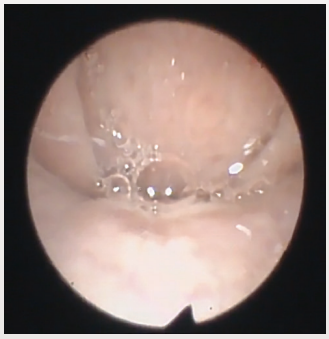


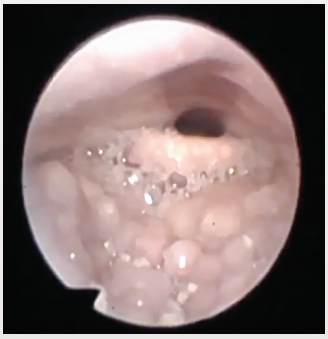
- Fully implanted system that uses well-established technologies and surgical techniques
- Breathing sensor monitors a patient's breathing cycle
- Rhythmic, mild stimulation is delivered to the hypoglossal nerve through the stimulation cuff
- Mild stimulation is delivered during inspiration, when the OSA patient's airway is most vulnerable to collapse

Stimulation Effect on Airway Anatomy

No Stimulation





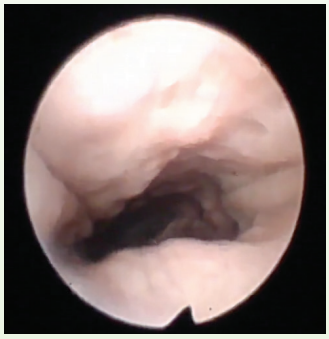


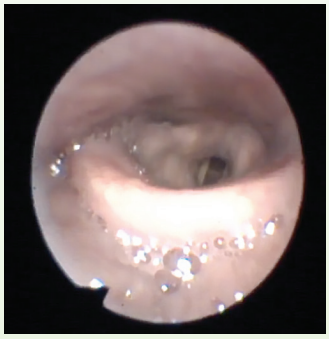
Palate

Tongue Base

Obstructed Airway

Mild Stimulation





Palate

180% increase
in airway dimension

Tongue Base

130% increase
in airway dimension

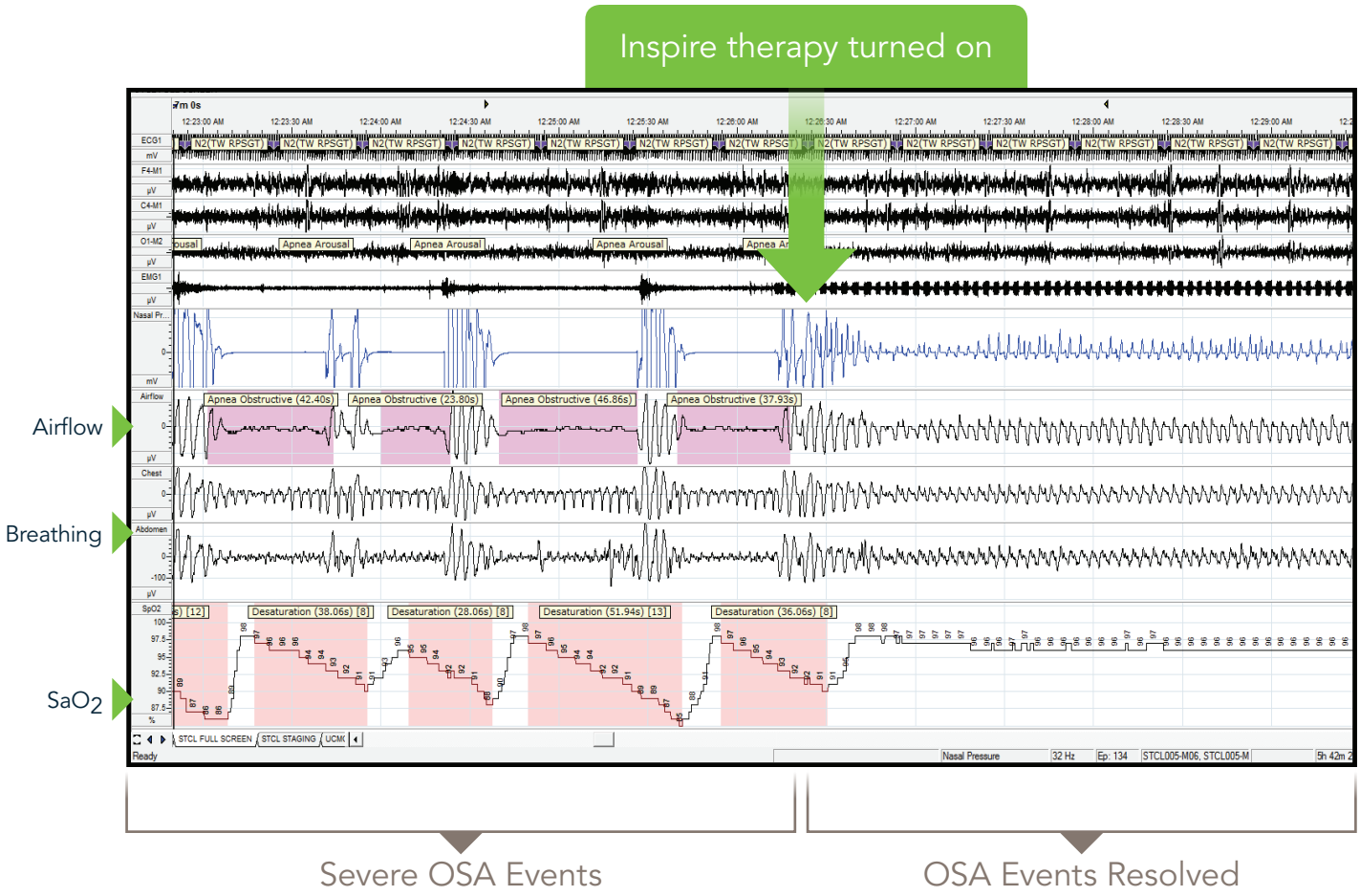
Open Airway

At therapeutic titrated levels, Inspire therapy prevents the airway from collapsing to facilitate unobstructed breathing

Safiruddin, et al. European Respiratory Journal, January 2015

*Endoscopy images of an Inspire therapy recipient

Stimulation Effect During Sleep



- Airflow and breathing stabilized
- Normal SaO_2 levels restored
- Uninterrupted sleep continues without arousals

*Sleep study of an Inspire therapy recipient

Inspire Therapy
Clinical Evidence Development

12 peer-reviewed publications as of November 2015

INSPIRE 1, 2, 3 FEASIBILITY STUDIES	STAR PHASE III TRIAL WITH RANDOMIZED CONTROLLED WITHDRAWAL STUDY	ONGOING STUDIES
First in Man	Safety/Efficacy	European Post-Approval Study
Patient Selection	FDA Approval	US Post-Approval Study
Implant Technique	Long-Term Follow-Up	Multiple Single Center Experience Projects
Safety/Efficacy	Cost Effectiveness	European Randomized Controlled Study
4 Peer-Reviewed Publications	**8 Peer-Reviewed Publications**	

Peer-Reviewed STAR Trial Outcomes Publications:

One Year: Upper Airway Stimulation for Obstructive Sleep Apnea. Strollo et al. *The New England Journal of Medicine*. January 2014

Randomized Study: Randomized Controlled Withdrawal Study of Upper Airway Stimulation on OSA. Woodson et al. *Otolaryngology Head and Neck Surgery*. September 2014

18 Months: Upper Airway Stimulation for Obstructive Sleep Apnea—Durability of the Treatment Effect at 18 months. Strollo et al. *SLEEP*. June 2015

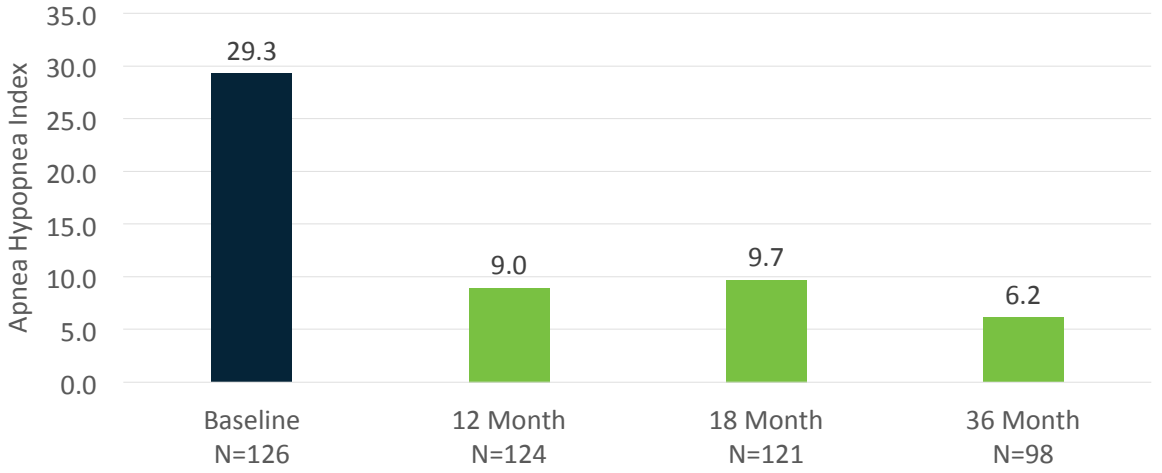
Two Year: Upper Airway Stimulation for Obstructive Sleep Apnea: Self-Reported Outcomes at 24 months. Soose et al. *Journal of Clinical Sleep Medicine*. July 2015

Three Year: Three Year Outcomes of Cranial Nerve Stimulation for Obstructive Sleep Apnea: The STAR Trial. Woodson et al. *Otolaryngology Head and Neck Surgery*. November 2015

Inspire Therapy
Long-Term Objective Outcomes

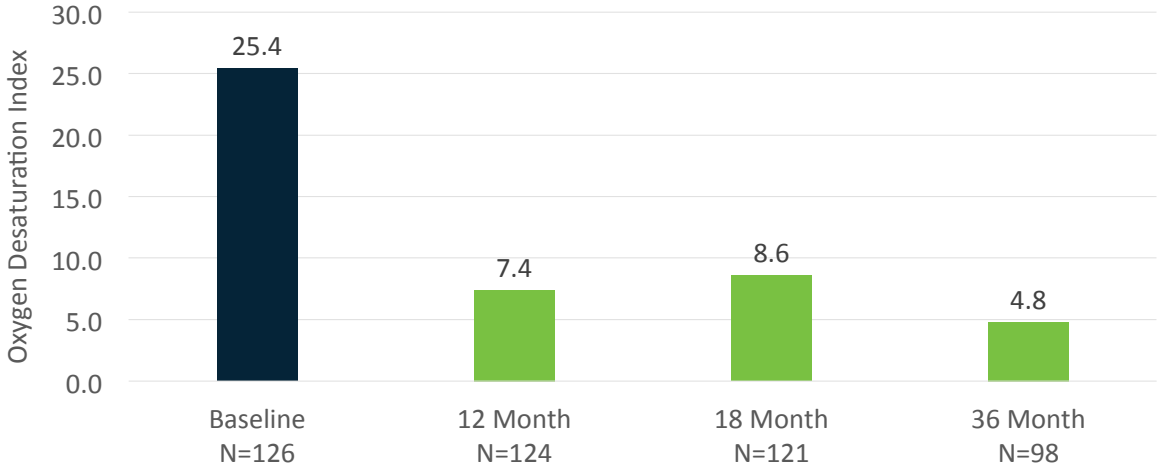
Patients using Inspire therapy experienced significant decreases in both AHI and ODI from baseline to 12 months. These significant improvements were maintained over the 36-month follow-up period.

APNEA HYPOPNEA INDEX (AHI)



All p values < 0.01 vs. baseline. Results in median.

OXYGEN DESATURATION INDEX (ODI)

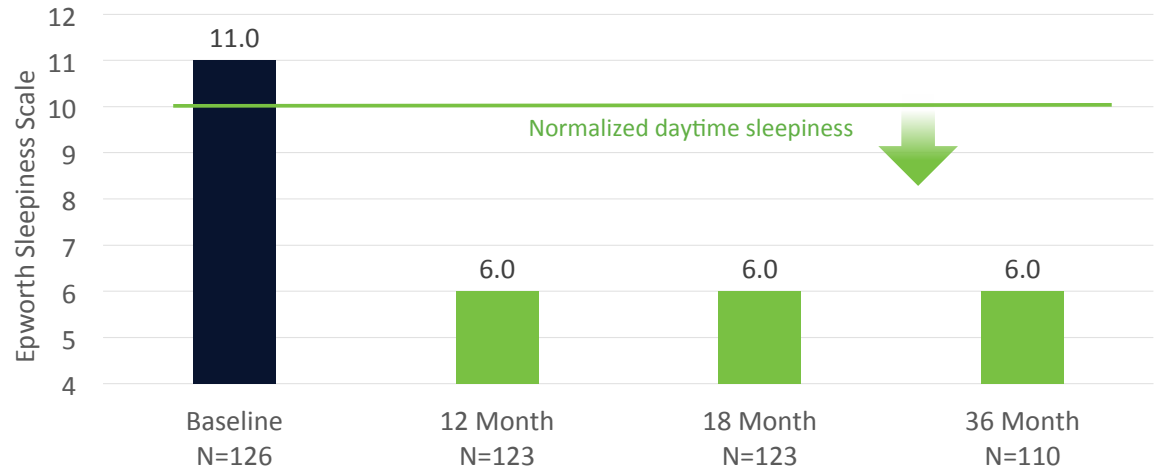


All p values < 0.01 vs. baseline. Results in median.

Inspire Therapy
Long-Term Patient Reported Outcomes

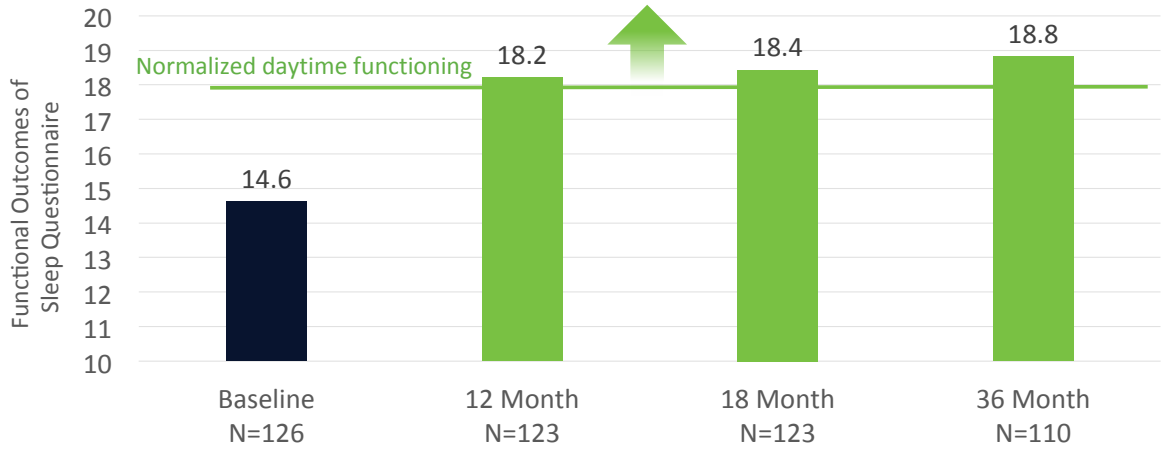
Patients using Inspire therapy reported significant improvements and normalization of both daytime sleepiness and daytime functioning. These significant improvements were reported at 12 months and were sustained at 36-month follow up.

EPWORTH SLEEPINESS SCALE (ESS)



All p values < 0.01 vs. baseline. Results in median.

FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE* (FOSQ)



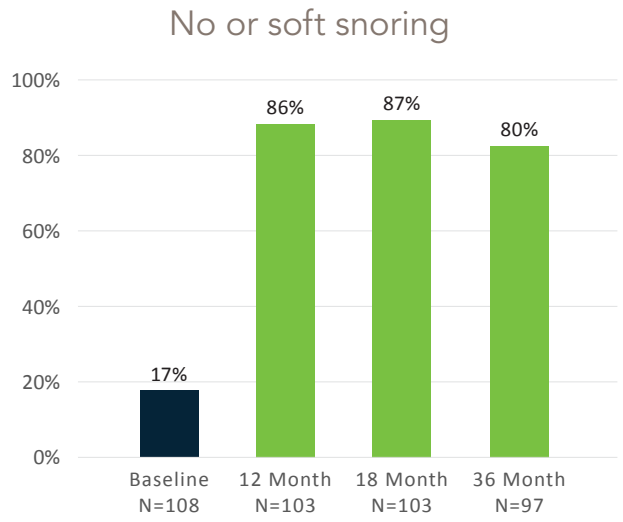
All p values < 0.01 vs. baseline. Results in median.

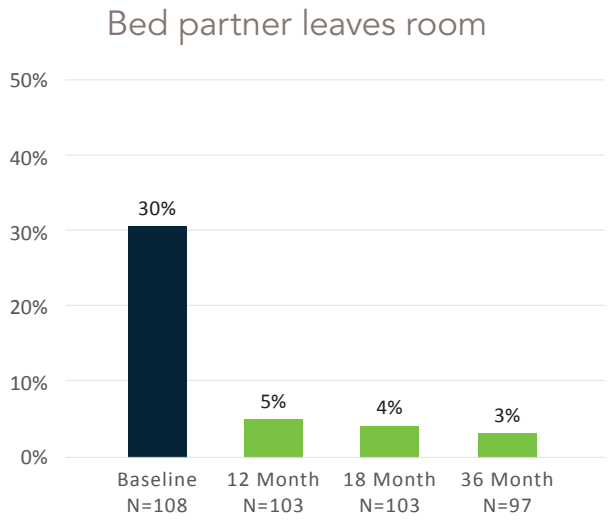
* Importantly, all 5 FOSQ subscale variables showed clinically significant improvements. FOSQ subscale variables include (1) activity, (2) productivity, (3) social, (4) intimacy and (5) vigilance.

Inspire Therapy
Patient and Partner Experience

Sleep apnea affects not only patients but their bed partners as well. Snoring, a common sleep apnea symptom, was significantly impacted in patients using Inspire therapy from baseline. Additionally, fewer partners left the room due to their partner's snoring.

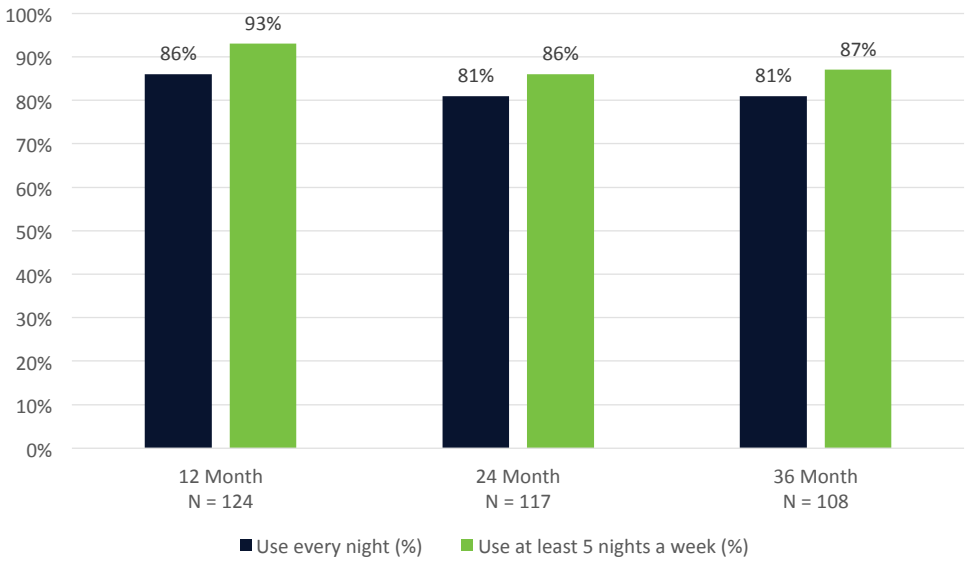
PARTER REPORTED SNORING OUTCOMES





Therapy adherence remained high throughout the three-year follow-up period.

THERAPY ADHERENCE



Inspire Therapy
Patient Selection Considerations

Patients use the handheld sleep remote to turn the therapy on before bed and off upon waking.

Inspire therapy is FDA-approved and available at over 50 leading medical centers in the United States. It is intended for people who:

- Have been diagnosed with moderate to severe OSA (AHI 20-65)
- Cannot tolerate or get consistent benefit from CPAP
- Are not significantly overweight

People who meet these basic criteria can be referred to a specialist who can evaluate sleep parameters, assess the airway anatomy and determine if Inspire therapy is right for them.

In addition, Inspire therapy is approved and available in over 8 European countries.

Visit www.inspiresleep.com to review risks, benefits and expectations associated with Inspire therapy. Risks associated with the surgical implant procedure are low but may include infection and temporary tongue weakness. Most patients acclimate well to the presence of the Inspire system and to the therapeutic stimulation. Some patients may require post-implant adjustments to the system's settings in order to improve effectiveness and ease acclimatization.

Additional Resources:

www.InspireSleep.com
844 OSA HELP (844-672-4357)

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Inspire Medical Systems

800-132-001 Rev A Nov 2015