2024

Inspire® Patient Experience Report

Market Surveillance & Quality Update

Inspire®

Overview:

Every Obstructive Sleep Apnea (OSA) patient experience is different, but one aspect rings true for all; it's excruciating to live with and ultimately manage. When it comes to OSA treatment, Continuous Pulmonary Air Pressure (CPAP) is the standard of care. While it works for many, it doesn't always work for everyone. When this happens, patients often feel like they're out of options and luck.

Inspire® therapy is a potential solution for these people. It is surgically implanted and tailored to the patient by a sleep medicine professional. The patient controls therapy with a small remote. Thousands of patients count on Inspire therapy for relief from OSA.

Since 2007, successful patient outcomes and care experiences are guiding tenants for Inspire Medical Systems. Dr. Glen Nelson, Inspire Medical Systems' first Board Chairman, established the motto, "If we put the patient first, we will never lose our way." This spirit guides and motivates us to publish an annual Patient Experience Report (PER). This report transparently shares therapy outcomes through a patient lens and aims to educate the reader on the experiences of others.

For a full bibliography of over 300 peer reviewed publications covering Inspire therapy, visit professionals.inspiresleep.com/publications.

Commitment to Quality

At Inspire Medical Systems, our focus on successful patient outcomes is paramount in everything we do each day. Our Quality Policy is our formal commitment to you that we will never waver in that regard.

Inspire Quality Policy:

- **Relentlessly** pursue safe, effective, and reliable treatment of obstructive sleep apnea.
- **Strive** to consistently improve the quality of life of our patients and exceed customer expectations.
- **Maintain** rigorous processes that ensure compliance with applicable global laws and regulations.

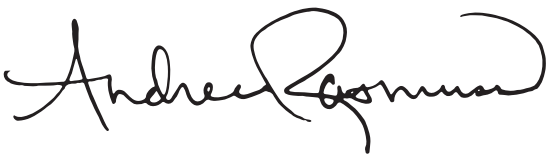
There are two primary data sources for the Inspire Patient Experience Report.

1. Post-market surveillance data

2. ADHERE, real-world global registry

Contact Information

Feedback plays a vital role in our effort to continuously improve our products and services. To contact our patient and physician support team, please visit inspiresleep.com/contact for 24x7 support or call 1-844-672-4386 (US) or +49 0800 00 09 78 99 (EU).



Andrea Rasmussen
Vice President, Quality
Inspire Medical Systems, Inc.

Dr. Glen D Nelson
Inspire Chairman of the Board 2006–2017

"Put the patient first and you will never lose your way."

Contents

Post-Market Surveillance System Overview 4
Patient Satisfaction 5
Quality of Life and Therapy Compliance 5
OSA Burden Reduction 6
Revision & Explant Tracking 7
Implant Complications
- ADHERE Registry 9
- Third Party Data 10

Post-Market Surveillance System Overview

Post-market surveillance is a systemic process used to collect and analyze experience gained from medical devices that have been commercially approved and placed on the market.

Post-market experience data is collected from patients, healthcare professionals, product registries, regulators and Inspire employees.

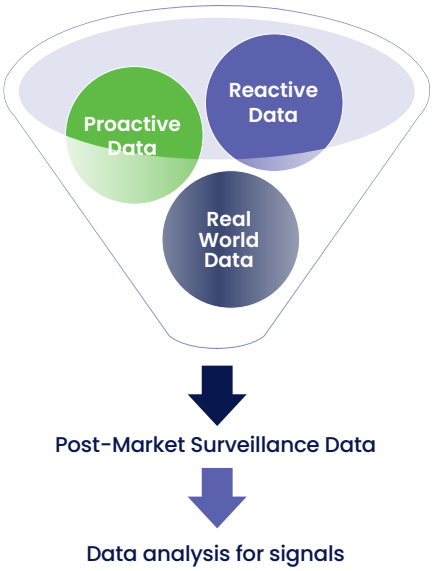
A post-market surveillance system has many critical inputs and outputs, as illustrated below.

Post-market surveillance system

Proactive Data Sources
- Post-Market Clinical Studies
- Literature Searches
- Product Service Data
- Customer Surveys
- Social Media

Reactive Data Sources
- Complaints
- Regulatory Safety Reports
- Non-conformance Reports
- Out-of-Tolerance Reports
- Audits

Data Signals Drive:
- Corrective & Preventive Action
- Training
- Design Improvements
- Product Recalls



Inspire Medical Systems uses both proactive and reactive data to monitor the performance of our products.

Data is collected from Inspire Medical Systems customers around the world. Data analysis from these sources may lead to corrective action, regulatory reporting, improvements to our products, and training.

Post-market surveillance data is collected from customer and patient-initiated complaints, product returns and Inspire employee reports. Underreporting of events is recognized throughout the medical device industry. Inspire Medical Systems is continuously improving the accuracy of the data through rigorous and regular employee training and customer awareness.

ADHERE Registry Overview

- Goal: Collect **real-world outcomes** data
- International multi-center, standard-of-care registry
- Eligibility – patients receiving Upper Airway Stimulation (UAS) for OSA

5,000 enrollments at 61 medical centers

US Centers

EU Centers (Belgium, Germany, Netherlands, Switzerland)

Registry Data Collection

Baseline

Medical Record
- Demographics
- OSA History
- AHI
- ESS

Implant
- Implant Time
- Adverse Events

Post-Titration (6mo.)
- AHI
- ESS
- Patient Experience
- Therapy Usage
- Clinical Global Impression

Annual Visit (12mo.)
- AHI
- ESS
- Patient Experience
- Therapy Usage
- Clinical Global Impression

AHI = Apnea Hypopnea Index
ESS = Epworth Sleepiness Scale

Patient Satisfaction

Patient satisfaction is a result of clinical outcomes, patient experience, and quality of life. It is a measure of the timely, efficient, and patient-centered delivery of quality care. Patient satisfaction is thus a very important indicator to measure the success of Inspire therapy.

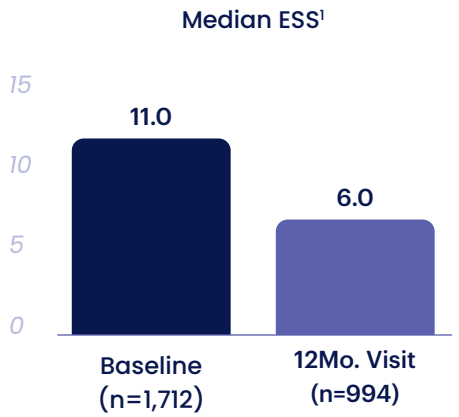
The ADHERE registry asks patients to answer four questions about their satisfaction with Inspire therapy.

How does Inspire therapy compare against your previous experience with CPAP?	91%[1]	Say Inspire therapy is better
I would recommend Inspire therapy to a friend or family member.	93%[1]	Agree or strongly agree
Given the chance, I would choose to receive Inspire therapy again.	92%[1]	Agree or strongly agree
Overall, how satisfied are you with Inspire therapy?	90%[1]	Satisfied or very satisfied

Quality of Life & Compliance

The Epworth Sleepiness Scale (ESS) is currently the most used subjective test of daytime sleepiness in clinical practice. It is a simple, self-administered, eight-item questionnaire that measures the risk of falling asleep in eight specific situations that are commonly met. A score of less than 10 is considered normal. The higher the score (from 10 to 24), the greater the reported subjective daytime sleepiness (Johns, 1991).

The ADHERE registry asks patients to complete an ESS survey at baseline and at 6 and 12-month follow-ups. ESS is the measure Inspire uses to quantify subjective benefit of therapy. Prior to Inspire therapy, patients were sleepy, and sleepiness is reduced to normal levels after treatment.



Compliance with therapy is a key factor required to gain the health benefits associated with treating obstructive sleep apnea. Longer CPAP usage has been shown to improve survival, cardiovascular events, blood pressure, excessive daytime sleepiness, cognitive function, and quality of life. However, average compliance to CPAP is often reported at less than 5 hours[2-3].

The ADHERE registry tracks average nightly compliance of Inspire therapy patients.

Hours of nightly use @ 12-months (n=913[1]) **5.7**

UAS usage of 5.7 hours/night at 12-months exceeds average CPAP usage levels from major clinical studies. [2-3]

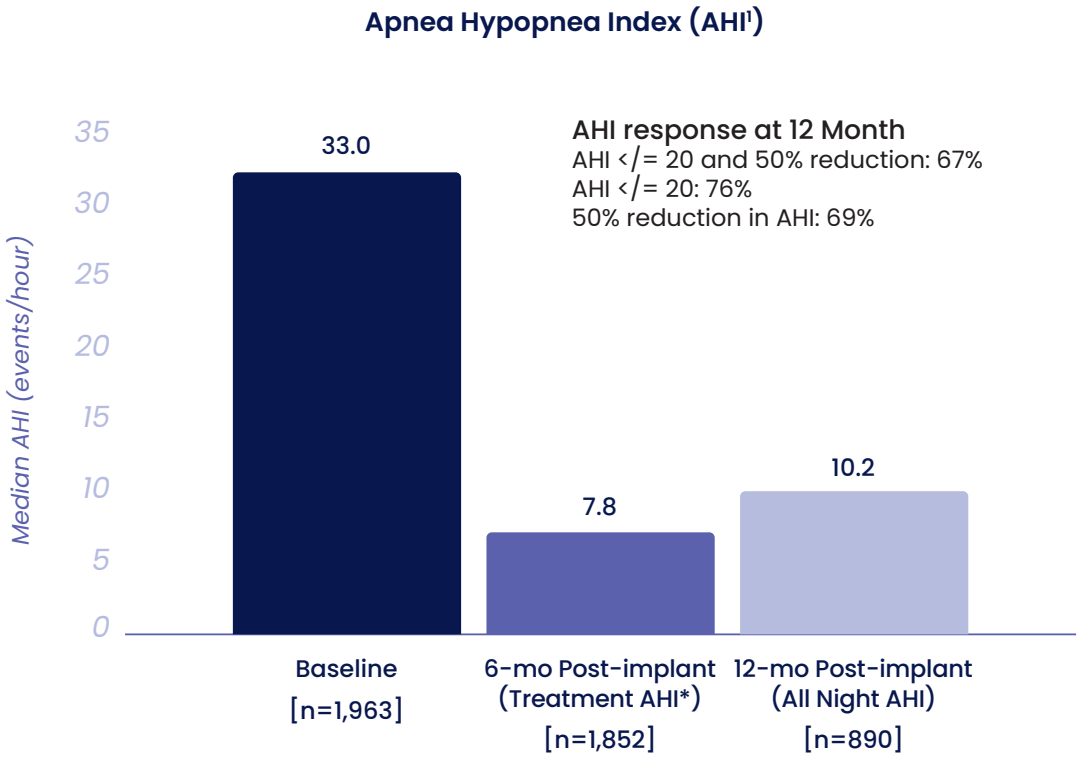
1 Data on File
2 Apnea Positive Pressure Long-term Efficacy 1: Study—Kushida et al, SLEEP, Vol. 35, No. 12, 2012
3 The HOME-PAP Study —Rosen et al, SLEEP, Vol. 35, No. 6, 2012

OSA Burden Reduction

The apnea-hypopnea index (AHI) is well established as the best studied metric of OSA severity. The AASM has identified the following severity grades based on the number of obstructive breathing events per hour:

- Mild: 5 to 15 events per hour
- Moderate: 15 to 30 events per hour
- Severe: greater than 30 events per hour

The ADHERE registry includes a follow-up PSG or HSAT at six months and twelve months post-implant.



**Treatment AHI is defined as the AHI measurement after stimulation has been activated and optimal therapy achieved. The treatment AHI may be assessed during an HST or a PSG while using the optimal therapeutic setting.*

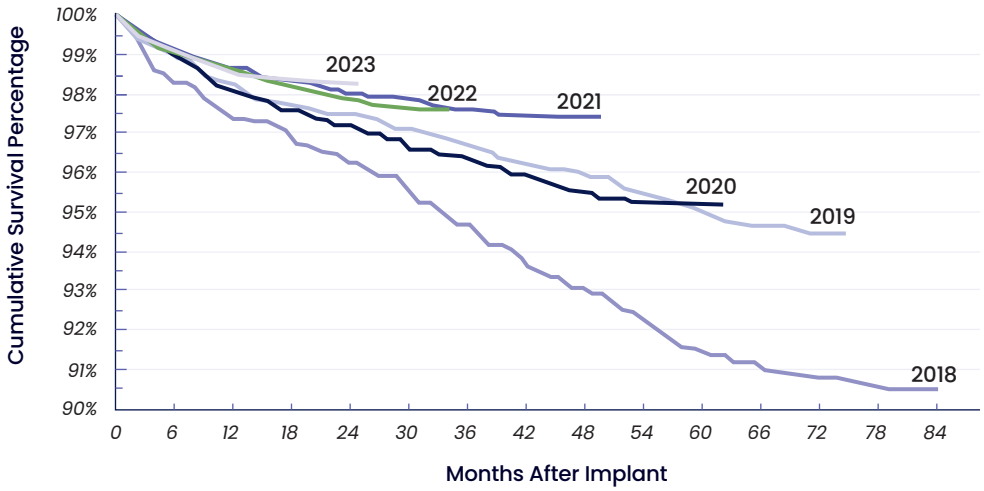
Surgical Revision & Device Explant Results

Inspire monitors and collects post-market surveillance data on surgical revisions and device explants. Our historical and go-forward improvements in product and patient outcomes are real and measurable. Year-over-year improvements are driven by:

- Continuous training and improvement to surgical technique
- Improved Inspire Medical Systems field support training
- Elective explant rates decreasing with improved patient selection
- Continuous improvements to the post-implant patient care pathways
- Regulatory approval of expanded labeling

Post-Market Surveillance (Revision Rates)

Figure 1: Inspire Global System Survivability to Revision by Implant Year[4]



2023 Primary Reasons for Revision:

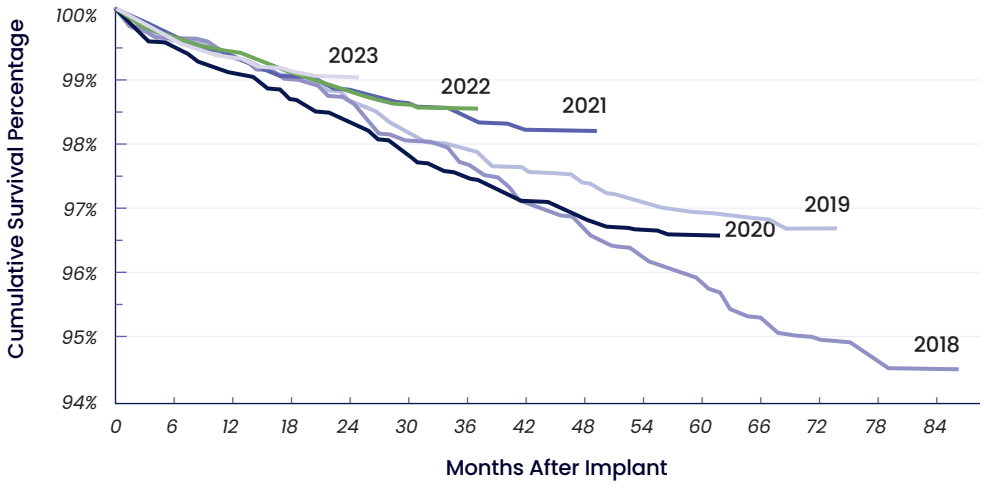
- **Device Movement** (device migration, erosion, tethering, dislodgement)
- **Device Deficiency** (related to the respiratory sensing lead [primary] or IPG)
- **Post-surgical Healing** (hematoma, incision dehiscence, resuture, seroma)

Top 3 reasons account for 71% of total revisions.

A device revision is a surgical event where a patient requires that an implanted system component be replaced or a surgical intervention is necessary to remedy an adverse event or patient complaint.

Post-Market Surveillance (Explant Rates)

Figure 2: Inspire Global System Survivability to Explant by Implant Year



2023 Primary Reasons for Explant:

- Elective Explant
- Infection
- MRI Compatibility

Top 3 reasons account for 93% of total explants.

A device explant is a surgical event where a patient requires the removal of the entire implanted system or removal of an implanted system component.

[4] *Huntley, et al. Real-World Evaluation of Upper Airway Stimulation System Survival Using Post-Market Surveillance Data. [Poster abstract]. SLEEP 2023 Conference.*

Figures 1 and 2 (on the preceding page) show the percentage of implanted patients that remain free from revision or explant-related events at various time points post implant. These are estimated using the Kaplan-Meier statistical method. These estimates intend to illustrate the probability that a patient is free from a surgical revision or device explant related event for a given period of time. As an example, a probability percentage of 97% indicates that through the stated follow-up time, the patient had a 3% risk of a surgical revision or device explant since the time of initial implant.

These statistical curves are estimates based on internal quality reporting systems. As our experience accumulates, the accuracy of the estimation improves.

In 2023, Inspire's post-market surveillance system (illustrated earlier) identified the Respiratory Sensing Lead as the top reason for device deficiency revisions, which prompted corrective actions.

1. **Respiratory Sensing Lead – Damage:** During routine office visits, physicians review each patient's diagnostic data. In a small number of patients, a revision surgery is required as the lead insulation is damaged and is detectable during check-up. Most revisions are related to the Inspire Model 4323 Respiratory Sensing Lead which is no longer manufactured. The Inspire Model 4340 Respiratory Sensing Lead, released to the US market in 2019 and currently in production, is more robust and designed specifically to mitigate this risk.

   In 2023, surgical revisions related to sense lead damage or other sensor defects have been reduced to 9.6% of all surgical revisions performed in the year.

2. **Respiratory Sensing Lead – Tip Failure:** This results in a revision surgery for a small number of patients because the sensing lead tip separated from the primary lead body. Three specific action items were formally implemented to mitigate this risk in 2021:

   - Best practice surgical training on the handling and insertion of the lead
   - An improved surgical technique for implanting the sensing lead; specifically, moving from a 3-incision procedure to a 2-incision procedure
   - Acknowledgment of possible sensing lead interactions with patient anatomy

   Implementation of these mitigations decreased the reported occurrence rate of this issue in patients post mitigation from approximately 1.1% (1 in 90 procedures) to 0.07% (1 in 1,400 procedures).

   There were no surgical revisions due to sensing lead tip failures in the post-mitigation implant population (patients implanted in 2022 & 2023). We expect the rate of occurrence for this event will continue to be less than 0.1%.

Complications – ADHERE Registry

The ADHERE Registry, which includes 5,000 patients, collects information related to serious complications with the Inspire implant or system. Complications are classified as either serious or non-serious. A serious complication (adverse event) is an event that is one or more of the following: requires hospitalization and/or surgical intervention; leads to a persistent or significant disability or incapacity; is life-threatening.

Serious complications, reported to date, are detailed in the table below according to the period in which they occurred (intraoperative or postoperative). The intraoperative period includes the operative and immediately post-operative period (<10 days post-implant). The postoperative period refers to the remainder of the follow-up period.

To date, 0.4% and 2.4% of patients in the ADHERE Registry have experienced serious intraoperative and postoperative complications, respectively.

Serious Intraoperative Complications[5]	% of Patients
Hematoma	0.1%
Arrhythmia	0.1%
Bleeding	<0.1%
Anesthesia-related Issues	<0.1%
Failed Implant	<0.1%
Pneumothorax	<0.1%
Other	<0.1%
Total	**0.4%**

Serious Intraoperative Complications[5]	% of Patients
Infection	0.1%
Explant (entire system)	0.4%
Revision (2 or more components)	0.3%
Revision (IPG only)	0.4%
Revision (Sense lead only)	0.8%
Revision (Stimulation lead only)	0.5%
Other	0.1%
Total	**2.4%**

In addition to the serious adverse events noted above, non-serious issues are also collected in the ADHERE Registry. Most frequent non-serious issues (with incidence rate > 2.0%) are detailed in the table below. The most common non-serious complication is stimulation-related discomfort, which is typically addressed with adjustments to the therapy settings.

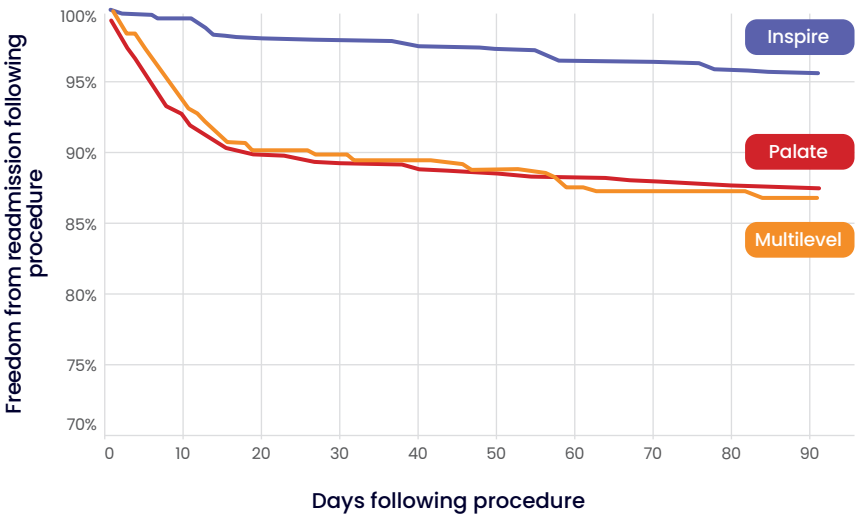
Most Common Non-Serious Issues[5]	% of Patients
Stimulation-related Discomfort	7.8%
Insomnia/Arousal	5.0%
Tongue Abrasion	3.1%

[5] *Data on file*

Comparison to Anatomy-Altering OSA Surgery – Third Party Data

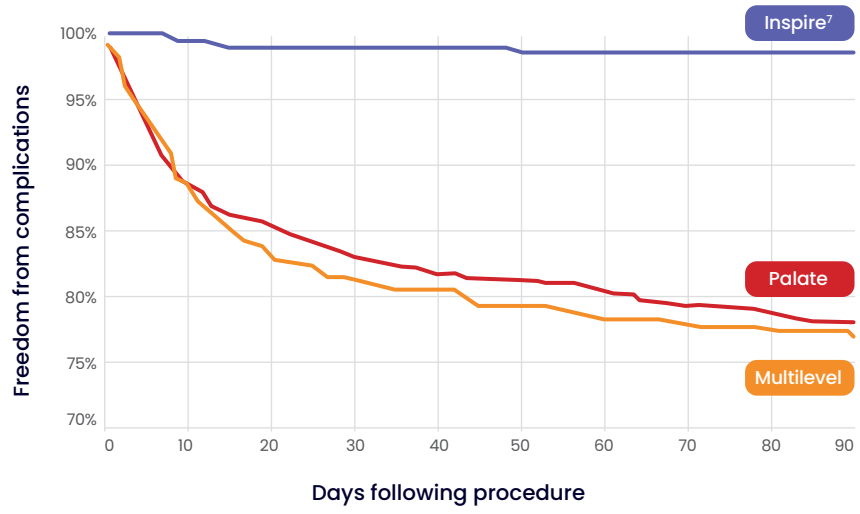
There are other CPAP alternatives available for moderate to severe OSA patients, including anatomy-altering surgeries. Nord, et. al evaluated readmissions and complications following Inspire Upper Airway Stimulation (UAS) compared to palatal or multilevel sleep surgery. Both hospital readmission and complications following the procedure were significantly lower in the UAS group compared to anatomy altering surgeries. This information is included in the Inspire Patient Experience Report to provide a reference point for the complication rates seen with the Inspire procedure.

Readmission Following Procedure[6]



- Palatal surgery had a higher risk of readmission or return to OR (12%vs 4%, p<0.0001), and a higher complication rate (21% vs 2%, p<0.0001) than Inspire therapy
- Multilevel surgery results had a similarly higher risk of readmission / return to OR (12% vs 4%, p<0.0001, complications: 22% vs 3%, p<0.0001)

Complications Following Procedure

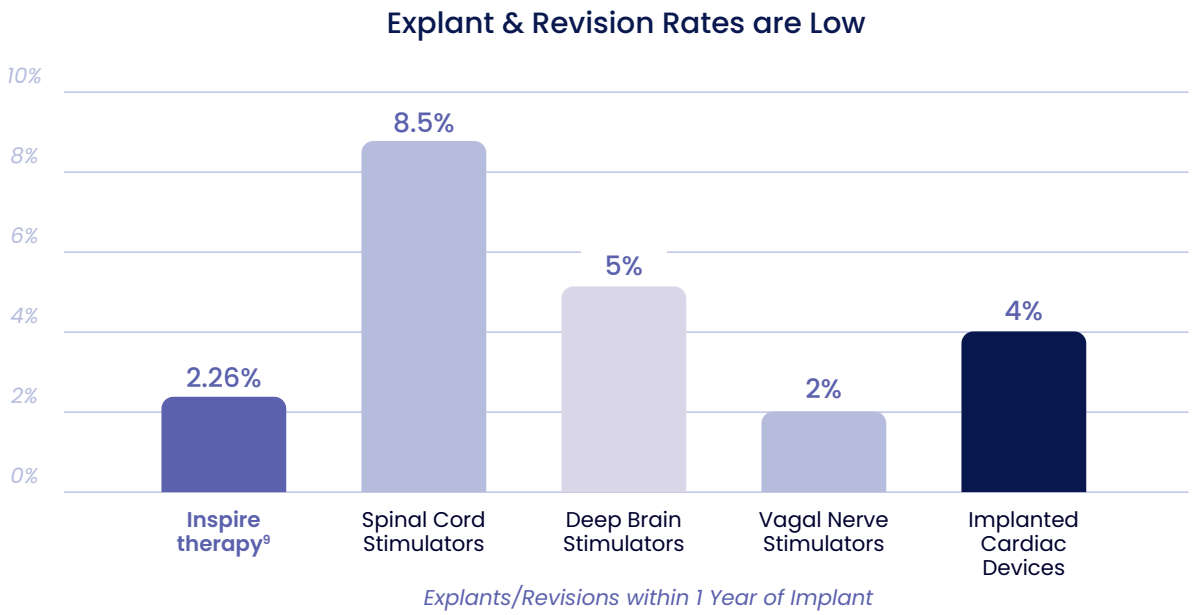


The first 20 days following surgery was most risky for readmission for both palate and multilevel surgeries, but the Inspire therapy group had relatively few complications, measured out to 90 days

[6] *Nord R, Fitzpatrick T, DeShazo JP, Reiter ER. Comparison of readmission and complication rates between traditional sleep surgery and hypoglossal nerve stimulation. Laryngoscope Investig Otolaryngol. 2022;7(5):1659-1666.*

[7] *Based on Inspire implants from April, 2014–March, 2021.*

A third-party review and analysis of Inspire therapy post-market data[8] has stated the real-world commercial performance of Inspire therapy is comparable to the observed clinical study data. The reported rates of explant and revision are very low and compare well against rates for other implanted stimulators.



[8] *Moroco, et al.*

[9] *Based on Inspire implants from January, 2018–March, 2022.*