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Three-Year Outcomes of Cranial Nerve Stimulation for Obstructive Sleep Apnea: The STAR Trial

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Objective. To describe the 36-month clinical and polysomnography (PSG) outcomes in an obstructive sleep apnea (OSA) cohort treated with hypoglossal cranial nerve upper airway stimulation (UAS).

Study Design. A multicenter prospective cohort study.

Setting. Industry-supported multicenter academic and clinical setting.

Subjects. Participants (n = 116) at 36 months from a cohort of 126 implanted participants.

Methods. Participants were enrolled in a prospective phase III trial evaluating the efficacy of UAS for moderated to severe OSA. Prospective outcomes included apnea-hypopnea index, oxygen desaturation index, other PSG measures, self-reported measures of sleepiness, sleep-related quality of life, and snoring.

Results. Of 126 enrolled participants, 116 (92%) completed 36-month follow-up evaluation per protocol; 98 participants additionally agreed to a voluntary 36-month PSG. Self-report daily device usage was 81%. In the PSG group, 74% met the a priori definition of success with the primary outcomes of apnea-hypopnea index, reduced from the median value of 28.2 events per hour at baseline to 8.7 and 6.2 at 12 and 36 months, respectively. Similarly, self-reported outcomes improved from baseline to 12 months and were maintained at 36 months. Soft or no snoring reported by bed partner increased from 17% at baseline to 80% at 36 months. Serious device-related adverse events were rare, with 1 elective device explantation from 12 to 36 months.

Conclusion. Long-term 3-year improvements in objective respiratory and subjective quality-of-life outcome measures are maintained. Adverse events are uncommon. UAS is a successful and appropriate long-term treatment for individuals with moderate to severe OSA.

Keywords

obstructive sleep apnea, cranial nerve, hypoglossal nerve, sleep, device, implant, long term, clinical, apnea hypopnea index, sleep, quality of life

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Obstructive sleep apnea (OSA) is a prevalent chronic disease affecting quality of life and sleep, and it is associated with increasing risks of hypertension, cardiovascular disease, metabolic abnormalities, traffic accidents, and mortality.[1,2] Successful treatment improves

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quality of life, reduces associated disease morbidity, and is associated with major reductions in downstream health care costs.[3] Treatment of moderate to severe OSA is a major health care concern.

The most widely accepted treatment is nasal continuous positive airway pressure (CPAP). CPAP use improves polysomnography (PSG) outcomes, quality of life, and medical morbidities, including new-onset cardiovascular disease and hypertension.[4] Although CPAP is a first-line treatment for moderate and severe sleep apnea, long-term use for many patients is suboptimal. Adherence in several large cohort studies over a period ≤6 months is only 39% to 50%.[5,6]

Cranial nerve stimulation of the hypoglossal nerve was Food and Drug Administration approved in 2014 for the treatment of moderate and severe OSA in adults. Favorable selection criteria included a body mass index (BMI) <32 kg/m^2, lack of central apnea, and a favorable pattern of palatal collapse during drug-induced sedation endoscopy (DISE).[7,8] Short-term results of feasibility trials were favorable, and a major prospective trial (STAR trial) demonstrated a 66% success rate based on primary outcome measures of apnea-hypopnea index (AHI) at 1 year with normalization of many secondary outcome measures.[9] A randomized therapy withdrawal study supported effectiveness at 13 months and durability at 18 months.[10] Treatment with upper airway stimulation versus no treatment is estimated to be a cost-effective therapy in the US health care system.[11]

The current study reports long-term outcomes and durability of the Inspire implantable hypoglossal nerve stimulation system (Inspire Medical Systems, Maple Grove, Minnesota) at 36 months.

Methods

Participants

The STAR trial multicenter cohort included adults with a history of moderate to severe OSA and intolerance or inadequate adherence to CPAP. Key study exclusion criteria included BMI >32 kg/m^2, neuromuscular disease (including hypoglossal nerve palsy or injury), severe cardiopulmonary disorders, active psychiatric disease, and comorbid nonrespiratory sleep disorders that would confound functional sleep-related assessments.

Participants who met inclusion/exclusion criteria underwent 3 screening tests: an in-laboratory attended PSG, a surgical consultation visit, and DISE. Participants were excluded after the PSG for an AHI <20 or >50 events/hour sleep, central and/or mixed apnea index >25% of the AHI, or a nonsupine AHI <10. Participants were excluded if pronounced anatomic abnormalities would prevent effective use of the device (eg, tonsil size 3 or 4). DISE assessed site and pattern of upper airway collapse under sedation (eg, propofol and/or midazolam) and excluded any participants with observed complete concentric collapse at the level of the velopharynx.

Study Procedures

Qualified participants who met preimplant screening criteria underwent device implantation. Details of the surgical technique are described in a prior publication.[12] The implanted system (Inspire Medical Systems) consists of 3 components: a stimulation cuff electrode that encircles a distal branch of the hypoglossal nerve, a pressure-sensing lead placed within the fourth or fifth intercostal space, and an implantable pulse generator inserted into a subcutaneous pocket beneath the clavicle. The therapy is designed to sense ventilatory effort and provide stimulation to the hypoglossal nerve in synchrony with respiration so that inspiration is unobstructed.

The device was activated 1 month after the implant procedure. During the first month of at-home use, participants gradually increased the stimulation amplitude to facilitate therapy acclimatization and to optimize both comfort and subjective effectiveness. Between 2 and 6 months, ≥1 in-laboratory PSG titration studies were conducted to optimize therapy. Additional titration studies were performed in some participants after 6 months based on previous titration results and participant feedback.

All participant self-reported outcomes were followed at 6-month intervals for 3 years. PSGs were collected at 12- and 18-month follow-up visits per the protocol. In addition, all participants were invited to complete a nonscheduled PSG at 36 months. The primary outcomes of AHI and ODI (oxygen desaturation index) were scored by an independent core laboratory, using standard 2007 scoring criteria,[13] with hypopnea score based on a 30% airflow reduction and a 4% oxygen desaturation. Secondary outcome measures included subjective sleepiness and sleep-related quality of life via the validated Epworth Sleepiness Scale (ESS) and the Functional Outcomes of Sleep Questionnaire (FOSQ). Clinical variables—including BMI, neck circumference, tongue function, speech, swallowing, daily use by self-report, and blood pressure—were measured at scheduled study visits to assess for any changes over the course of the study. Subjective report of snoring was collected from participants and bed partners' reports on a categorical scale (no snoring, soft snoring, loud snoring, very intense snoring, or bed partner leaves room)

All reported adverse events were reviewed and coded by the Clinical Events Committee. Serious adverse events were defined as any that led to death, life-threatening illness, permanent impairment, or new or prolonged hospitalization. Adverse events were categorized as either procedure related if related to the surgical procedure or device related if secondary to use of the device after therapy activation. Adverse events could also be judged as not related to either circumstance. The trial was approved by the institutional review board (United States) or medical ethics committee (Europe) in each participating center. An independent Clinical Events Committee and a Data Safety Monitoring Board provided review and adjudication of safety data.

Statistical Analysis

The sample size was calculated on the basis of previous studies.[7] Approximately 108 participants were required for the primary end point evaluation, with the exact 1-sided binomial test at a significant level of 2.5% with 80% power.

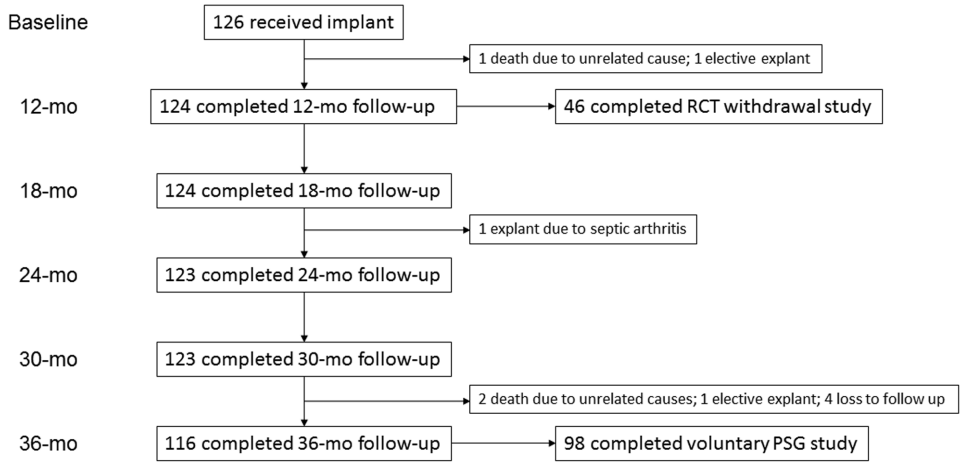

Figure 1. Consort diagram. PSG, polysomnography; RCT, randomized controlled trial.

For primary outcome, the AHI and ODI at the 12-, 18-, and 36-month follow-ups were compared with the baseline measurement. A 2-sided paired *t* test was used to evaluate the difference between baseline and 12 months and between 12 and 36 months at the 5% significant level. For participants who did not complete PSG study at 36 months, a ''last value carried forward'' analysis was conducted by using the PSG results from the 18- or 12-month visit.

Results

After enrollment and screening, the original cohort consisted of 126 participants; a total of 124, 123, and 116 completed follow-up at the 12-, 24-, and 36-month visits postimplant, respectively (**Figure 1**). Baseline characteristics and measures did not differ between the follow-up participants and the original cohort. The mean BMI in the follow-up cohort was unchanged from baseline to 12 and 36 months.

Ninety-eight participants voluntarily completed an interim PSG study at 36 months. This group did not differ in baseline BMI and AHI from the original or 12-month group data (**Table 1**). The primary efficacy outcome measures of AHI and ODI decreased from baseline to the 12-month assessment and remained stable at 36 months. Mean AHI for the cohort decreased from baseline to 12 months and remained stable at 36 months (32.0 ± 11.8 to 15.3 ± 16.1 and 11.5 ± 13.9 events/hour). ODI demonstrated a small further reduction at 36 months versus 12 months (**Figure 2** and **Table 2**). Per the Sher criteria (an AHI decrease of >50% to <20), which was the a priori definition of success, 74% of the interim PSG group achieved a response to treatment. An AHI of <5 or 10 events/hour was observed in 44% and 69%, respectively. A total of 51 (52%) showed consistently favorable responses at 12, 18, and 36 months, while 9 (9%) participants did not meet response status at any period (see appendix at www.otojournal.org/supplemental). In the 17 noninterim PSG participants, 54% were nonresponders at the 12-month evaluation. Using the ''last value carried forward'' analysis from the cohort at 12 or 18 months, the average AHI at 36 months was 14.2 ± 15.9, with a median AHI of 7.3 and a response rate of 65% (2 withdrawn participants, 1 death and 1 elective explant, were counted as nonresponders).

When long-term responders and nonresponders were compared, univariate analysis demonstrated differences in AHI, ODI, and prior uvulopalatopharyngoplasty between groups; however, in a stepwise logistic model, only AHI remained significantly associated. BMI was not associated with responders versus nonresponders (**Table 3**).

Secondary Outcomes

A total of 113 participants completed self-reported outcomes at 36 months. Improvements observed at 12 months persisted at 36 months (**Table 4**). At baseline, only 33% reported a normal ESS score (≤10), and 15% reported a normal FOSQ score (>17.9). At 36 months, this was increased to 77% and 63%, respectively (**Figure 3**). Improvements in the percentage time of oxygen saturation <90% at 12 months were maintained at 36 months. There were improvements of sleep architecture with an increase of N3 sleep and a reduction of arousal index from baseline to 36 months (see online appendix).

Long-term bed partner– and patient-reported subjective snoring reports demonstrated improvement from baseline and were stable versus 12 months. The percentage of bed partner–reported no scoring or soft snoring increased from 17% at baseline to 86% at 12 months and remained stable at 80% at 36 months (**Figure 4**). Participants' subjective report of nightly therapy use was at 86% at 12 months and 81% at 24 and 36 months. Twenty-one participants at 36 months reported not using therapy every night. Of these, 10 reported therapy use for at least 4 nights each week. The other 11 participants, who reported <4 nights per week of use, described this as the result of discomfort related to stimulation (n = 5), forgetting to turn device on (n = 2), other sleep disorders (n = 2), and 1 each because of lost remote or a return to CPAP.

Adverse Events

The largest number of nonserious adverse events were related to implant procedure and were reported within the

Table 1. Baseline Characteristics of the Study Population at Enrollment.[a]

Characteristics	Baseline (n = 126)	Completed 12 mo (n = 124)	Completed 36 mo (n = 116)
Age, y	54.5 ± 10.2	54.3 ± 10.2	54.3 ± 10.3
Body mass index, kg/m^2	28.4 ± 2.6	28.5 ± 2.6	28.6 ± 2.6
Apnea-hypopnea index, events/h	32.0 ± 11.8	31.7 ± 11.6	31.1 ± 10.9

[a]Results in mean ± SD.

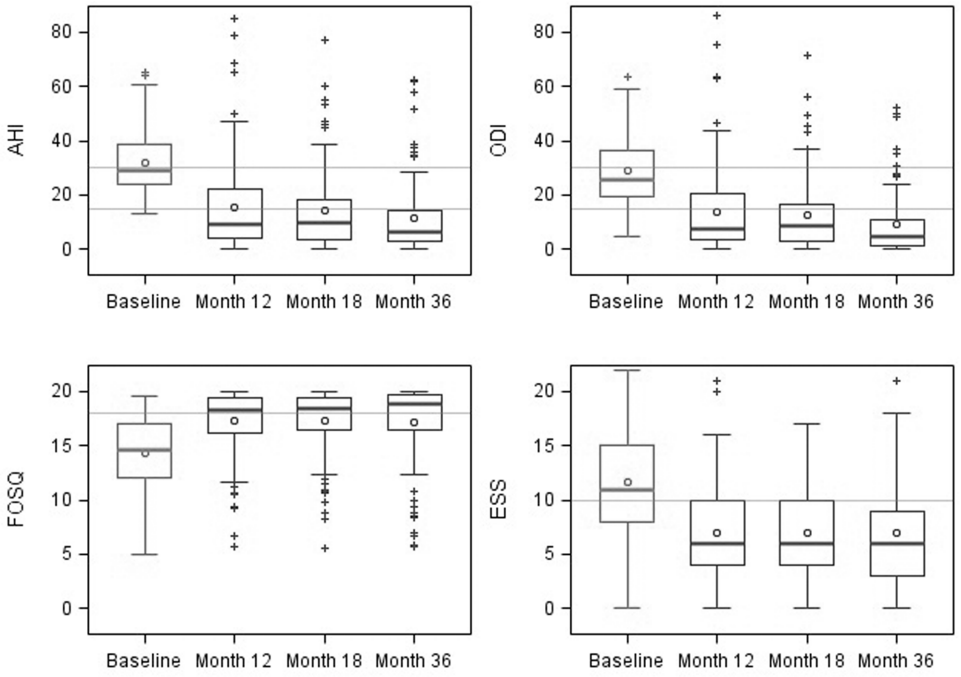

Figure 2. Polysomnographic and self-report measures at baseline and 12, 18, and 36 months. Tukey box plots: box lines mark 25th to 75th percentiles and median ("o" marks mean); outside lines mark distribution limits (outliers represented as +). AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; ODI, oxygen desaturation index.

Table 2. PSG Outcome Measures for Participants Completed PSG at 36 months (N = 98).

				Change (95% CI; *P* Value)		
	Baseline	12 mo	36 mo	Baseline to 12 mo	Baseline to 36 mo	12 to 36 mo
AHI, event/h	30.4 ± 10.4	13.5 ± 14.3	11.5 ± 13.9	16.9 (13.9, 19.9; <.001)	18.8 (16.1, 21.6; <.001)	1.95 (–1.0, 4.9; .20)
Median	28.2	8.7	6.2	17.4	19.4	0.6
ODI, event/h	27.1 ± 10.8	12.0 ± 13.6	9.1 ± 11.7	15.1 (12.3, 17.9; <.001)	18.0 (15.5, 20.4; <.001)	2.86 (0.4, 5.3; .02)
Median	24.3	7.1	4.8	15.5	17.2	1.1
SaO_2 <90%	7.9 ± 9.7	5.0 ± 11.2	5.7 ± 10.2	2.9 (1.0, 4.8; 0.01)	2.2 (–0.1, 4.5; .06)	–0.73 (–2.7, 1.2; .46)
Median	4.8	0.7	1.0	2.1	1.5	0.0

Abbreviations: AHI, apnea-hypopnea index; CI, confidence interval; ODI, oxygen desaturation index; PSG, polysomnography; SaO_2, oxygen saturation.
[a]Baseline and 12-month values are from the cohort that completed PSG at 36 months (n = 98). Results in mean ± SD or median as noted. Statistical significance, $P < .05$.

first month of implantation as previously reported. After 12 months, the only serious adverse events were elective device removal due to insomnia (n = 1) and due to device-unrelated septic arthritis (n = 1). Three participants continued to report numbness at the incisional sites lasting for ≥12 months. Discomfort due to electrical stimulation was reported 80 times in the first year and 23 and 24 times in the second and third years of the follow-up. Tongue

Table 3. Comparison of Baseline Characteristics between Responders and Nonresponders at 36 Months.[a]

Baseline Characteristics	Month 36		Odds Ratio	95% CI (*P* Value)
	Responders (n = 73)	Nonresponders (n = 25)		
Age, y	56.4 ± 10.4	51.6 ± 10.2	1.05	1.00, 1.10 (.0496)
Male, %	82	92	0.37	0.08, 1.74 (.21)
Body mass index	28.5 ± 2.8	29.2 ± 2.0	0.88	0.72, 1.08 (.22)
Neck size	41.1 ± 3.5	41.6 ± 2.5	0.95	0.82, 1.10 (.48)
Baseline AHI	28.8 ± 9.3	35.0 ± 12.4	0.95	0.91, 0.99 (.01)
Baseline ODI	25.6 ± 9.5	31.5 ± 13.0	0.95	0.91, 0.99 (.02)
Prior UPPP, %	25	4	0.13	0.02, 1.01 (.05)
Baseline FOSQ	14.6 ± 3.2	15.3 ± 2.6	0.92	0.79, 1.07 (.28)
Baseline ESS	11.1 ± 4.8	11.1 ± 4.3	1.01	0.91, 1.11 (.92)

Abbreviations: AHI, apnea-hypopnea index; CI, confidence interval; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; ODI, oxygen desaturation index; UPPP, uvulopalatopharyngoplasty. Results in mean ± SD or percentage.
[a]Based on a stepwise logistic regression analysis with the 3 significant covariates, apnea-hypopnea index remained statistically significant (odds ratio, 0.95; 95% CLs: 0.93, 0.99; $P = .01$).

Table 4. Self-reported Quality-of-Life Outcome for Participants Who Completed Follow-up at 36 months (n = 113).[a]

				Change (95% CI; *P* Value)		
	Baseline	12 mo	36 mo	Baseline to 12 mo	Baseline to 36 mo	12 to 36 mo
FOSQ	14.6 ± 3.0	17.6 ± 2.4	17.4 ± 3.5	–3.0 (–3.5, –2.5; <.001)	–2.7 (–3.4, –1.9; <.001)	0.4 (–0.2, 1.0; .20)
Median	15.1	18.3	18.8	–2.5	–2.6	0.0
ESS	11.4 ± 5.1	6.9 ± 4.3	7.0 ± 5.0	4.5 (3.6, 5.5; <.001)	4.3 (3.3, 5.4; <.001)	–0.04 (–0.7, 0.6; .92)
Median	11	6	6	4	4	0

Abbreviations: ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire.
[a]Baseline and 12-month values are from the cohort that completed follow-up at 36 months (n = 113). Normal FOSQ value is a score >17.9; normal ESS is a score ≤10. Results in mean ± SD or median as noted. Statistical significance, $P < .05$.

abrasions caused by movement of the tongue over mandibular dentition decreased from 28 in the first year to 4 in the third year. In 12 participants, recurrent tongue abrasions or discomfort related to tongue movement along the teeth was successfully treated with plastic dental guards. After an mean ± SD follow-up of 40 ± 6 months (range, 10-51 months), there were 2 device- or disease-unrelated deaths (1 cardiac arrest after a fall and 1 homicide). Three participants were lost to follow-up. A detailed list of adverse events is provided in the online appendix.

Discussion

The objective of the current report was to assess the long-term clinical effectiveness of cranial nerve stimulation of the hypoglossal nerve using an implanted system. In a prospectively followed cohort, objective primary metrics (AHI and ODI) and secondary outcomes were improved at 36 months. Although the study suffers from the weakness of not having a control group for comparison, it has the strength of demonstrating large and meaningful changes over a long duration of evaluation. Improvements observed at 12 months were maintained at 3 years of follow-up. Additionally, the study benefits from a high level of clinical follow-up at 3 years: 116 participants (92%) completed the scheduled 36-month follow-up.

An additional 98 participants (78%) also volunteered for an interim 36-month PSG. For the group having a PSG, mean AHI decreased from 30.4 ± 10.4 events/hour at baseline to 13.5 ± 14.3 at 12 months and 11.5 ± 13.9 at 36 months. Although the 36-month PSG group did not significantly differ in baseline characteristics from the 12-month group in baseline characteristics, it did differ in having a lower percentage of 12-month nonresponders than did the group that did not volunteer. This potentially confounds the 36-month mean AHI when compared with other time points. It is important, however, to understand that the means data do not describe individual differences in treatment response. With upper airway stimulation, AHI response varies within individuals at different time points (see Figure S2, available online). In the cohort, the majority of responders demonstrated a stable reduction in AHI at multiple time points over 3 years. However, a second group of responders had a more variable response in reducing AHI over multiple sleep studies. When a threshold ''cut point'' is applied on any single night, some individuals may be classified as responders or nonresponders. The

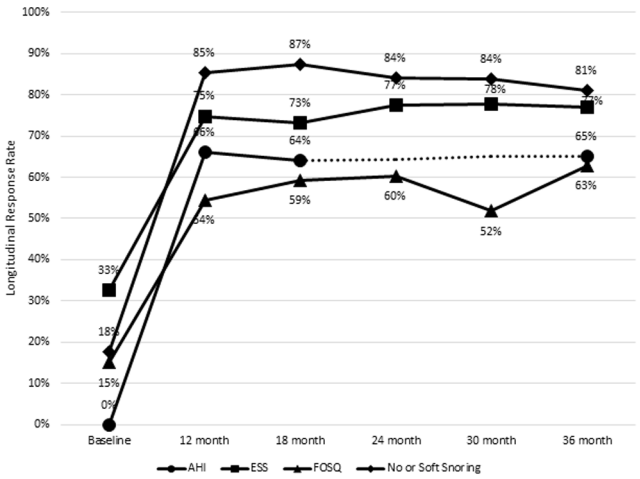

Figure 3. Longitudinal outcome definitions: AHI >50% reduction to <20; ESS score <10; FOSQ score >17.9; snoring self-report of no or soft snoring. AHI not measured at 24 and 30 months (dotted line). AHI, apnea-hypopnea index; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire.

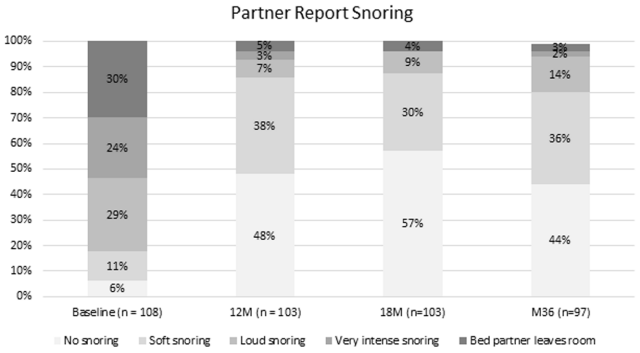

Figure 4. Bed partner report of snoring.

clinical importance of this residual AHI is unknown. However, using AHI as an isolated metric of disease may be questioned, and experience with nasal CPAP demonstrates that meaningful clinical benefit occurs when used for a fraction of the night.[14,15] Understanding that each night's AHI with upper airway stimulation may vary and may require individuals to use the patient programmer to adjust therapy on some nights, mean data support an ongoing long-term clinical effectiveness of the device.

The goal of OSA treatment is to improve not only surrogate sleep study metrics but also clinical outcomes. It is these clinical outcome measures that are important to patients. At 36 months, improvements in self-reported quality of life and validated sleep outcomes, which were abnormal at baseline and markedly improved at 12 months, demonstrated durability of the clinical response. The clinical outcomes of the therapy continue to be robust. Of the 36-month follow-up group (n = 116), 81% use the device regularly. When accounting for individuals that use the device at least 4 nights a week, 84% of the initial implanted cohort (n = 126) still are frequently (≥4 nights) reporting activating the device. A large percentage of the participants achieved normalization of clinical outcomes at 3 years. Normalization of sleepiness (ESS) increased from 33% to 77%, while the percentage of participants reporting a normal sleep-related quality of life (FOSQ) increased from 15% to 63% from baseline to 36 months (**Figure 3**).

The number of adverse events associated with the therapy continue to be acceptable. The majority of device-related events occurred in association with device implantation and have been discussed in earlier publications. The rate of device-related events continued to decrease, with most events being minor and related to sensation of tongue stimulation and tongue abrasions. These have been managed with adjustment of stimulation parameters and dental adjustments. The only serious device-related adverse effects included 3 device explants: 2 were at participants' request due to other sleep disorders, and 1 was in a device responder due to an unrelated systemic septic arthritis. At the beginning of the trial, there was a question whether fibrosis would occur between the stimulation cuff and the nerve, which would require a gradual increase in stimulation threshold over time. For the group, there have been no changes in stimulation thresholds (sensation, functional, or subdiscomfort; see online appendix), which indicates that fibrosis or nerve-related changes are not a concern at this time. Based on these data, device harm or risk is low at 3 years.

The data from this study provide additional important evidence supporting neuromodulation as a method of treatment of OSA. In contrast to other surgical procedures that directly alter the upper airway to prevent its obstruction, upper airway stimulation using the Inspire implant reduces obstruction by physically increasing muscle tone to selected upper airway muscles innervated by the hypoglossal nerve. The current long-term effectiveness of the procedure demonstrates that it is a pharyngeal procedure and not just a ''tongue base'' procedure. Activation of tongue musculature not only mechanically opens the oropharyngeal airway directly with tongue protrusion but also has effects on the retropalatal airway. The presence of this tongue palate mechanical linkage has been observed experimentally,[16] and the current data provide support that activation of the tongue protrusor muscles maintains a clinical effect for a long duration of therapy.

Fluoroscopy and DISE studies examining stimulator mechanism of action demonstrate that unilateral hypoglossal nerve stimulation mechanically affects the entire pharynx.[17,18] Selection criteria support that success is ultimately determined by the effects on the palatal airway. Factors that worsen or improve palatal collapsibility (possibly factors affecting the lateral retropalatal wall) are likely important to clinical outcomes of UAS. While all these participants with a BMI <32 and restrained AHI had ''favorable'' palatal collapse of an anterior-posterior manner, effectiveness is further determined by how favorable the linkage is between nerve stimulation and palatal opening.[17]

Independent studies using several devices now provide data to support cranial nerve upper airway stimulation for

the treatment of OSA. Eastwood,[19] Van de Heyning,[7] Mwenge,[20] and Kezirian[21] published data demonstrating improvement in sleep apnea. A cost-benefit analysis using surrogate metrics places this therapy in a favorable position when compared with no treatment in patients with CPAP intolerance.[11] The STAR trial provides the strongest data supporting neuromodulation as durable and effective therapy for OSA. Data at 1 year and a randomized withdrawal effect at 12 and 18 months have been published.[10] The current study provides prospective results at 3 years and indicates substantial use and clinical improvement in individuals who have moderate to severe OSA, who have failed conventional therapy, and who meet favorable inclusion criteria. Weaknesses of the current report include a potential selection bias in the group agreeing to have sleep studies and the lack of a control group. Although the mean AHI of the cohort may be affected by those agreeing or not agreeing to polysomnograms, 84% of patients available for 3 years of study underwent sleep studies, and responders in the group demonstrated a durable treatment effect. A control group for such a long-term study is not feasible. This trial is unique in that other sleep apnea treatment is often assessed in terms of months rather than years of therapy, and the long clinical effectiveness of these therapies, which are widely accepted, is not based on long-term prospective trials. The effect size of clinical outcomes for the therapy is in the range of a large effect at 24 months, and this study supports the durability of effect.[22] This is important, as sleep apnea is most commonly a chronic condition requiring long-term management.

In conclusion, 3-year improvements in objective respiratory and subjective quality-of-life outcome measures are maintained. Adverse events are uncommon. Cranial nerve stimulation is a successful and appropriate long-term treatment for individuals with moderate to severe OSA.

Acknowledgment

We acknowledge all investigators who participated in the STAR trial (see online appendix). Ms Teri Yurik (Namsa, Inc) provided statistical analysis of results presented in this study.

Author Contributions

B. Tucker Woodson, data collection, analysis, interpretation and writing; **Ryan J. Soose,** data collection, interpretation, and writing; **M. Boyd Gillespie,** data collection, interpretation, and writing; **Kingman P. Strohl,** data collection, interpretation, and revising; **Joachim T. Maurer,** data collection, interpretation, and writing; **Nico de Vries,** data collection, interpretation, and revising; **David L. Steward,** data collection, interpretation, and revising; **Jonathan Z. Baskin,** data collection, interpretation, and revising; **M. Safwan Badr,** data collection, interpretation, and revising; **Ho-sheng Lin,** data collection, interpretation, and revising; **Tapan A. Padhya,** data collection, interpretation, and revising; **Sam Mickelson,** data collection, interpretation, and revising; **W. McDowell Anderson,** data collection, interpretation, and revising; **Olivier M. Vanderveken,** data collection, interpretation, and revising; **Patrick J. Strollo Jr,** data collection, interpretation, and revising.

Disclosures

Competing interests: B. Tucker Woodson, Inspire Medical Systems—study investigator, consultant; Medtronic—consultant, royalty; Siesta Medical—consultant. Ryan J. Soose, Inspire Medical Systems—study investigator, consultant; Philips Respironics—consulting. M. Boyd Gillespie, Inspire Medical Systems—study investigator, consultant; Medtronic, Olympus, Arthrocare—consultant; Surgical Specialties—consultant, research support. Kingman P. Strohl, Inspire Medical Systems—study investigator, consultant; Somnetrics LLC—consultant (not related to report); Seven Dreamers LLC—consultant (not related to report). Joachim T. Maurer, Inspire Medical Systems—study investigator, consultant; GlaxoSmithKline, Weinmann, Olympus, ResMed, Neuwirth, Medtronic, and Heinen & Löwenstein—personal fees outside the submitted work; Philips—Consultant. Nico de Vries, Inspire Medical Systems—study investigator, consultant; Philips, Olympus—consultant; Night Balance/ReVent—medical advisor, shareholder, funding from company. David L. Steward, Inspire Medical Systems—study investigator, consultant. Jonathan Z. Baskin, Inspire Medical Systems—study investigator, consultant. M. Safwan Badr, Inspire Medical Systems—study investigator, consultant. Ho-sheng Lin, Inspire Medical Systems—study investigator, consultant; Intuitive Surgical—proctor. Tapan A. Padhya, Inspire Medical Systems—study investigator, consultant. Sam Mickelson, Inspire Medical Systems—study investigator. W. McDowell Anderson, Inspire Medical Systems—study investigator. Olivier M. Vanderveken, Inspire Medical Systems—study investigator, consultant; Somnomed Inc—grant; Nyxoah—study investigator, consultant; Philips Electronics BV—consultant. Patrick J. Strollo Jr, Inspire Medical Systems—study investigator, consultant; ResMed—scientific advisory board, research grant; Philips Respironics—research grant; Jazz Pharmaceuticals—consultant, research grant.

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Supplemental Material

Additional supporting information may be found at http://otojournal.org/supplemental.

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