PRODUCT PERFORMANCE REPORT

SUMMARY OF DATA FROM THE MEDTRONIC POST-MARKET REGISTRY

2019

v.1.0 03Apr2020

Medtronic
Further, Together

Contents

1 Overview

1.1 Registry Background

Medtronic uses a prospective, long-term multi-center registry to monitor the performance of certain products at selected centers titled the Product Surveillance Registry (PSR). This registry was initially created by Medtronic to monitor the performance of commercially available target drug delivery (TDD) and spinal cord stimulation (PSTM) systems. Later on deep brain stimulation (DBS) and sacral neuromodulation (SNM) were added to the registry. This 2019 Product Performance Report (PPR) provides data on the devices followed in the registry. Medtronic also incorporates the findings of Returned Product Analysis (RPA) for devices followed in the registry that are returned to Medtronic.

Depending upon geography, this report may contain information outside approved labeling for the Medtronic commercially available devices. It is recognized that healthcare providers prescribe approved therapies to meet specific patient needs; however, Medtronic only directs the use of its products according to geography-specific, approved labeling.

The registry has collected data from centers across North America, Europe, South America, and Asia. There have been 76 centers that have contributed data for TDD systems, 84 centers for PSTM systems, 43 centers for DBS systems, and 23 centers for SNM systems. Each registry center received Institutional Review Board or Medical Ethics Committee approval of the registry protocol and associated Informed Consent Forms (ICF). Registry patients signed an ICF prior to enrollment. Each registry center followed its standard clinical practice for device system implantation including patient selection, implant methods, and post-implant therapy management. Centers were activated after receipt of the necessary documentation, completion of training, and approval to access the web-based registry system.

1.2 Commitment to Quality

The Medtronic commitment to quality has long been stated in our Mission, "To strive without reserve for the greatest possible reliability and quality in our products; to be the unsurpassed standard of comparison and to be recognized as a company of dedication, honesty, integrity, and service."

In line with this commitment we remain focused on sharing information and appropriate updates with customers on a regular basis. Thus, we are pleased to share the 12th Annual Medtronic Neuromodulation Product Performance Report.

We are proud of our pioneering history at Medtronic and we realize the responsibility that comes with driving innovation in technology. As the first and only company to offer a full line of Spinal Cord Stimulation, Deep Brain Stimulation, Sacral Neuromodulation and Targeted Drug Delivery therapies, we believe that performance reporting is of critical importance as we strive for better performance with every new product and therapy we develop. This report shows the evolution of product performance over time and also reveals advances in therapies that come with this experience and knowledge. Through this sharing of information we can enable physicians to best leverage state-of-the-art therapy delivery and also understand the performance of our devices to best manage patients.

We have tracked 18,572 patients in our ongoing post-market registry. The registry has enrolled 56,563 Neuromodulation system components. Components include pumps, catheters, neurostimulators, leads, and extensions. Data on other events not directly attributed to product performance are also included to provide additional information that may be important for patient management. Although gastric electrical stimulation also involves neurostimulation, the performance of these systems is not included in this report.

We welcome your suggestions on content, format, and any information you may have regarding the performance of Medtronic products. If you have questions or comments, please contact us through the information provided below.

Thank you for your support.

Todd Weaver, PhD, MPH
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Medtronic

1.3 Contact Information

We invite our customers to use this telephone number to call with suggestions, inquiries, or specific problems related to our products or this report.

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1.5 Trademarks of Medtronic, Inc.

Therapy	Trademarks
Targeted Drug Delivery	Ascenda™ intrathecal catheter
	SynchroMed™ implantable drug pump
Spinal Cord Stimulation	AnkerStim™
	Intellis™ neurostimulator
	Itrel™ 3 neurostimulator
	Pisces-Octad™ lead
	Pisces-Quad™ lead
	PrimeAdvanced™ neurostimulator
	PrimeAdvanced™ SureScan™ MRI neurostimulator
	Restore™ implantable neurostimulator
	RestoreAdvanced™ neurostimulator
	RestoreAdvanced™ SureScan™ MRI neurostimulator
	RestoreSensor™ neurostimulator
	RestoreSensor™ SureScan™ MRI neurostimulator
	RestoreUltra™ neurostimulator
	RestoreUltra™ SureScan™ MRI neurostimulator
	Resume™ TL lead
	Specify™ lead
	Synergy Versitrel™ neurostimulator
	Synergy™ neurostimulator
	SynergyCompact™ neurostimulator
	SynergyPlus+™ neurostimulator
	Vectris™ SureScan™ lead
Deep Brain Stimulation	Activa™ neurostimulator
	Kinetra™ neurostimulator
	Soletra™ neurostimulator
Sacral Neuromodulation	InterStim™ neurostimulator

2 Methodology

2.1 Event Classification

Events currently collected in the registry include all events that appear or worsen during the registry and are a result of:

- Implanted or external components (device related),
- Implant or modification procedure (procedure related), or
- Infusion or stimulation therapy (therapy related).

Information on all deaths is also collected regardless of their relatedness to the device, implant procedure, and/or therapy.

For centers participating in the PSR protocol, specific therapy relevant events for deep brain stimulation are also collected and include:

- Negative changes in behavior from baseline,
- New or worsening depression from baseline, and
- New or worsened suicidal ideation from baseline, attempted suicide or completed suicide.

For some events related to implanted neuromodulation systems that did not exist in the MedDRA dictionary, Medtronic used their own coding system, and all results were integrated for reporting purposes.

2.1.1 Registry Definitions

In the registry, the events are defined as follows (see Figure 2.1 for the procedure to detemine the event types):

- **Adverse Event:** any death or undesirable experience (associated with signs, symptoms, illnesses, or other medical events) occurring to the patient that appears or worsens during the clinical study and is possibly related to the device, procedure, and/or therapy.
- **Device Event:** an issue with any of the implantable or external system components.
- **Therapy Relevant Event:** a therapy specific event type that may or may not be related to the device, procedure, or therapy.

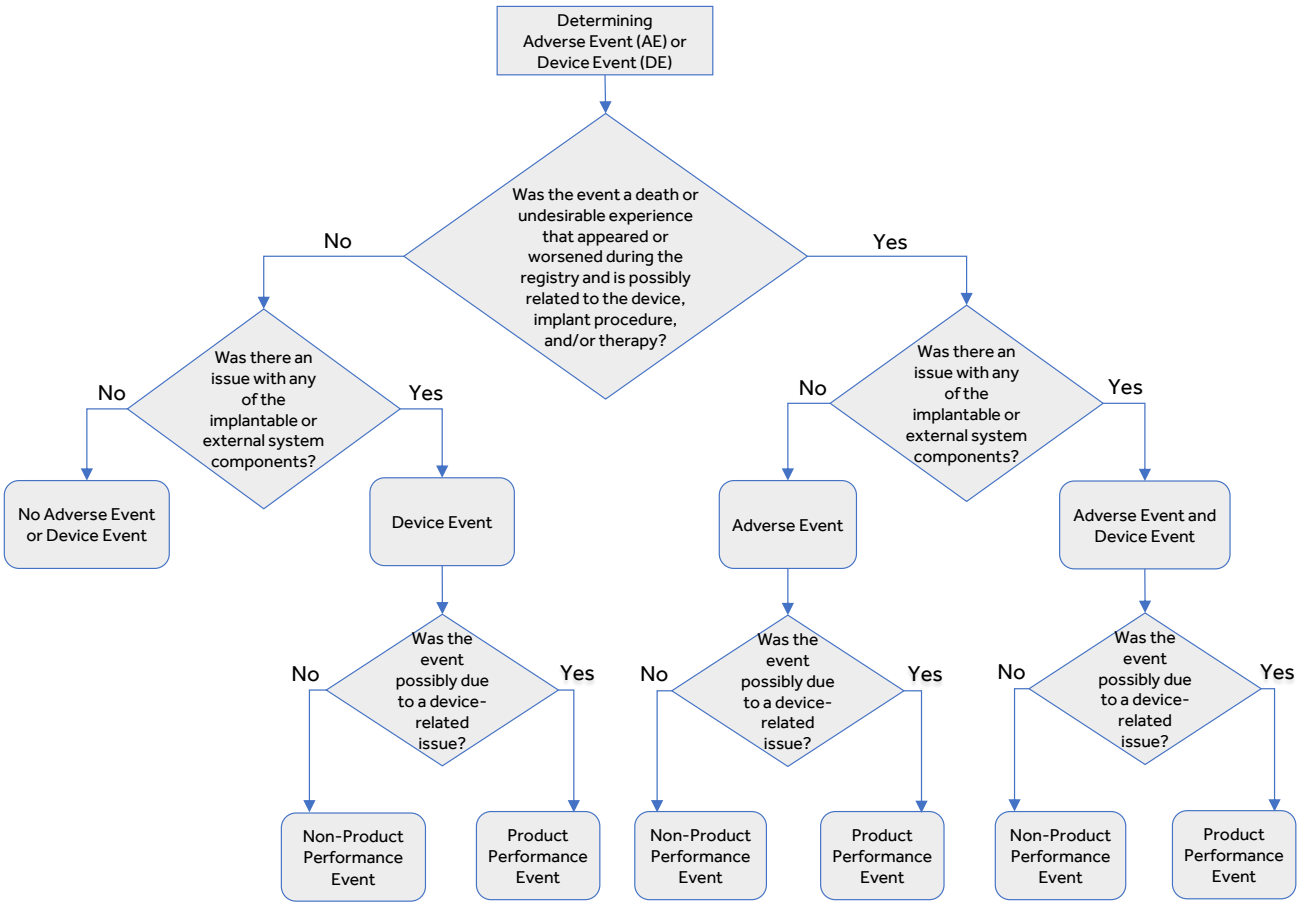


Figure 2.1: Adverse Event/Device Event Flowchart

2.1.2 Product Performance and Non-Product Performance Categorization

For analysis purposes, events collected were collapsed into two categories: product performance events and non-product performance events. All events were reviewed by Medtronic to determine if they were product performance-related (product performance events are events that are possibly due to a device-related issue). A non-product performance related event, or a clinical event not related to product performance, was any undesirable experience (associated with signs, symptoms, illnesses, or other medical events) occurring to the patient, and that appears or worsens during the clinical study. These clinical events not related to product performance possibly resulted from or were related to the implant procedure, or modification between implant and procedure, therapy, or delivery of therapy, and cannot be classified as product performance-related. All clinical events not related to a product performance and reported as a serious adverse event were summarized by MedDRA System Organ Class (SOC) if the event met a patient percentage threshold (0.5% to 1.0%).

2.1.3 Consistency and Accuracy

Consistency and accuracy of event reporting is monitored at four levels: through logic checks built into the study database as center personnel enter information; through review of each event by the study team as it is received by Medtronic; review by the Medical Advisor when necessary; and through routine monitoring at each center per Medtronic standard operating procedures. Monitoring is accomplished through a risk-based approach that aligns with the current FDA guidance on monitoring. Through this approach not every data field is monitored but an emphasis is placed on data related to the primary objective (e.g., events). Clarification and subsequent adjudication of events may be required for, but is not limited to, the following reasons:

- Inconsistency with the protocols,
- Inconsistency with the instructions provided to the centers through training materials,
- Incomplete or inaccurate event description that makes a reported event reason, event reason detail, and the clinical data appear inadequate or inconsistent,
- Medtronic Customer Support and Vigilance Complaint management requirement for additional information, or
- Center personnel initiated corrections or additions.

2.2 Device Survival Analyses

Device performance is expressed in terms of device survival estimates, where "survival" refers to freedom from a product performance event, not the survival of the patient. These survival probabilities are estimated using the Kaplan-Meier method [1]. The estimates are intended to illustrate the probability that a device will survive for a given number of years without a product performance related event.

Active surveillance normally begins at the time of implant and continues until a product performance or censoring event occurs. In some cases in the registry, active surveillance of a device starts after the device was implanted, which is called left truncation [1]. The survival probability of such a device is conditional on survival to the time when the device enters the registry. For the PPR analysis, a statistical method to incorporate data from these retrospectively enrolled devices was applied. Left truncation provides a statistical technique that uses data from existing devices while appropriately adjusting the device survival curves for the time the device was not actively followed in the registry. Thus, in some cases sample sizes may fluctuate from one time interval to the next interval.

Throughout this report, cumulative device survival plots are presented. These figures show the percentage of implanted devices that remain free from product performance-related events at various time points. This survival estimate is a good representation of the probability a device will survive a period of time without a product performance event. For example, a device survival probability of 90% indicates that through the stated follow-up time, the device had a 10% risk of incurring a product performance event since the time of implant.

The survival curves are statistical estimates. As performance experience accumulates, the accuracy of the estimation improves. Confidence intervals are provided as a way to indicate the degree of certainty of the estimates. Greenwood's formula is used to calculate the standard errors, and the log-log method is used to produce the 2-sided 95% confidence bounds [2]. This can be roughly interpreted as meaning that the true survival of the device will fall somewhere in the interval, with 95% probability. When confidence intervals for device models overlap, estimates of survival from product performance-related events may not be different between models. When confidence intervals do not overlap, estimates of survival from product performance-related events may be different between models. Statistical significance may be further evaluated using the Log-rank test or Wilcoxon test as appropriate.

The device survival curves are presented through all continuous time points where there are at least 20 devices, and are cut off at the last 3-month time point where at least 20 total devices were still being followed. Since the survival estimate can become very imprecise with small sample sizes, a minimum of 20 devices must have at least 12 months of follow-up as of the report cut-off date to present a survival curve in this report. Device survival estimates are presented at the device level, not at the system level which involves the combination of two or more devices.

2.3 Returned Product Analysis

Registry devices that are returned to Medtronic are analyzed via a Returned Product Analysis (RPA) process following protocols to confirm proper functioning or identification of root cause for any failure or deficiency. For registry pumps and neurostimulators that are returned, and for which RPA establishes a root cause or finds no anomaly, results reported herein reflect the RPA finding unless otherwise indicated in this report. When available, RPA findings are also used as one of the sources to identify the root cause of failure or deficiency for catheters and leads. In cases where the center does not explant and/or return a device, the physician-reported event reason is used for classification and analysis purposes.

Medtronic uses data from RPA as well as complaint reports from non-returned product for ongoing quality monitoring and improvement efforts. This report presents data from the registry including the results of RPA for returned devices from registry centers and patients. Data from RPA outside the registry centers and patients are not presented in this report.

REFERENCES

1. Klein, John P., Moeschberger, Melvin L. Survival Analysis Techniques for Censored and Truncated Data, New York: Springer-Verlag New York, Inc., 1997.
2. Lee, Elisa T. (2003) Statistical Methods for Survival Data Analysis — 3rd Edition (Wiley Series in Probability and Statistics).

3 Targeted Drug Delivery Systems

3.1 Study Participants

3.1.1 Centers

The targeted drug delivery tables and graphs were generated based on data collected between August 7, 2003 and the report cut-off date of October 31, 2019. Seventy-six centers spanning 12 countries in North America, Europe and South America, enrolled patients and contributed patient data to the targeted drug delivery systems section of this report. Figure 3.1 shows a World Map, in which the countries that enrolled TDD patients are highlighted.

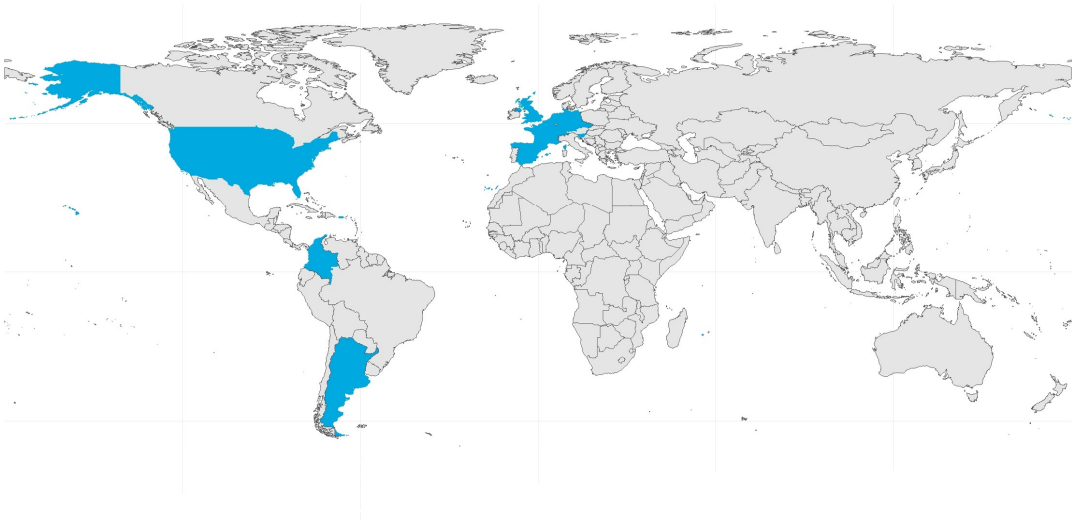


Figure 3.1: Countries with Targeted Drug Delivery Therapy Patients in Registry (Highlighted)

3.1.2 Patients

There were 8,997 total targeted drug delivery system patients enrolled through October 31, 2019. In Table 3.1 and Figure 3.2, 57.9% of patients were implanted with a targeted drug delivery system for treatment of non-malignant pain (pain not related to cancer and its treatment), followed by 22.4% for treatment of spasticity, and 17.6% for treatment of malignant pain (pain

related to cancer). Primary treatment indication is provided by the physician. The sites of pain for the malignant pain patients are presented in Table 3.2, while the sub-indications for the non-malignant pain and the spasticity patients are presented in Table 3.3 and Table 3.4, respectively.

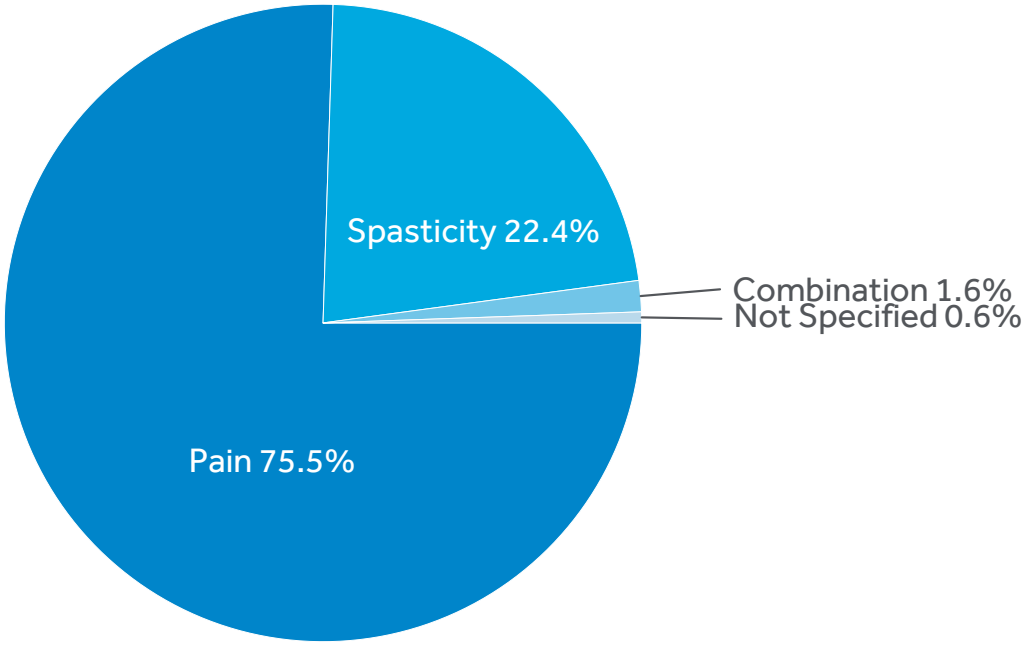


Figure 3.2: Targeted Drug Delivery Primary Treatment Indications

Table 3.1: Targeted Drug Delivery Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Pain	**6,793 (75.5%)**
Non-malignant pain	5,208 (57.9%)
Malignant pain	1,584 (17.6%)
Pain, Not specified	1 (0.0%)
Spasticity	**2,012 (22.4%)**
Combination	**142 (1.6%)**
Non-malignant pain & Spasticity	141 (1.6%)
Malignant pain & Spasticity	1 (0.0%)
Not Specified[b]	**50 (0.6%)**
Total Patients	**8,997 (100%)**

[a] For approved indications refer to product labeling for your geography.

[b] Includes incomplete data forms at the time of the data snapshot and exited patients where indication was never provided.

Table 3.2: Targeted Drug Delivery Malignant Pain: Site of Pain

Malignant Pain: Site of Pain	Count
Spine/Back	587
Abdominal/Visceral	365
Extremity	255
Pelvic	217
Thoracic	180
Head/Neck	95
Other	139
Not Specified	439
Total Sites of Pain[a]	**2,277**

[a] In 1,585 patients with indications of malignant pain and a combination of malignant pain and spasticity.

Table 3.3: Targeted Drug Delivery Non-Malignant Pain: Sub-Indications

Non-Malignant Pain: Sub-Indications	Enrolled Patients (%)
Back Pain with Leg Pain	1,724 (32.2%)
Back Pain without Leg Pain	1,533 (28.7%)
General Neuropathic Condition	229 (4.3%)
CRPS I[a]	167 (3.1%)
Peripheral Neuropathy	82 (1.5%)
Joint Pain/Arthritis	70 (1.3%)
General Nociceptive Condition	51 (1.0%)
CRPS II[a]	37 (0.7%)
Osteoporosis	20 (0.4%)
Other	481 (9.0%)
Not Specified	955 (17.9%)
Total Patients[b]	**5,349**

[a] CRPS is complex regional pain syndrome.
[b] Includes patients with indications of non-malignant pain and combinations of non-malignant pain with spasticity.

Table 3.4: Targeted Drug Delivery Spasticity: Sub-Indications

Spasticity: Sub-Indications	Pediatrics (%) (<18 years)	Adults (%) (>= 18 years)	All Patients (%)
Cerebral Palsy	345 (77.5%)	231 (13.5%)	576 (26.7%)
Multiple Sclerosis	0 (0.0%)	528 (30.9%)	528 (24.5%)
Spinal Cord Injury	7 (1.6%)	336 (19.7%)	343 (15.9%)
Brain Injury	36 (8.1%)	118 (6.9%)	154 (7.1%)
Stroke	1 (0.2%)	88 (5.1%)	89 (4.1%)
Other	12 (2.7%)	178 (10.4%)	190 (8.8%)
Not Specified	44 (9.9%)	230 (13.5%)	274 (12.7%)
Total Patients[a]	**445**	**1,709**	**2,154**

[a] Includes patients with indications of non-malignant pain and combinations of non-malignant pain with spasticity.

It is recognized that health care providers prescribe therapies to meet specific patient needs; however, Medtronic only directs the use of its products based on approved regulatory labeling. Product labeling varies by geography. Contact a local Medtronic representative for region-specific product labeling.

3.2 Event Summary

There were 2,118 product performance events reported between August 7, 2003 and October 31, 2019, in patients with targeted drug delivery systems. These events represent 22.1% of the total reported events (2,118/9,564), which occurred in 1,373 (15.3%) of the 8,997 total patients enrolled, and are presented graphically within this report (e.g. events per patient years as well as survival curves). As an ongoing registry, events not coded at the time of the data snapshot (waiting for further information) will be included in future reports (n=40).

All registry devices that are returned to Medtronic are analyzed via a Returned Product Analysis (RPA) process. If available, RPA findings assist in the classification of the events. Within this report, Table 3.5 and the event tables in the pump and catheter sections differentiate the events by those determined by the RPA process versus those determined by the physician. Please refer to the Methodology section for more information.

There were 2,221 deaths reported for patients with targeted drug delivery systems (see Table 3.11). None of these deaths were reported as a direct result of a product performance event. Early versions of the protocol required events to be reported only when the event required a surgical intervention, resulted in therapy abandonment, or resulted in death. The required event reporting definition was expanded in April 2010 to include all adverse events related to the device, implant procedure, and/or therapy. Table 3.5 includes combined data from these versions of the protocol.

3.2.1 Product Performance Events

Table 3.5: Targeted Drug Delivery System Product Performance Events

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=8,997[b]
RPA Determination	**285**	**0.99**	**259 (2.88%)**
Pump Motor Stall[c]	155	0.54	150 (1.67%)
Laboratory Overinfusion Finding[d]	30	0.10	29 (0.32%)
Corrosion And/Or Gear Wear	28	0.10	28 (0.31%)
Battery High Resistance	11	0.04	11 (0.12%)
Confirmed Overinfusion[e]	11	0.04	5 (0.06%)
Reduced Battery Performance	10	0.03	10 (0.11%)
Deformed Pump Tube	8	0.03	7 (0.08%)
Motor Feedthrough Anomaly	7	0.02	7 (0.08%)
Reservoir Access Issues Due To Residue	7	0.02	6 (0.07%)
Alarm And/Or Resonator Anomaly	2	0.01	2 (0.02%)
Hole In Pump Tube	2	0.01	1 (0.01%)
Other[f]	14	0.05	14 (0.16%)
Physician's Determination	**1,833**	**6.38**	**1,235 (13.73%)**
Catheter Occlusion	402	1.40	359 (3.99%)
Catheter Dislodgement	367	1.28	309 (3.43%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=8,997[b]
Catheter Break/Cut	230	0.80	205 (2.28%)
Catheter Kink	203	0.71	179 (1.99%)
Pump Motor Stall[g]	106	0.37	87 (0.97%)
Device Malfunction[h]	102	0.35	91 (1.01%)
Catheter Related Complication	83	0.29	78 (0.87%)
Catheter Leakage	63	0.22	60 (0.67%)
Pump Reservoir Volume Discrepancy	53	0.18	39 (0.43%)
Catheter Disconnection At Pump	48	0.17	47 (0.52%)
Pump Unable To Enter/Withdraw From Catheter Access Port	36	0.13	30 (0.33%)
Device Difficult To Use	19	0.07	19 (0.21%)
Pump Underinfusion	19	0.07	16 (0.18%)
Medical Device Complication[i]	18	0.06	16 (0.18%)
Pump Connector Break/Cut	18	0.06	17 (0.19%)
Device Issue[j]	10	0.03	10 (0.11%)
Catheter Disconnection Between Catheter Segments	7	0.02	7 (0.08%)
Catheter Access Port Issue	6	0.02	6 (0.07%)
Device Breakage	6	0.02	6 (0.07%)
Catheter Damage	5	0.02	5 (0.06%)
Device Alarm Issue	4	0.01	4 (0.04%)
Device Connection Issue	4	0.01	4 (0.04%)
Pump Not Infusing	3	0.01	3 (0.03%)
Device Damage	2	0.01	2 (0.02%)
Physician Reported Overinfusion[k]	2	0.01	2 (0.02%)
Other[f]	17	0.06	17 (0.19%)
Total	**2,118**	**7.37**	**1,373 (15.26%)**

[a] Medical Dictionary for Regulatory Activities (MedDRA) Lower-Level Term or Medtronic's coding system term for events that do not exist in the MedDRA dictionary.

[b] The total number of patients with events may not represent the sum of all rows, as a patient may have experienced more than one type of event.

[c] Of the 155 RPA determined motor stalls, 154 had a pump etiology and 1 had other etiology. Motor stall count does not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. The SynchroMed II pump is designed to temporarily stop the rotor of the pump motor and suspend drug infusion for the duration of the MRI exposure for patient safety.

[d] Includes pumps that had a laboratory finding but the patient did not have clinical signs or symptoms consistent with pump overinfusion.

[e] Patient had clinical signs and symptoms consistent with pump overinfusion, pump returned and positive laboratory test.

[f] Composed of event codes with 1 event each.

[g] Of the 106 physician determined motor stalls, 93 had a pump etiology; 1 had another etiology and 12 had a MRI etiology. Of the 12 MRI etiology, 2 pumps were replaced and 10 remain active in the patients. Motor stall count does not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. The SynchroMed II pump is designed to temporarily stop the rotor of the pump motor and suspend drug infusion for the duration of the MRI exposure for patient safety.

[h] Includes 66 PTM malfunctions, 11 unexpectedly locked out of PTM, 6 pump malfunctions, 4 PTM unable to sync with pump, 2 pump reset occurred, 2 PTM displayed incorrect alarm date, 2 pump stopped mode, 1 clinician programmer malfunction, 1 patient felt pump not working, 1 unspecific difficulties with PTM, 1 PTM bonding issue, 1 possibly due to antenna, 1 suspected rotor problem, 1 possible pump malfunction, 1 PTM not providing boluses, 1 PTM displayed incorrect reservoir alarm.

[i] Includes 5 worn catheter connector, 2 possible corrosion of catheter due to concentration of drug, 1 metal clips on sutureless connector appear bent, 1 pump unable to interrogate/program, 1 pump in safe state, 1 worn proximal connector, 1 telemetry was stopped secondary to error code, 1 worn catheter, 1 sutureless connector failure, 1 pumped beeped, 1 wear and tear of connector pin, 1 pocket of air detected in dye study, 1 sutureless attachment worn off.

[j] Includes 6 unable to activate PTM, 3 PTM Error Codes and 1 de-coupled PTM.

[k] Patient had clinical signs and symptoms, but pump not returned and analyzed.

A total of 1,459 (68.9%) of the 2,118 product performance events were related to the catheter only. There were 475 (22.4%) events related to the pump only. There were 134 (6.3%) related to other component and 50 (2.4%) related to other etiologies. Relatedness is reported by the physician.

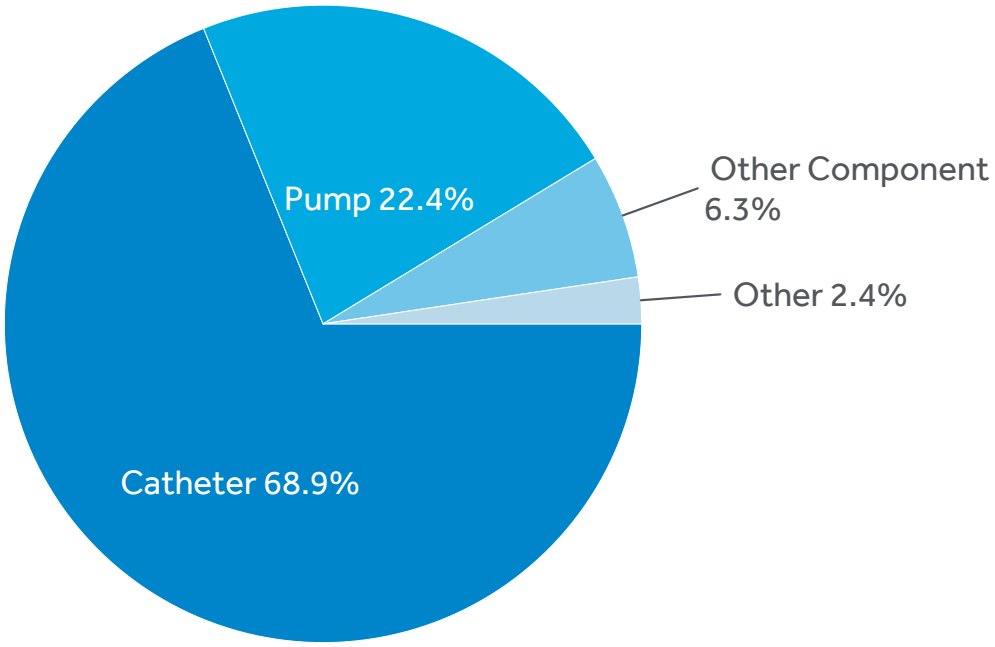


Figure 3.3: Targeted Drug Delivery System Product Performance Events by Relatedness

3.2.2 Clinical Events Not Related To Product Performance

The clinical events not related to product performance are summarized if:

- The patient was enrolled in the PSR at the time in which the clinical event collection was initiated (N=2,421)
- Categorized as serious adverse events
- Occurred with a System Organ Class (SOC) threshold $\geq$1% of patients
- Other Considerations
  - Some events are described in high level group terms (HLGT) to provide more specificity, if needed
  - Some therapies will provide therapy relevant events (e.g., Inflammatory Mass, Cerebrospinal Fluid Leaks)

Table 3.6: Targeted Drug Delivery Clinical Events Not Related To Product Performance

Event Type	Number of SAE	Patients with SAE n (%) N=2,421	SAE Per 100 Patient Months	Patients with SAE Requiring Surgical Intervention n (%) N=2,421
General disorders and administration site conditions	**72**	**67 (2.77%)**	**0.18**	**13 (0.54%)**
Therapeutic and nontherapeutic effects (excl toxicity)	47	43 (1.78%)	0.12	2 (0.08%)
Complications associated with device	16	16 (0.66%)	0.04	10 (0.41%)
General system disorders NEC	7	7 (0.29%)	0.02	1 (0.04%)
Other[a]	2	2 (0.08%)	0.00	1 (0.04%)
Infections and infestations	**57**	**52 (2.15%)**	**0.14**	**44 (1.82%)**
Infections - pathogen unspecified	40	37 (1.53%)	0.10	34 (1.40%)
Bacterial infectious disorders	17	17 (0.70%)	0.04	11 (0.45%)
Nervous system disorders	**33**	**31 (1.28%)**	**0.08**	**12 (0.50%)**
Neurological disorders NEC	15	15 (0.62%)	0.04	7 (0.29%)
Neuromuscular disorders	6	6 (0.25%)	0.01	2 (0.08%)
Other[a]	12	12 (0.50%)	0.03	3 (0.12%)
Injury, poisoning and procedural complications	**29**	**28 (1.16%)**	**0.07**	**8 (0.33%)**
Overdoses and underdoses NEC	12	12 (0.50%)	0.03	0 (0.00%)
Procedural related injuries and complications NEC	12	12 (0.50%)	0.03	6 (0.25%)
Other[a]	5	5 (0.21%)	0.01	2 (0.08%)
Other SOC Terms (<1.0% Threshold)	**20**	**20 (0.83%)**	**0.05**	**4 (0.17%)**
Total	**211**	**178 (7.35%)**	**0.53**	**74 (3.06%)**

[a] Composed of high level group term event codes with fewer than 5 events each.

3.2.3 Therapy Relevant Events

3.2.3.1 Cerebrospinal Fluid Leaks

Potential cerebrospinal fluid leak (CSF) events are identified and assessed by Medtronic personnel and the site physician of the case to ascertain the case definition using Table 3.7.

Table 3.7: Cerebrospinal Fluid Leak Event Definition

Case Definition	Ascertainment
Definitive CSF Leak	▪ Observation of clear fluid leaking from the wound, or ▪ Dye study demonstrates extravasation of dye outside dura, or ▪ Patient with persistent post-operative ***positional*** headache, plus one of the following: – Blood patch or suturing relieves headaches, or – Subcutaneous ***persistent*** fluid collection on the catheter tract, or – Meningeal enhancement on MRI with contrast.
Probable CSF Leak	**Reproducible** post-operative **positional** headache for >14 days with or without report of subcutaneous fluid collection. No dye study performed or dye study result inconclusive.
Possible CSF Leak	**Intermittent** post-operative **positional** headache for >14 days without report of subcutaneous fluid collection. No dye study performed or dye study result inconclusive.
Not CSF Leak	Acute post-operative non-positional headache lasting less than 14 days.

The potential CSF leak status (N=313) at the time of this analysis is presented in Table 3.8 with a definitive and probable CSF leak rate of 1.1% (99/8,997). The causality of the CSF leak event is dependent on the individual cases.

Table 3.8: Summary of Cerebrospinal Fluid Leak Adjudication

Cases Reviewed	Definitive CSF Leak	Probable CSF Leak	Possible CSF Leak	Not CSF Leak	Unspecified[a]
313	91	8	18	166	30

[a] Unadjudicated due to the timing of the data or due to the site no longer being active.

3.2.3.2 Inflammatory Masses

Inflammatory mass, also sometimes reported as catheter-tip inflammatory mass or an intrathecal granuloma, is a potential complication of intrathecal opioid drug therapy. In order to better quantify the incidence of inflammatory mass, all events were evaluated for a report of inflammatory mass. For these identified cases, the medical records were reviewed by Medtronic personnel together with radiographic images when available. The radiographic images were reviewed to determine if there was evidence of an intradural extramedullary enhancing lesion.

The adjudication team assessed each case based upon the case definition and ascertainment guideline presented in Table 3.9. A summary of cases evaluated for IM through the data cut-off is shown in Table 3.10.

Table 3.9: Case Definition and Ascertainment of Inflammatory Mass

Case Definition	Ascertainment
Definitive IM	Surgical and histological verification or clinical symptoms plus contrast enhanced MRI or CT myelogram and resolution of lesion following cessation of drug exposure
Probable IM	No surgical or histological verification, but clinical criteria and enhanced MRI or CT myelogram criteria are present
Possible IM	Medical records document IM, but there is no surgical or histological verification, there are no clinical criteria, and no radiographic data are available
Not IM	Surgical and histological verification that lesion is another disease process rather than IM, or radiographic data do not show an intrathecal lesion

There were a total of 124 suspected cases of inflammatory mass (Table 3.10) that were discerned from evaluation of patient records and reviewed by the adjudication team. Medtronic will continue to evaluate reports of inflammatory mass. Any previously classified case of IM will be re-evaluated if new evidence is received after this report. An analysis of the adjudicated definitive and probable inflammatory mass cases in the PSR from 2003 through October 2019 indicates an incidence of 0.22% (15/6,793) for pain patients and 0% (0/2,012) for the spasticity patients.

Table 3.10: Summary of Inflammatory Mass Adjudication

Year of Event	Cases Reviewed	Definitive IM	Probable IM	Possible IM	Not IM
2004	4				4
2005	4	1		1	2
2006	7	1	1	2	3
2007	9	1	1	2	5
2008	4		1		3
2009	3	1			2
2010	11		1	1	9
2011	11	1	2	1	7
2012	13			1	12
2013	6			4	2
2014	10			2	8
2015	21	1		6	14
2016	10	1	1	2	6
2017	8				8
2018	2				2
2019	1	1			
Total	**124**	**8**	**7**	**22**	**87**

3.2.4 Patient Deaths

In earlier versions of the protocol, deaths were only assessed for the relatedness to the device product performance. After 2010, death assessments were expanded to also include the relationship to the implant procedure and/or therapy. As of the report cut-off, a total of 2,221 patients in the registry had expired. As with previous reports, no deaths were reported as a direct result of a product performance event. Although, three deaths were assigned by the physician as possibly related to the implant procedure and/or therapy.

Of the three deaths possibly related to the procedure and/or therapy, one death was due to a pulmonary embolism where the treating physician stated that the event could be possibly related to the withdrawal of the intrathecal medications. The patient had experienced a lack of therapy due to a missed refill visit leading to the withdrawal and not to the device malfunctioning. Medtronic Medical Safety assessed this death event as possibly related to the to the lack of therapy. A second death was reported by the treating physician as due to acute respiratory failure possibly related to the procedure and/or therapy. This patient had a history of persistent upper respiratory tract problems, difficulties swallowing and chronic aspiration as the result of cancer related treatments. Medtronic Medical Safety assessed this death event as possibly related to the surgery/anesthesia during the implant procedure and therapy. The third death was reported by the physician as due to respiratory distress possibly related to the

intrathecal medication. This patient had multiple comorbidities with multiple concomitant medications and a decreased level of physical activity. The death records state the cause of death as probable arteriosclerotic cardiovascular disease. Medtronic Medical Safety assessed this event as unassessable due to incomplete information.

Since 2003, a total of 1,265 (57.0%) deaths have been reported in this patient registry study based upon patients receiving therapy for malignant pain, 728 (32.8%) for non-malignant pain, 213 (9.6%) for spasticity, 11 (0.5%) for non-malignant pain & spasticity, and 4 (0.2%) for not specified primary indication (see Table 3.11). The percentage is based upon the total patient death events and not based upon the rate of occurrence. **All tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 3.11: Targeted Drug Delivery System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Malignant pain	1,265 (57.0%)
Non-malignant pain	728 (32.8%)
Spasticity	213 (9.6%)
Non-malignant pain & Spasticity	11 (0.5%)
Not Specified	4 (0.2%)
Total	**2,221 (100%)**

[a] For approved indications refer to product labeling for your geography.

3.3 Pumps

From August 7, 2003, to the report cut-off date of October 31, 2019, there were 11,132 pumps followed in the registry. The difference between the total number of patients (n=8,997) versus the total number of pumps is due to the fact that some patients were subsequently re-implanted with a pump multiple times. The aggregate prospective follow-up time for all pumps was 336,694 months (28,058 years). Table 3.12 provides the number and percentage of pumps by model.

3.3.1 SynchroMed II Design Change: Pump Enhancements

Design changes to the SynchroMed II 20 mL and 40 mL pump models were implemented to reduce the likelihood of non-recoverable motor stalls. These changes were released incrementally, allowing for the pumps to be considered in three groups: 1) Pre-Enhancements (prior to 2016), 2) the Modified Gear Wheel Material and Encapsulated Feedthroughs (GW3/FT) enhancements (released January 2016) and 3) the Applied Diamond Like Coating (GW3/FT/DLC) enhancement (released July 2017). All enhancements were communicated in the August 2017 Medical Device Safety Notification: SynchroMed II Implantable Drug Infusion Pump Design Change Model Numbers 8637-20, 8637-40. For details, please visit

https://www.medtronic.com/content/dam/medtronic-com/professional/documents/product-advisories/tdd/synchromed-pump-design-change-august-2017-hcp-letter.pdf. Table 3.12 provides the number and percentage of pumps by model and pump enhancement.

Table 3.12: Targeted Drug Delivery Pump Counts by Model and Pump Enhancement

Model Name	N (%)
SynchroMed II 40 mL	**6,044 (60.78%)**
Pre-enhancements[a]	4,785 (48.12%)
GW3/FT/DLC enhancements	723 (7.27%)
GW3/FT enhancements[a]	536 (5.39%)
SynchroMed II 20 mL	**3,900 (39.22%)**
Pre-enhancements[a]	3,046 (30.63%)
GW3/FT/DLC enhancements	491 (4.94%)
GW3/FT enhancements[a]	363 (3.65%)
SynchroMed EL 18 mL[a]	**1,146 (5.40%)**
SynchroMed EL 10 mL[a]	**34 (0.16%)**
SynchroMed Classic[a]	**5 (0.02%)**
Other/Unspecified	**3 (0.01%)**
Total	**11,132 (100%)**

[a] No longer manufactured.

The pump product performance-related events by model, pre-SynchroMed II enhancements and SynchroMed II enhancements are summarized in the pump models section. Please visit http://synchromed2enhancements.medtronic.com for specific pump details by serial number.

3.3.2 Pump Events

There were 480 product performance-related events with an underlying reported etiology related to pump function. This includes 475 events with a pump etiology and 5 events with both a pump and other etiology (including device and non-device etiologies). Of these, 396 were the initial product performance event that affected pump survival estimates. For pumps in the registry, the current return rate to Medtronic Returned Product Analysis (RPA) was 28.5% (1,508/5,283). The proportion was based upon the number of registry pumps received by RPA, divided by the sum of the total number of explanted devices and the total number of pumps in patients who have expired. In the 480 pump events, 41.7% (200/480) were assigned as device related by the physician, not returned to Medtronic RPA (see Figure 3.4).

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For pumps:

- 396 had follow up time cut-off due to product performance-related events.

- 8,156 were censored in the survival analysis for the following reasons: patient expired, pump explanted, site termination, patient discontinued, patient lost to follow-up, or therapy suspended.
- 2,580 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

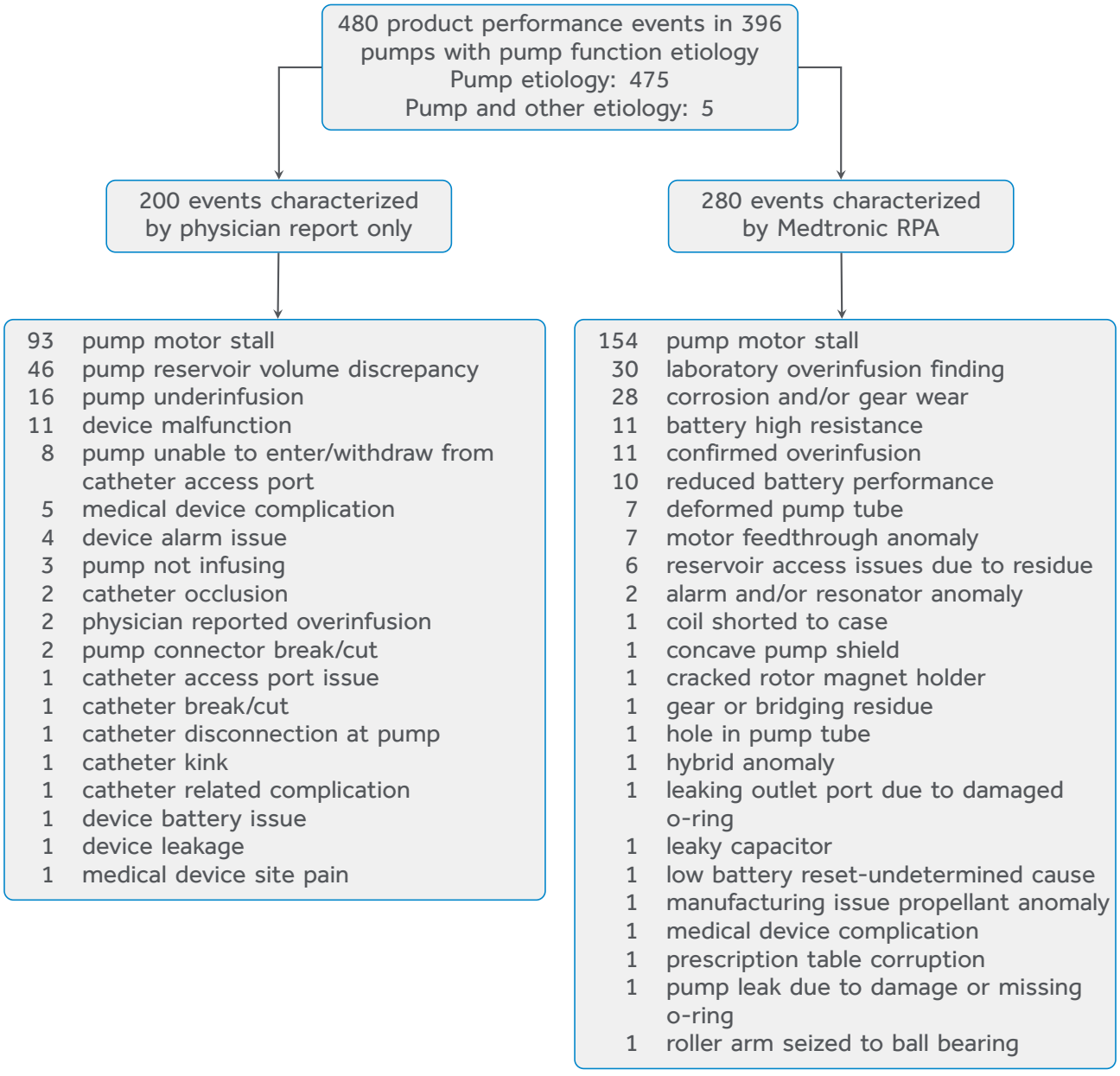


Figure 3.4: Distribution of Pump Function Etiology Product Performance Events

3.3.2.1 Overinfusion

Medtronic executed a field action in March 2014 informing healthcare professionals of overinfusion associated with the SynchroMed II Infusion System. In September 2016, an updated customer letter (https://www.medtronic.com/content/dam/medtronic-com/professional/documents/product-advisories/tdd/hcp_overinfusion_letter.pdf) was provided which stated an overinfusion occurrence rate for registry patients. This rate was based on pumps which had both laboratory overinfusion through returned product analysis and an in-vivo complaint of either clinical overinfusion symptoms or lower than expected residual volume. This definition was used because environmental factors during shipping may impact the results of returned product testing. As of October 31, 2019, there were 5 pumps in the registry that met this definition as stated in the customer letter. The 5 pumps with overinfusion provided 95% confidence that the occurrence rate is less than 0.0011 (0.11%). The use of non-indicated drug formulations (such as admixtures, compounded drugs and unapproved drug concentrations) increases the likelihood for overinfusion. Medtronic continues to monitor pump performance relative to overinfusion.

Table 3.13: Overinfusion Rate

	In Vivo and Laboratory Overinfusion[a]
Number of Pumps	5
Ocurrence Rate[b]	0.11%

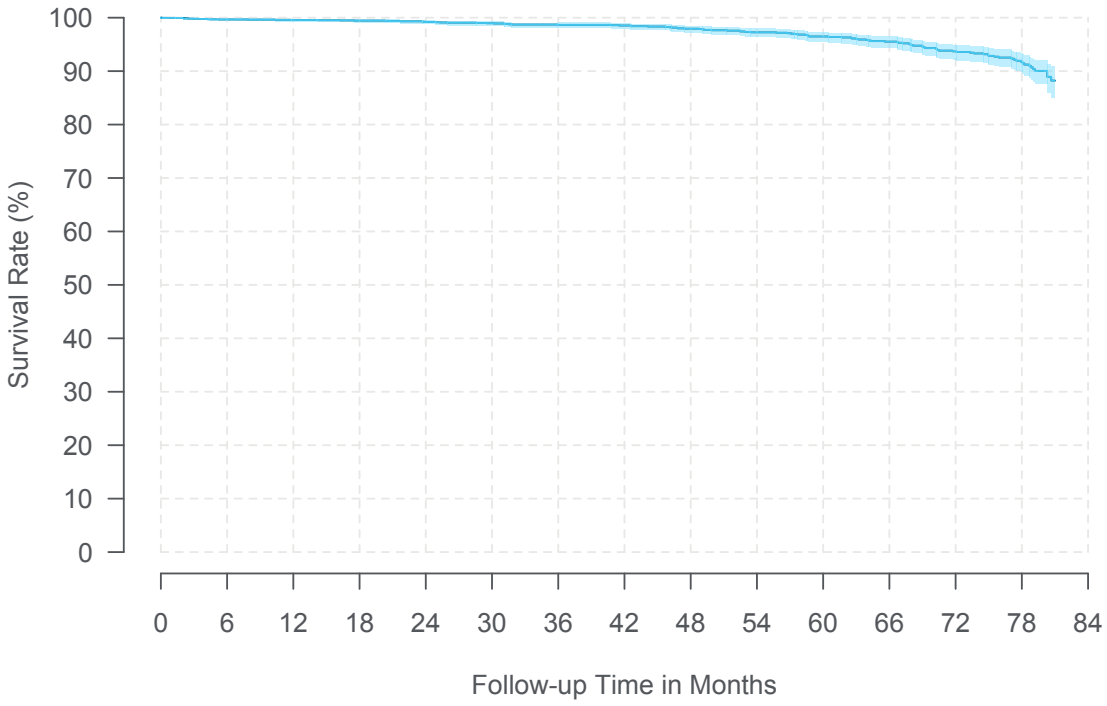
[a] Based on definition of in-vivo and laboratory overinfusion in September 2016 Field Action letter.
[b] Upper one-sided exact 95% confidence interval.

3.3.3 Pump Models

The following figures and tables represent the SynchroMed II pump characteristics, survival (including 95% confidence intervals), specifications and events by model. Since the survival estimate may become very imprecise with smaller sample sizes, the device survival curves below are truncated when the sample size is less than 20 active devices for each 3-month interval. The survival of SynchroMed EL model was not shown since it has no active devices in the PSR. For information on this model, please refer to the 2017 or earlier reports.

3.3.3.1 Model SynchroMed II 20 mL

Model/Name	SynchroMed II 20 mL
FDA Approval Date	September 2003
Pumps Enrolled	3,900
Pumps Currently Active in Study	1,081
Device Events	112
Median Follow-up Time (Months)	30.8
Cumulative Follow-up Time (Months)	139,297



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (99.2%, 99.7%)	99.2% (98.8%, 99.5%)	98.7% (98.1%, 99.0%)	97.9% (97.2%, 98.5%)	96.5% (95.5%, 97.3%)
Sample Size	2,735	2,252	1,783	1,398	1,057

Time Interval	6 Years	At 81 Months			
Survival (95% CI)	93.7% (92.2%, 94.9%)	88.2% (84.9%, 90.9%)			
Sample Size	738	100			

Specification: SynchroMed II 20 mL	
Expected battery life[a]	6-7 years
Thickness	0.77 in (19.5 mm)
Diameter	3.4 in (87.5 mm)
Capacity	20.0 mL
Minimal Programmable Flow Rate[b]	0.048 mL/day
Maximum Programmable Flow Rate[b]	24 mL/day
Minimum Rate Infusion Mode[c]	0.006 mL/day

[a] Dependent on flow rate. Designed to shut off at 84 months.

[b] Actual limits depend on pump calibration constant and selected infusion mode.

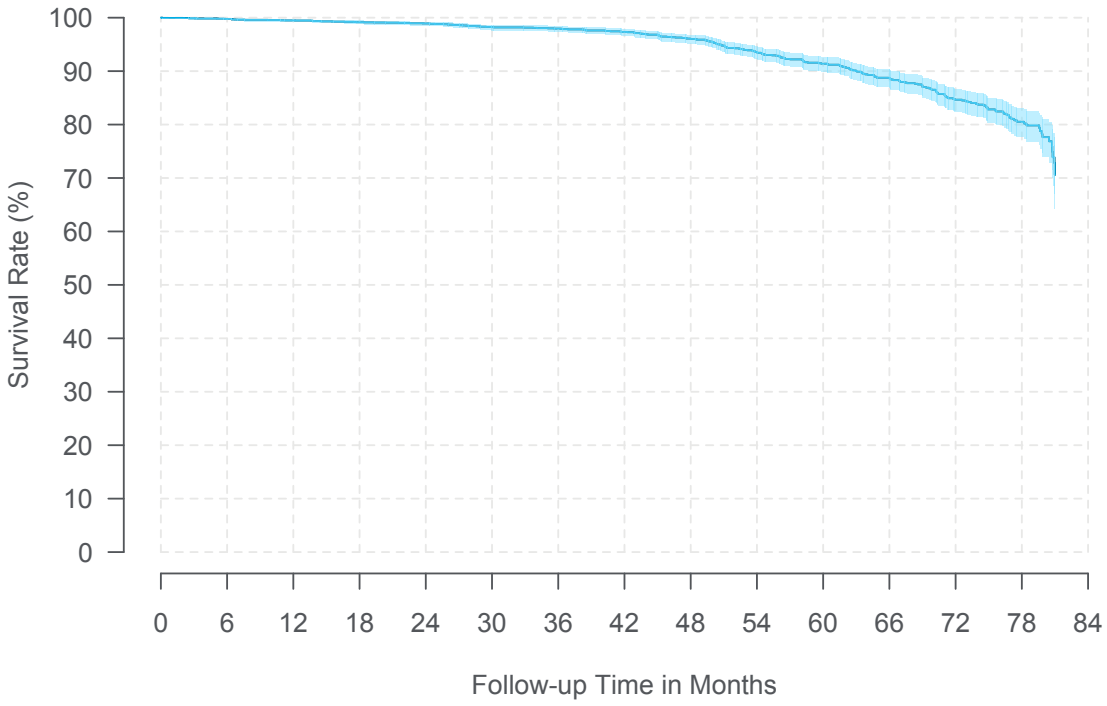
[c] Nontherapeutic (if therapy is to be temporarily discontinued).

Pump Event Summary: SynchroMed II 20 mL	N
RPA Determination	**58**
Pump Motor Stall	30
Battery High Resistance	6
Laboratory Overinfusion Finding	5
Corrosion And/Or Gear Wear	4
Motor Feedthrough Anomaly	3
Reduced Battery Performance	2
Other[a]	8
Physician's Determination	**54**
Pump Motor Stall	23
Pump Reservoir Volume Discrepancy	10
Device Malfunction	4
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Device Alarm Issue	3
Medical Device Complication	3
Other[a]	7
Total	**112**

[a] Composed of event codes with 1 event each.

3.3.3.2 Model SynchroMed II 40 mL

Model/Name	SynchroMed II 40 mL
FDA Approval Date	September 2003
Pumps Enrolled	6,044
Pumps Currently Active in Study	1,519
Device Events	250
Median Follow-up Time (Months)	19.1
Cumulative Follow-up Time (Months)	165,150



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (99.2%, 99.7%)	98.9% (98.5%, 99.2%)	98.0% (97.4%, 98.4%)	96.0% (95.1%, 96.8%)	91.4% (89.9%, 92.7%)
Sample Size	3,541	2,733	2,059	1,462	973

Time Interval	6 Years	At 81 Months			
Survival (95% CI)	84.6% (82.4%, 86.6%)	70.6% (64.2%, 76.1%)			
Sample Size	601	62			

Specification: SynchroMed II 40 mL	
Expected battery life[a]	6-7 years
Thickness	1.0 in (26 mm)
Diameter	3.4 in (87.5 mm)
Capacity	40.0 mL
Minimal Programmable Flow Rate[b]	0.048 mL/day
Maximum Programmable Flow Rate[b]	24 mL/day
Minimum Rate Infusion Mode[c]	0.006 mL/day

[a] Dependent on flow rate. Designed to shut off at 84 months.

[b] Actual limits depend on pump calibration constant and selected infusion mode.

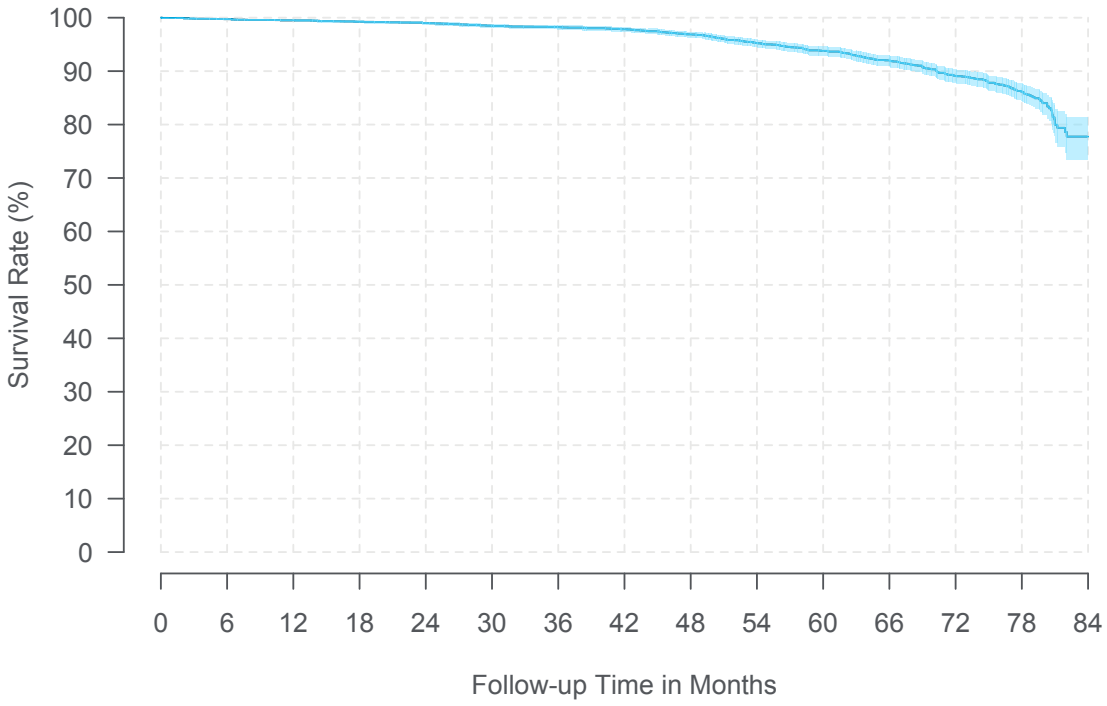
[c] Nontherapeutic (if therapy is to be temporarily discontinued).

Pump Event Summary: SynchroMed II 40 mL	N
RPA Determination	**160**
Pump Motor Stall	101
Laboratory Overinfusion Finding	22
Reduced Battery Performance	7
Corrosion And/Or Gear Wear	6
Deformed Pump Tube	5
Confirmed Overinfusion	4
Battery High Resistance	3
Reservoir Access Issues Due To Residue	3
Motor Feedthrough Anomaly	2
Other[a]	7
Physician's Determination	**90**
Pump Motor Stall	39
Pump Reservoir Volume Discrepancy	24
Pump Underinfusion	8
Device Malfunction	5
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Pump Not Infusing	2
Other[a]	8
Total	**250**

[a] Composed of event codes with 1 event each.

3.3.3.3 SynchroMed II 20 mL and 40 mL: Pre-enhancements

Model/Name	Pre-enhancements
FDA Approval Date	September 2003
Pumps Enrolled	7,831
Pumps Currently Active in Study	1,060
Device Events	353
Median Follow-up Time (Months)	32.9
Cumulative Follow-up Time (Months)	276,588



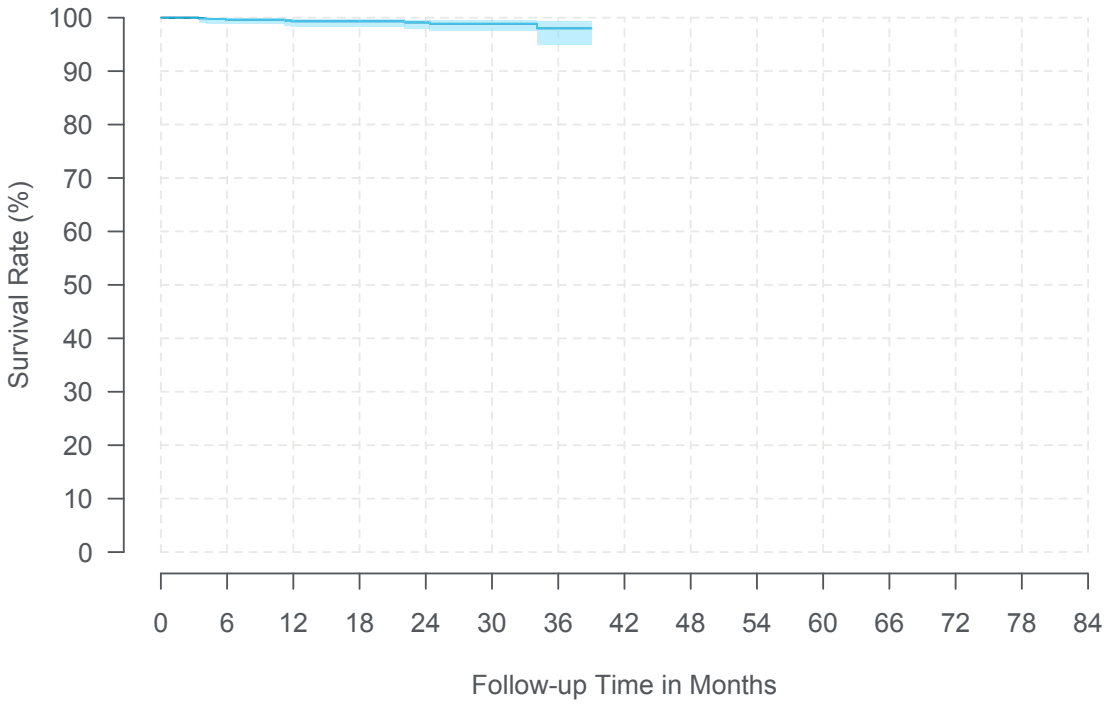
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (99.3%, 99.7%)	99.0% (98.7%, 99.2%)	98.2% (97.8%, 98.6%)	96.9% (96.3%, 97.3%)	93.8% (92.9%, 94.6%)
Sample Size	5,290	4,566	3,775	2,860	2,030

Time Interval	6 Years	7 Years			
Survival (95% CI)	89.1% (87.8%, 90.3%)	77.7% (73.5%, 81.4%)			
Sample Size	1,339	25			

Pump Event Summary: SynchroMed II Pre-enhancements	Total
RPA Determination	**217**
Pump Motor Stall	131
Laboratory Overinfusion Finding	27
Corrosion And/Or Gear Wear	10
Battery High Resistance	9
Reduced Battery Performance	9
Deformed Pump Tube	6
Confirmed Overinfusion	5
Motor Feedthrough Anomaly	5
Reservoir Access Issues Due To Residue	4
Alarm And/Or Resonator Anomaly	2
Other[a]	9
Physician's Determination	**136**
Pump Motor Stall	60
Pump Reservoir Volume Discrepancy	31
Device Malfunction	8
Pump Unable To Enter/Withdraw From Catheter Access Port	8
Pump Underinfusion	8
Device Alarm Issue	4
Medical Device Complication	4
Pump Not Infusing	3
Catheter Occlusion	2
Physician Reported Overinfusion	2
Pump Connector Break/Cut	2
Other[a]	4
Total	**353**

3.3.3.4 SynchroMed II 20 mL and 40 mL: GW3/FT Enhancements

Model/Name	GW3/FT enhancements
FDA Approval Date	September 2015 (GW3)/November 2015 (FT)
Pumps Enrolled	899
Pumps Currently Active in Study	536
Device Events	8
Median Follow-up Time (Months)	22.6
Cumulative Follow-up Time (Months)	18,935



Time Interval	1 Year	2 Years	3 Years	At 39 Months
Survival (95% CI)	99.3% (98.4%, 99.7%)	99.1% (98.0%, 99.6%)	98.0% (94.9%, 99.2%)	98.0% (94.9%, 99.2%)
Sample Size	668	414	67	30

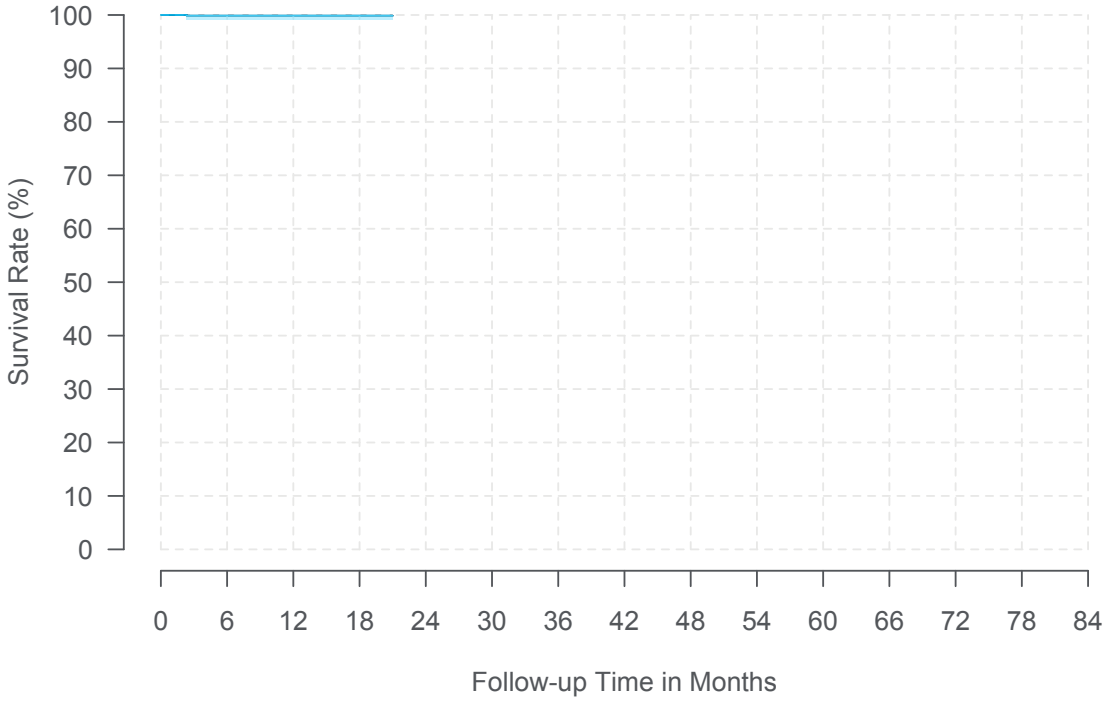
Pump Event Summary: SynchroMed II GW3/FT Enhancements	Total
RPA Determination	**0**
Physician's Determination	**8**
Pump Reservoir Volume Discrepancy	3
Pump Motor Stall[a]	2
Other[b]	3
Total	**8**

[a] The 2 stalls were reported as temporary and recovered within 24 hours wthout sequelae.

[b] Composed of event codes with 1 event each.

3.3.3.5 SynchroMed II 20 mL and 40 mL: GW3/FT/DLC Enhancements

Model/Name	GW3/FT/DLC enhancements
FDA Approval Date	April 2017 (DLC)
Pumps Enrolled	1,214
Pumps Currently Active in Study	1,004
Device Events	1
Median Follow-up Time (Months)	6.2
Cumulative Follow-up Time (Months)	8,924



Time Interval	1 Year	At 21 Months
Survival	99.9%	99.9%
(95% CI)	(99.1%, 100%)	(99.1%, 100%)
Sample Size	318	38

Pump Event Summary: SynchroMed II GW3/FT/DLC Enhancements	Total
RPA Determination	**1**
Pump Leak Due To Damage Or Missing O-Ring	1
Physician's Determination	**0**
Total	**1**

3.3.4 Pump Summary

Table 3.14: Targeted Drug Delivery Pump Characteristics

Model/Name	FDA Approval Date	Pumps Enrolled	Pumps Active	Pump Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
SynchroMed II 20 mL	September 2003	3,900	1,081	112	30.8	139,297
SynchroMed II 40 mL	September 2003	6,044	1,519	250	19.1	165,150
SynchroMed II Pre-enhancements[a]	September 2003	7,831	1,060	353	32.9	276,588
SynchroMed II GW3/FT enhancements[a]	September 2015 (GW3) November 2015 (FT)	899	536	8	22.6	18,935
SynchroMed II GW3/FT/DLC enhancements[a]	April 2017 (DLC)	1,214	1,004	1	6.2	8,924

[a] For explanation of enhancements see Section 3.3.1.

Table 3.15: Targeted Drug Delivery Pump Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
SynchroMed II 20 mL	99.6% (99.2%, 99.7%)	99.2% (98.8%, 99.5%)	98.7% (98.1%, 99.0%)	97.9% (97.2%, 98.5%)	96.5% (95.5%, 97.3%)
SynchroMed II 40 mL	99.5% (99.2%, 99.7%)	98.9% (98.5%, 99.2%)	98.0% (97.4%, 98.4%)	96.0% (95.1%, 96.8%)	91.4% (89.9%, 92.7%)
SynchroMed II Pre-enhancements	99.5% (99.3%, 99.7%)	99.0% (98.7%, 99.2%)	98.2% (97.8%, 98.6%)	96.9% (96.3%, 97.3%)	93.8% (92.9%, 94.6%)
SynchroMed II GW3/FT enhancements	99.3% (98.4%, 99.7%)	99.1% (98.0%, 99.6%)	98.0% (94.9%, 99.2%)		
SynchroMed II GW3/FT/DLC enhancements	99.9% (99.1%, 100%)				

Model Name	6 Years	7 Years			
SynchroMed II 20 mL	93.7% (92.2%, 94.9%)				
SynchroMed II 40 mL	84.6% (82.4%, 86.6%)				
SynchroMed II Pre-enhancements	89.1% (87.8%, 90.3%)	77.7% (73.5%, 81.4%)			
SynchroMed II GW3/FT enhancements					
SynchroMed II GW3/FT/DLC enhancements					

Table 3.16: Targeted Drug Delivery SynchroMed II Pump Events by Enhancements

Pump Event	Pre-Enhancements	GW3/FT Enhancements	GW3/FT/DLC Enhancements
RPA Determination	**217**	**0**	**1**
Pump Motor Stall	131	0	0
Laboratory Overinfusion Finding	27	0	0
Corrosion And/Or Gear Wear	10	0	0
Battery High Resistance	9	0	0
Reduced Battery Performance	9	0	0
Deformed Pump Tube	6	0	0
Confirmed Overinfusion	5	0	0
Motor Feedthrough Anomaly	5	0	0
Reservoir Access Issues Due To Residue	4	0	0
Alarm And/Or Resonator Anomaly	2	0	0
Other[a]	9	0	1
Physician's Determination	**136**	**8**	**0**
Pump Motor Stall	60	2	0
Pump Reservoir Volume Discrepancy	31	3	0
Device Malfunction	8	1	0
Pump Unable To Enter/Withdraw From Catheter Access Port	8	0	0
Pump Underinfusion	8	0	0
Device Alarm Issue	4	0	0
Medical Device Complication	4	0	0
Pump Not Infusing	3	0	0
Catheter Occlusion	2	0	0
Physician Reported Overinfusion	2	0	0
Pump Connector Break/Cut	2	0	0
Other[a]	4	2	0
Total	**353**	**8**	**1**

[a] Composed of event codes with 1 event each.

3.4 SynchroMed II Pumps Exposed to On-Label and Off-Label Medications

The purpose of this analysis is to provide additional information regarding the product performance of SynchroMed II pumps exposed to On-Label and Off-Label medications. This report contains information outside the FDA approved labeling for the Medtronic SynchroMed II Infusion System. Infumorph®, Prialt®, Lioresal®, Gablofen®, and MITIGO™ are the only FDA approved intrathecal formulations. The long-term drug stability/compatibility and safety and/or efficacy of drugs not FDA approved for use with the SynchroMed II Infusion System have not been established in the United States. It is recognized that healthcare providers prescribe therapies to meet specific patient needs; however, Medtronic only directs the use of its products based on approved regulatory labeling. For the purposes of this report, On-Label and Off-Label determinations have been made based on the United States FDA approved labeling. However, product labeling varies by geography, so please contact your local Medtronic representative (http://www.medtronic.com/us-en/about/locations.html) for region-specific product labeling.

In this registry, patient status updates were obtained at least annually, until discontinuation of therapy, or until the patient was lost to follow-up. Medications within the pump were recorded at least annually. The interim data collection provided a snapshot of medication use at these points in time.

3.4.1 Pump Groups On/Off-Label Categorization

Through October 31, 2019, 8,069 patients (55.9% female, mean/SD age 54/17.5 years) have enrolled in the registry and have been implanted with 9,944 SynchroMed II pumps. At least one drug record was available on each of 9,563 pumps; if no drug records were available (n=381 pumps), the pump was excluded from this analysis. Pumps were categorized as being On- or Off-Label using the following criteria:

- **On-Label:** If a pump has at least one drug record in the registry, and none of the records show Off-Label drug exposure, that pump is considered On-Label even if the complete drug history of that pump is unknown.
  - For pumps used for pain patients, if the drug record has only one drug and it was Infumorph® (preservative-free morphine sulfate sterile solution), Prialt® (preservative-free ziconotide sterile solution) or MITIGO™ (preservative-free morphine sulfate sterile solution), these pumps were considered On-Label. Note: The classification was based on the name of the drug only, not the reported concentration of the drug. For this analysis, if only the generic chemical classification, such as morphine or ziconotide, was entered then the assumption was that the drug is On-Label.
  - For pumps used for spasticity patients, if the drug record has only one drug, and it is either Lioresal® (bacoflen injection) or Gablofen® (bacoflen injection), that drug record was considered On-Label. Note: The classification was based on the name of the drug only, not the reported concentration of the drug. For this analysis, if only the generic chemical classification, such as baclofen, was entered then the assumption was that the drug is On-Label.
  - Pumps with an On-Label drug history and currently containing preservative free water or preservative free saline, or if previously contained preservative free water/saline and currently containing On-Label drug were considered On-Label.
- **Off-Label:** Any drugs not within the approved indications specified above are considered Off-Label. Additionally, any drug record with more than one drug at a time in the pump (admixture) was considered Off-Label.
  - If a pump had any known exposure to Off-Label drugs (i.e., the Off-Label data have been collected in the registry), that pump was considered Off-Label, regardless of the amount of exposure time.
  - If a pump is filled with a medication that was reported as compounded, that pump was considered Off-Label.

The pumps were not stratified by design change sub-groups (GW3/FT and GW3/FT/DLC) due to the limited follow-up time.

3.4.2 Data Analysis

Survival estimates were calculated using the methods described in the Methodology section of this report. Statistical testing that compared survival curves was performed using a Cox proportional-hazards model. Since the survival estimate may become very imprecise with small sample sizes, Medtronic Neuromodulation's registry truncates device survival curves when the sample size is less than 20 active devices. At this threshold, one device failure yields a 5% decrease in cumulative survival. Additionally, the standard error for this survival estimate is approximately 5% (depending on previous conditional survival estimates), with 95% confidence intervals of approximately ± 10%. Overall, this large variability of 20% around the cumulative survival estimate would greatly reduce the precision for the point estimate.

Pump survival from product performance-related events was calculated and compared for the following groups:

- Total study population: On-Label vs. Off-Label Drugs (including all indications)
- Pain study population: On-Label vs. Off-Label Drugs (including all pain indications)
- Spasticity study population: On-Label vs. Off-Label Drugs (including all spasticity indications)

Additionally, the cumulative failure rate (i.e., the estimated probability that a pump will have a product performance-related event by a given time point) is presented in table and graph formats for each of the sub-groups listed above.

3.4.3 Results

A total of 2,956 (30.9%) SynchroMed II pumps were classified as On-Label where there was no evidence of Off-Label drug/admixture exposure. A total of 6,607 (69.1 %) pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. There were a total of 362 reported SynchroMed II pump product performance events during the study observation period. In addition to the 362 pump failures, there were 15 SynchroMed II pumps explanted due to normal battery depletion by the physician, which were returned to Medtronic and had an RPA observation of high battery resistance. For this analysis, these pumps were not considered failures, because they represented normal implant duration (ranging from 5.6 to 6.8 years) with no associated physician or patient complaint.

Three of the 362 pump failure events occurred in pumps with no drug records available. Of the remaining 359 SynchroMed II pump failures, 193 were classified as pump failure due to motor stall (with or without documented motor corrosion). The remaining pump failures were due to events such as inconsistent pump reservoir volume, overinfusion, corrosion and/or gear wear, device malfunction, reduced battery performance, pump underinfusion, and other non-conforming reasons. Overall, the rate of pump failures in this cohort was 3.8% (359/9,563) with a median follow-up of 25.1 months.

For the 193 pump failures due to motor stall, 93 of the events were associated with the patient presenting clinical signs or symptoms of possible drug withdrawal or increasing pain or spasticity. The other 100 events had no patient reported signs or symptoms associated with the event, but had a physician report of a motor stall occurrence.

Table 3.17: Targeted Drug Delivery Primary Indications by On/Off-Label Pump Groups

Primary Indication[a]	On-Label N=2,956	Off-Label N=6,607
Non-malignant Pain	903 (15.8%)	4,821 (84.2%)
Malignant Pain	46 (3.2%)	1,403 (96.8%)
Spasticity	2,007 (89.8%)	229 (10.2%)
Multiple/Unknown	0 (0.0%)	154 (100.0%)

[a] For approved indications refer to product labeling for your geography.

3.4.3.1 Total Study Population

A total of 2,956 SynchroMed II pumps were classified as On-Label for all therapies, where there was no evidence of Off-Label drug/admixture exposure. A total of 6,607 pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. The cumulative survival and failure of the SynchroMed II pump for all indications, stratified by the On-Label or Off-Label pump group, are shown in Figure 3.5 and Figure 3.6 respectively.

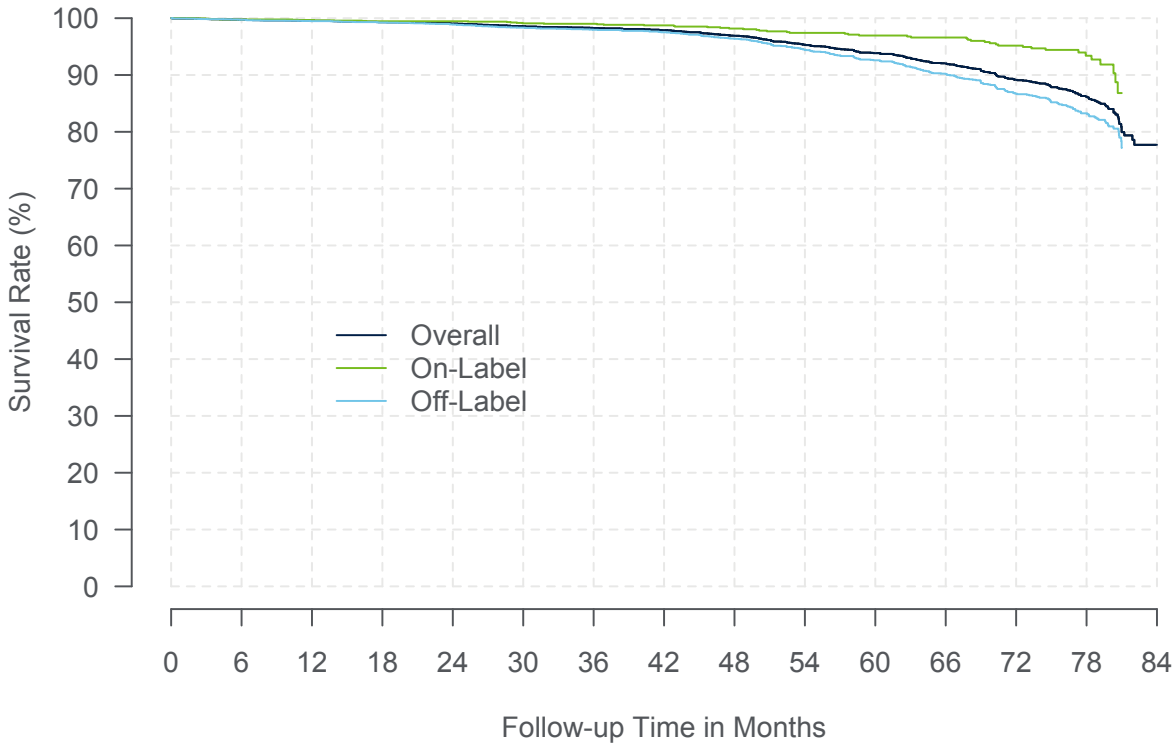


Figure 3.5: SynchroMed II Cumulative Survival (All Therapies)

Table 3.18: Survival Summary Table: All Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 81 Mos	7 Yrs
Overall	Survival	99.5%	99.1%	98.3%	96.9%	93.8%	89.1%	79.9%	77.7%
	Sample Size	6,174	4,924	3,807	2,831	2,017	1,334	161	25
On-Label	Survival	99.7%	99.5%	99.0%	98.2%	96.9%	95.2%	86.8%	
	Sample Size	1,929	1,497	1,114	824	586	413	38	
Off-Label	Survival	99.5%	98.9%	98.0%	96.4%	92.6%	86.7%	77.2%	
	Sample Size	4,245	3,427	2,693	2,007	1,431	921	123	

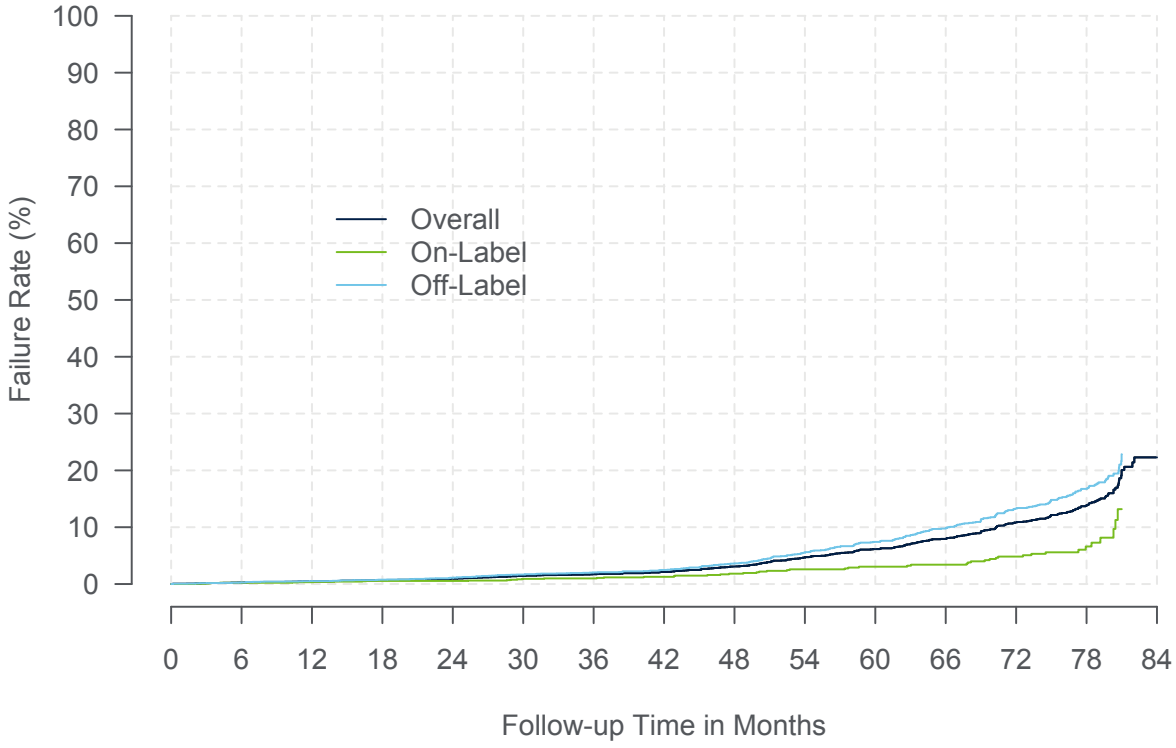


Figure 3.6: SynchroMed II Cumulative Failure (All Therapies)

Table 3.19: Failure Summary Table: All Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 81 Mos	7 Yrs
Overall	Failure	0.5%	0.9%	1.7%	3.1%	6.2%	10.9%	20.1%	22.3%
	Sample Size	6,174	4,924	3,807	2,831	2,017	1,334	161	25
On-Label	Failure	0.3%	0.5%	1.0%	1.8%	3.1%	4.8%	13.2%	
	Sample Size	1,929	1,497	1,114	824	586	413	38	
Off-Label	Failure	0.5%	1.1%	2.0%	3.6%	7.4%	13.3%	22.8%	
	Sample Size	4,245	3,427	2,693	2,007	1,431	921	123	

3.4.3.2 Pain Study Population

A total of 949 SynchroMed II pumps were classified as On-Label for pain therapies, where there was no evidence of Off-Label drug/admixture exposure. A total of 6,224 pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. The cumulative survival and failure of the SynchroMed II pump for pain indications, stratified by the On-Label or Off-Label pump group, are shown in Figure 3.7 and Figure 3.8 respectively.

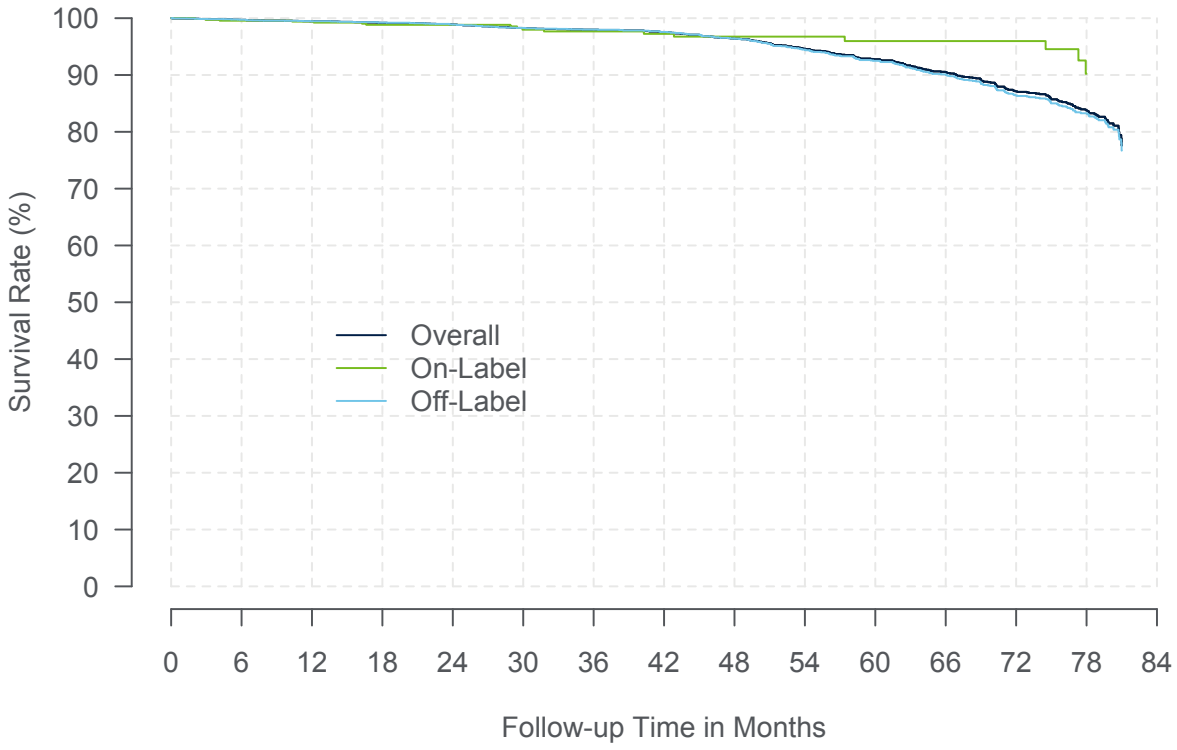


Figure 3.7: SynchroMed II Cumulative Survival (Pain Therapies)

Table 3.20: Survival Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Survival	99.5%	98.9%	98.0%	96.4%	92.8%	87.1%	83.8%	77.6%
	Sample Size	4,539	3,609	2,786	2,031	1,440	930	483	121
On-Label	Survival	99.4%	98.8%	97.7%	96.8%	96.0%	96.0%	90.2%	
	Sample Size	577	407	269	171	111	74	36	
Off-Label	Survival	99.5%	98.9%	98.0%	96.4%	92.5%	86.4%	83.3%	76.7%
	Sample Size	3,962	3,202	2,517	1,860	1,329	856	447	113

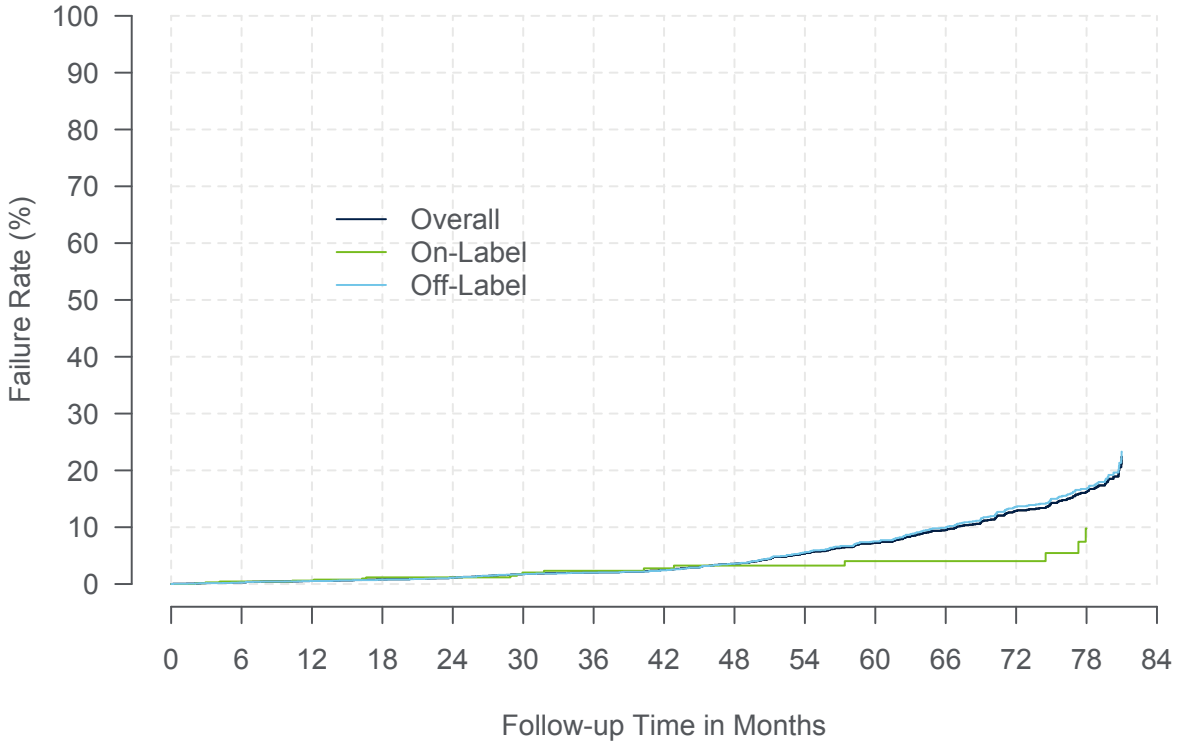


Figure 3.8: SynchroMed II Cumulative Failure (Pain Therapies)

Table 3.21: Failure Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Failure	0.5%	1.1%	2.0%	3.6%	7.2%	12.9%	16.2%	22.4%
	Sample Size	4,539	3,609	2,786	2,031	1,440	930	483	121
On-Label	Failure	0.6%	1.2%	2.3%	3.2%	4.0%	4.0%	9.8%	
	Sample Size	577	407	269	171	111	74	36	
Off-Label	Failure	0.5%	1.1%	2.0%	3.6%	7.5%	13.6%	16.7%	23.3%
	Sample Size	3,962	3,202	2,517	1,860	1,329	856	447	113

3.4.3.3 Spasticity Study Population

A total of 2,007 SynchroMed II pumps were classified as On-Label for spasticity therapies, where there was no evidence of Off-Label drug/admixture exposure. A total of 229 pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. The cumulative survival and failure of the SynchroMed II pump for spasticity indications, stratified by the On-Label or Off-Label pump group, are shown in Figure 3.9 and Figure 3.10 respectively.

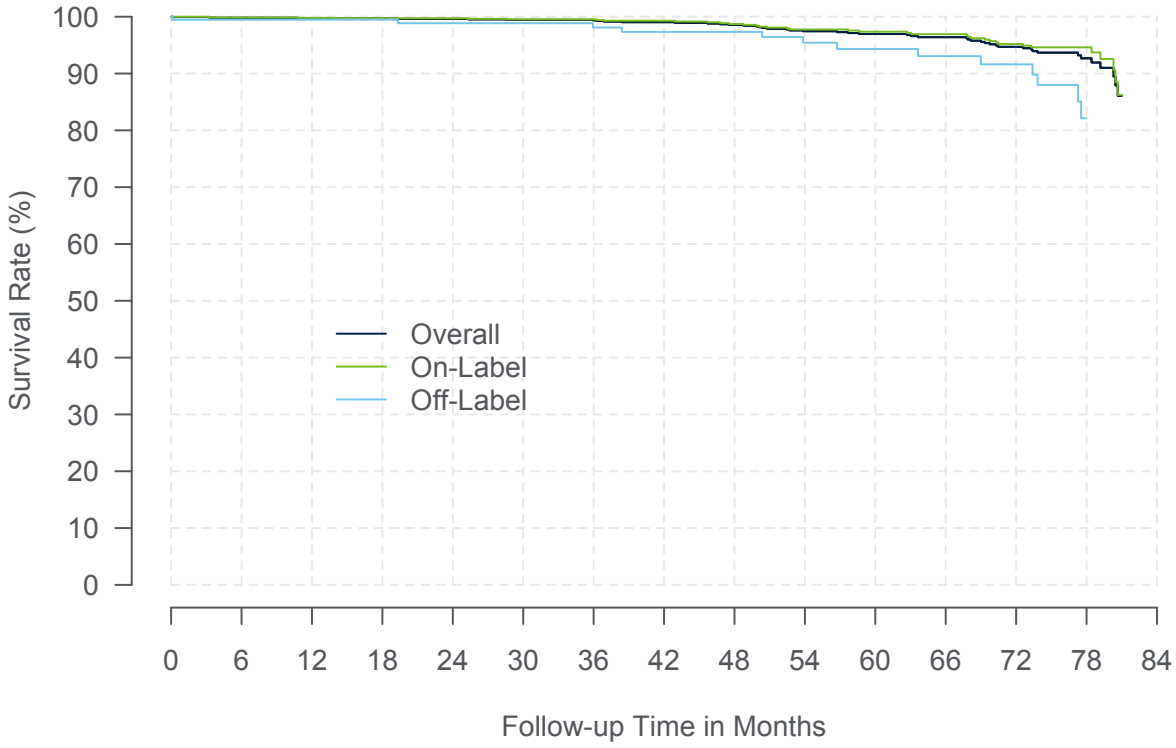


Figure 3.9: SynchroMed II Cumulative Survival (Spasticity Therapies)

Table 3.22: Survival Summary Table: Spasticity Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Survival	99.8%	99.6%	99.3%	98.5%	97.0%	94.7%	92.7%	86.1%
	Sample Size	1,530	1,242	973	763	554	395	142	39
On-Label	Survival	99.8%	99.7%	99.5%	98.7%	97.4%	95.2%	94.6%	86.2%
	Sample Size	1,352	1,090	845	653	475	339	121	30
Off-Label	Survival	99.5%	98.9%	98.1%	97.3%	94.3%	91.6%	82.1%	
	Sample Size	178	152	128	110	79	56	21	

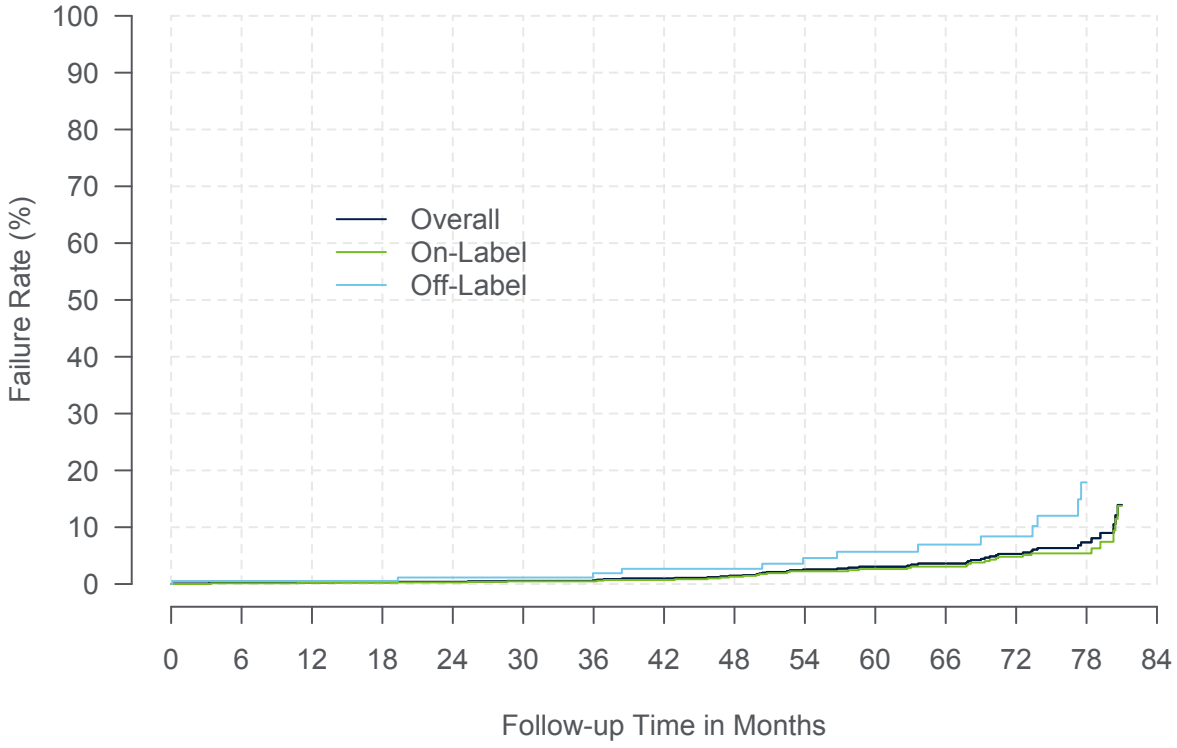


Figure 3.10: SynchroMed II Cumulative Failure (Spasticity Therapies)

Table 3.23: Failure Summary Table: Spasticity Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Failure	0.2%	0.4%	0.7%	1.5%	3.0%	5.3%	7.3%	13.9%
	Sample Size	1,530	1,242	973	763	554	395	142	39
On-Label	Failure	0.2%	0.3%	0.5%	1.3%	2.6%	4.8%	5.4%	13.8%
	Sample Size	1,352	1,090	845	653	475	339	121	30
Off-Label	Failure	0.5%	1.1%	1.9%	2.7%	5.7%	8.4%	17.9%	
	Sample Size	178	152	128	110	79	56	21	

3.4.4 Overall Summary and Limitations

- Pump failures have been observed in pumps with both On-Label and Off-Label medications used for all indications over the follow-up period.
- Off-Label medication exposure is associated with an overall 2.4 times greater risk of pump failure (95% confidence interval [1.763, 3.145]) compared to On-Label medication exposure for the entire pump population. The rate of pump failure accelerates in the Off-Label group after 48 months of follow-up. At 81 months of follow-up the survival from

pump failure for On-Label pumps was 86.8% compared to a survival of 77.2% for Off-Label pumps.

- The data represent the reported registry experience with a median follow-up time of 25.1 months. The longer-term data are based on a lower number of pumps and are subject to change as more follow-up data are obtained via the registry. Survival curve truncation or plateaus do not imply that the implanted devices will not be adversely impacted beyond the time points of the current data.
- The On-Label pump group was comprised of 67.9% of pumps with Spasticity as the indication (2,007 vs. 949: Spasticity versus Pain pumps respectively). While the Off-Label group consisted of 94.2% of pumps with pain indications (6,224 vs. 229: Pain versus Spasticity pumps respectively).
- Medication use was recorded as a snapshot at the time of follow-up. It is possible that some On-Label pumps received Off-Label medications in between follow-up periods. In addition, it is possible that some pumps designated as On-Label received compounded formulation of an On-Label equivalent but was not designated as such in the registry database. The time a pump was exposed to an Off-Label medication was not assessed. It is possible that some Off-Label pumps were exposed only for a brief period of time (e.g. < 6 months).
- The risk of pump failure by type of drug was not assessed. Many Off-Label pumps were exposed to multiple medications over the life span of the pump. This limits the ability to associate a specific drug, compounded drug, drug concentration, or drug combination with increased pump failure risk.

3.5 Catheters

From August 7, 2003, to the report cut-off date of October 31, 2019, there were 10,102 catheters followed in the registry. The total number of catheters was not equal to the total number of pumps (n=11,132) because patients may have undergone pump replacements but used the same catheters, or patients may have been implanted with Medtronic pumps and non-Medtronic catheters which were not registered with Medtronic Device And Registrant Tracking (DART) system. The aggregate prospective follow-up time for all catheters was 333,245 months (27,770 years). Table 3.24 provides the number and percentage of catheters by model.

Table 3.24: Targeted Drug Delivery Catheter Counts by Model

Model Name	N (%)
Currently Manufactured[a]	**2,529 (25.0%)**
8780 (US & OUS)	1,256 (12.4%)
8781 (US & OUS)	995 (9.9%)
8731SC (OUS)	278 (2.8%)
Revised Catheters	**1,906 (18.9%)**
Revised Not As Designed[b]	708 (7.0%)
Grafted Not As Designed[c]	485 (4.8%)
Revised As Designed[d]	396 (3.9%)
Ascenda Revised As Designed[e]	317 (3.1%)
No Longer Manufactured	**5,344 (52.9%)**
8709	2,888 (28.6%)
8709SC	1,090 (10.8%)
8711	655 (6.5%)
8731	526 (5.2%)
8703W	185 (1.8%)
Other/Unspecified	**323 (3.2%)**
Total	**10,102 (100%)**

[a] Manufactured for designated region; US=United States; OUS =Outside United States.

[b] Medtronic non-Ascenda catheters repaired with a Medtronic revision kit, but not for the model it was intended.

[c] Catheters that involve the ad-hoc assembly of components other than a Medtronic repair kit or brand-new catheter.

[d] 8731 catheters repaired with an 8596 proximal or 8598 distal revision kit.

[e] 8780 or 8781 Ascenda catheters repaired with the 8782 or 8784 revision kit.

3.5.1 Catheter Events

There were 1,469 product performance-related events with an underlying reported etiology related to catheter function. This includes 1,459 events with a catheter etiology and 10 events with both a catheter and other etiology (including device and non-device etiologies). The majority of the events were catheter occlusion (n=396), catheter dislodgement (n=361), catheter break/cut (n=228), or catheter kink (n=200). Of the 1,469 events, 1,261 were the initial product performance event that affected catheter survival estimates.

The catheter product performance-related events are summarized by model in the catheter models section.

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For catheters:

- 1,261 had follow-up time cut-off due to product performance-related events.
- 6,435 were censored in the survival analysis for the following reasons: patient expired, catheter explanted/capped, site termination, patient discontinued, patient lost to follow-up, or therapy suspended.
- 2,406 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

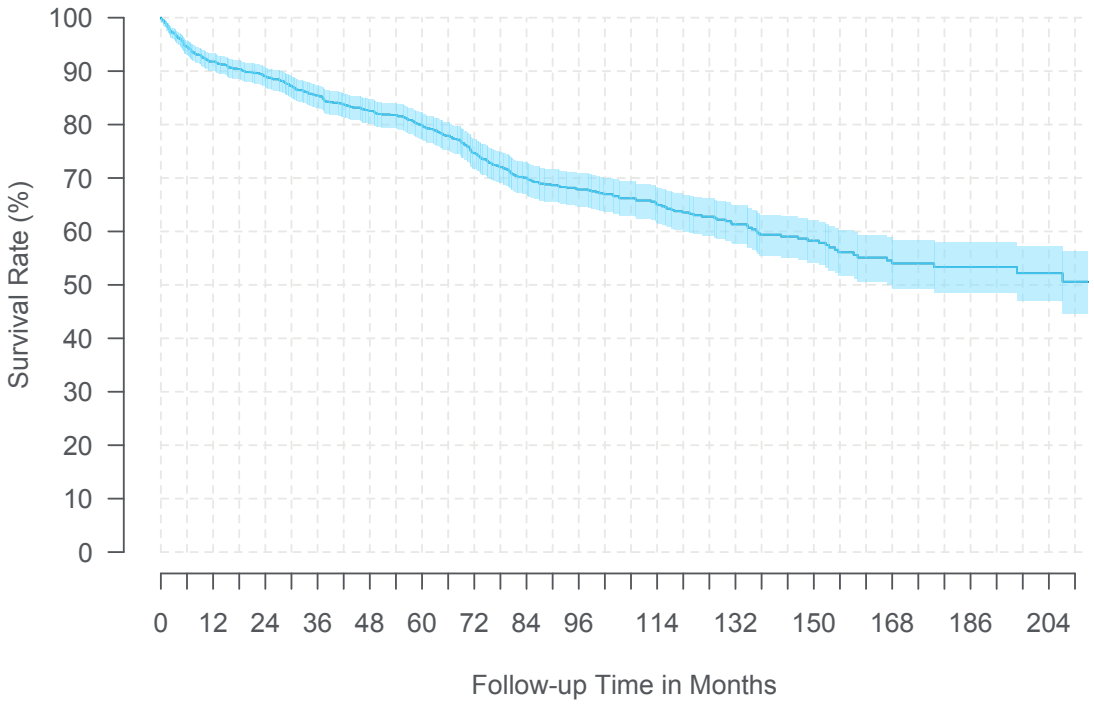
3.5.2 Catheter Models

The figures and tables below represent catheter survival and 95% confidence intervals where at least 20 catheters contributed to each 3-month interval. Survival curves are only shown if more than 20 devices had at least 12 months of follow-up at the time of the report cut-off for each model.

Medtronic catheter repair kits and 2-piece catheters include specially designed connector pins and strain relief sleeves to splice the catheter segments together. Catheters grafted not as designed, by definition, involve the ad-hoc assembly of components other than those from a Medtronic repair kit or brand-new catheter. Medtronic recommends that clinicians follow the labeling for the catheter revision kits.

3.5.2.1 Model 8709

Model/Name	8709/InDura
FDA Approval Date	May 1998
Catheters Enrolled	2,888
Catheters Currently Active in Study	178
Device Events	356
Median Follow-up Time (Months)	17.4
Cumulative Follow-up Time (Months)	94,664



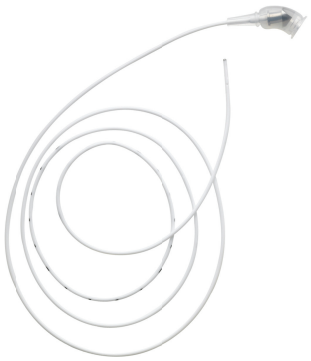
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.8% (90.0%, 93.2%)	89.0% (87.1%, 90.7%)	85.5% (83.2%, 87.4%)	82.5% (80.1%, 84.7%)	79.9% (77.3%, 82.2%)
Sample Size	983	928	866	772	662

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	74.7% (71.8%, 77.3%)	70.1% (67.0%, 73.0%)	67.8% (64.6%, 70.8%)	66.2% (62.9%, 69.3%)	63.5% (60.0%, 66.8%)
Sample Size	570	500	413	320	261

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	61.3% (57.6%, 64.8%)	59.0% (55.1%, 62.8%)	56.1% (51.7%, 60.2%)	54.0% (49.3%, 58.4%)	53.3% (48.5%, 57.9%)
Sample Size	208	162	119	95	73

Time Interval	16 Years	17 Years	At 213 Months		
Survival (95% CI)	53.3% (48.5%, 57.9%)	52.2% (47.0%, 57.1%)	50.6% (44.6%, 56.2%)		
Sample Size	54	34	21		

Specification: 8709	
Total Length	89 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Pump end

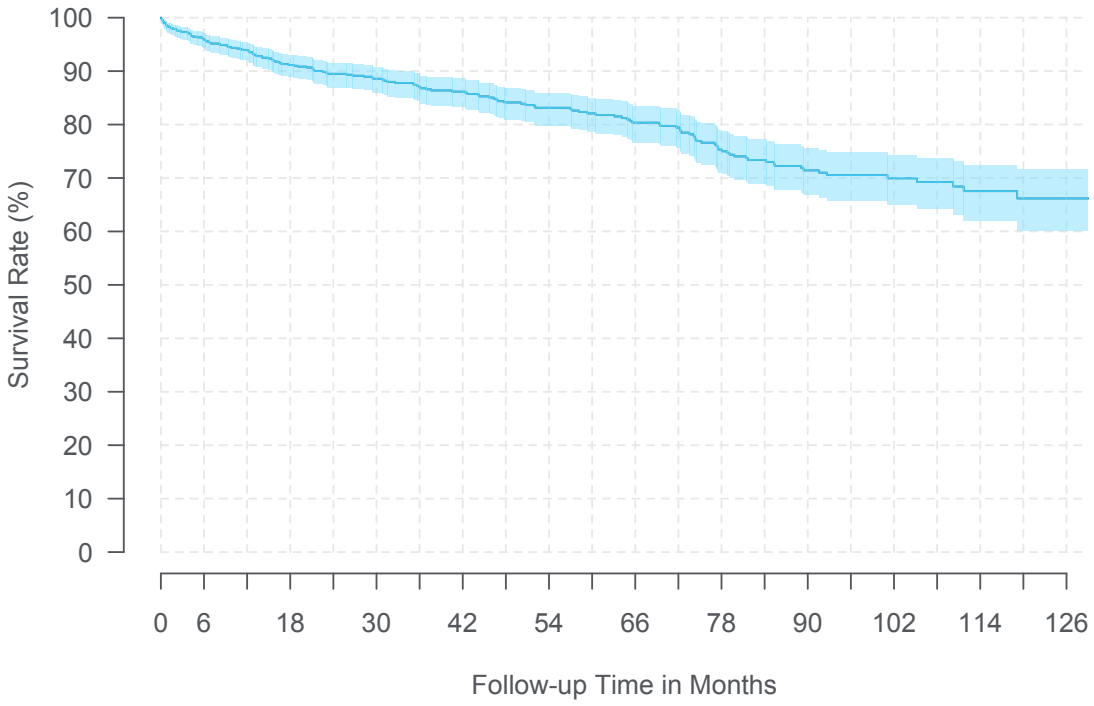


Catheter Event Summary: 8709	N
Catheter Dislodgement	97
Catheter Occlusion	82
Catheter Break/Cut	76
Catheter Kink	31
Catheter Disconnection At Pump	20
Catheter Leakage	13
Catheter Related Complication	13
Pump Connector Break/Cut	10
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Medical Device Complication	2
Other[a]	9
Total	**356**

[a] Composed of event codes with 1 event each.

3.5.2.2 Model 8709SC

Model/Name	8709SC/InDura 1P
FDA Approval Date	March 2006
Catheters Enrolled	1,090
Catheters Currently Active in Study	208
Device Events	151
Median Follow-up Time (Months)	25.4
Cumulative Follow-up Time (Months)	42,063



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.9% (92.0%, 95.4%)	89.5% (87.0%, 91.5%)	87.0% (84.2%, 89.3%)	84.1% (81.0%, 86.8%)	82.1% (78.7%, 85.0%)
Sample Size	664	514	432	358	297

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	79.4% (75.7%, 82.7%)	73.4% (69.0%, 77.3%)	70.5% (65.8%, 74.8%)	69.3% (64.2%, 73.7%)	66.2% (60.1%, 71.6%)
Sample Size	253	201	131	89	45

Time Interval	At 129 Months
Survival (95% CI)	66.2% (60.1%, 71.6%)
Sample Size	26

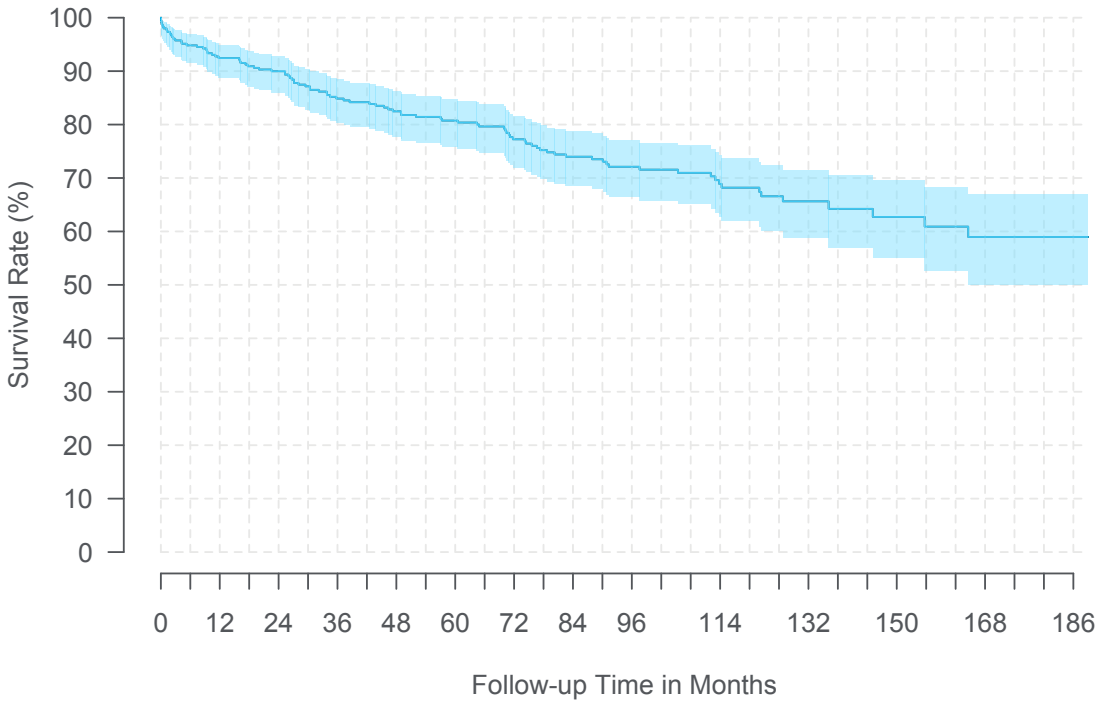
Specification: 8709SC	
Total Length	89 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed tip, radiopaque, titanium with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Pump end

Catheter Event Summary: 8709SC	N
Catheter Occlusion	38
Catheter Dislodgement	37
Catheter Break/Cut	34
Catheter Related Complication	9
Catheter Leakage	8
Catheter Kink	7
Catheter Disconnection At Pump	5
Medical Device Complication	3
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Catheter Damage	2
Other[a]	5
Total	**151**

[a] Composed of event codes with 1 event each.

3.5.2.3 Model 8711

Model/Name	8711/InDura
FDA Approval Date	October 1999
Catheters Enrolled	655
Catheters Currently Active in Study	87
Device Events	94
Median Follow-up Time (Months)	31.0
Cumulative Follow-up Time (Months)	29,460



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.4% (88.8%, 94.9%)	90.0% (86.0%, 92.9%)	84.9% (80.4%, 88.4%)	82.5% (77.7%, 86.3%)	80.7% (75.8%, 84.7%)
Sample Size	306	286	258	238	225

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	77.2% (72.0%, 81.6%)	74.0% (68.5%, 78.7%)	72.1% (66.4%, 77.0%)	71.0% (65.1%, 76.0%)	68.2% (61.9%, 73.6%)
Sample Size	190	174	137	114	87

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	65.6% (58.9%, 71.5%)	64.2% (57.0%, 70.5%)	60.9% (52.6%, 68.2%)	59.0% (50.0%, 66.9%)	59.0% (50.0%, 66.9%)
Sample Size	57	41	33	28	23

Time Interval	At 189 Months
Survival (95% CI)	59.0% (50.0%, 66.9%)
Sample Size	20

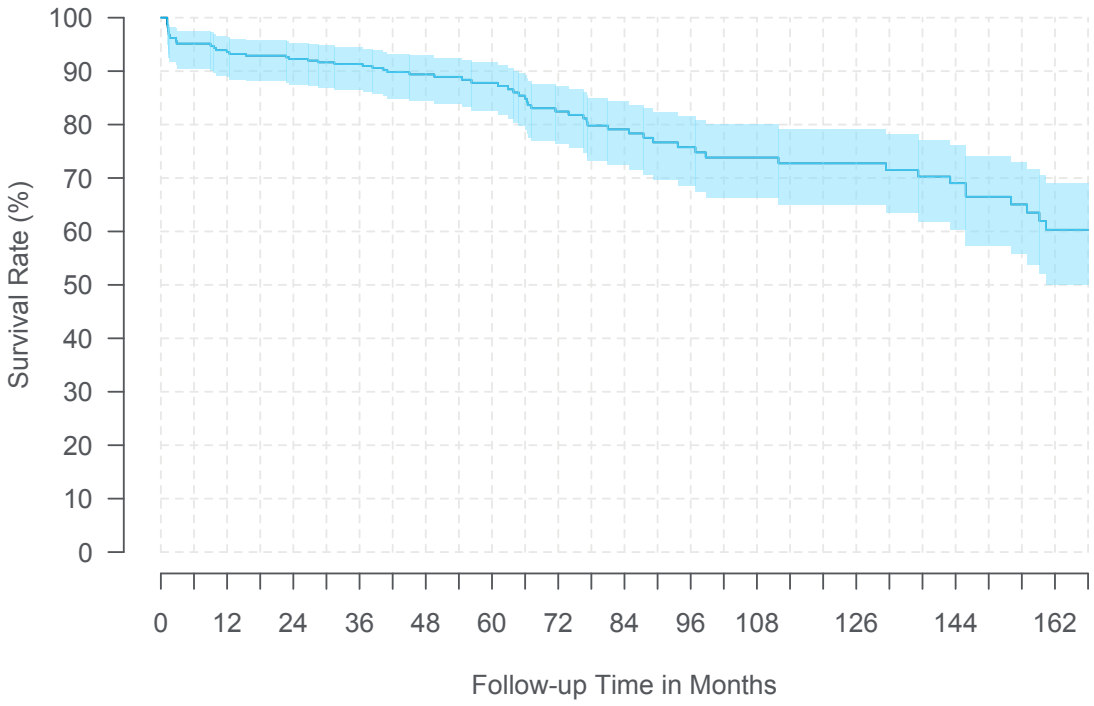
Specification: 8711	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Spinal and pump ends

Catheter Event Summary: 8711	N
Catheter Occlusion	28
Catheter Break/Cut	19
Catheter Related Complication	14
Catheter Dislodgement	13
Catheter Kink	7
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Catheter Leakage	3
Catheter Disconnection At Pump	2
Other[a]	4
Total	**94**

[a] Composed of event codes with 1 event each.

3.5.2.4 Model 8731

Model/Name	8731
FDA Approval Date	October 2002
Catheters Enrolled	526
Catheters Currently Active in Study	48
Device Events	60
Median Follow-up Time (Months)	31.6
Cumulative Follow-up Time (Months)	22,797



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.6% (88.9%, 96.3%)	92.3% (87.5%, 95.3%)	91.3% (86.5%, 94.5%)	89.4% (84.4%, 92.8%)	87.8% (82.5%, 91.6%)
Sample Size	261	305	255	196	148

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	82.4% (76.3%, 87.1%)	79.1% (72.5%, 84.3%)	75.8% (68.5%, 81.6%)	73.8% (66.2%, 80.0%)	72.7% (64.9%, 79.1%)
Sample Size	133	105	80	68	63

Time Interval	11 Years	12 Years	13 Years	14 Years	
Survival (95% CI)	71.5% (63.4%, 78.1%)	69.0% (60.4%, 76.2%)	65.1% (55.7%, 72.9%)	60.3% (50.1%, 69.1%)	
Sample Size	58	54	43	24	

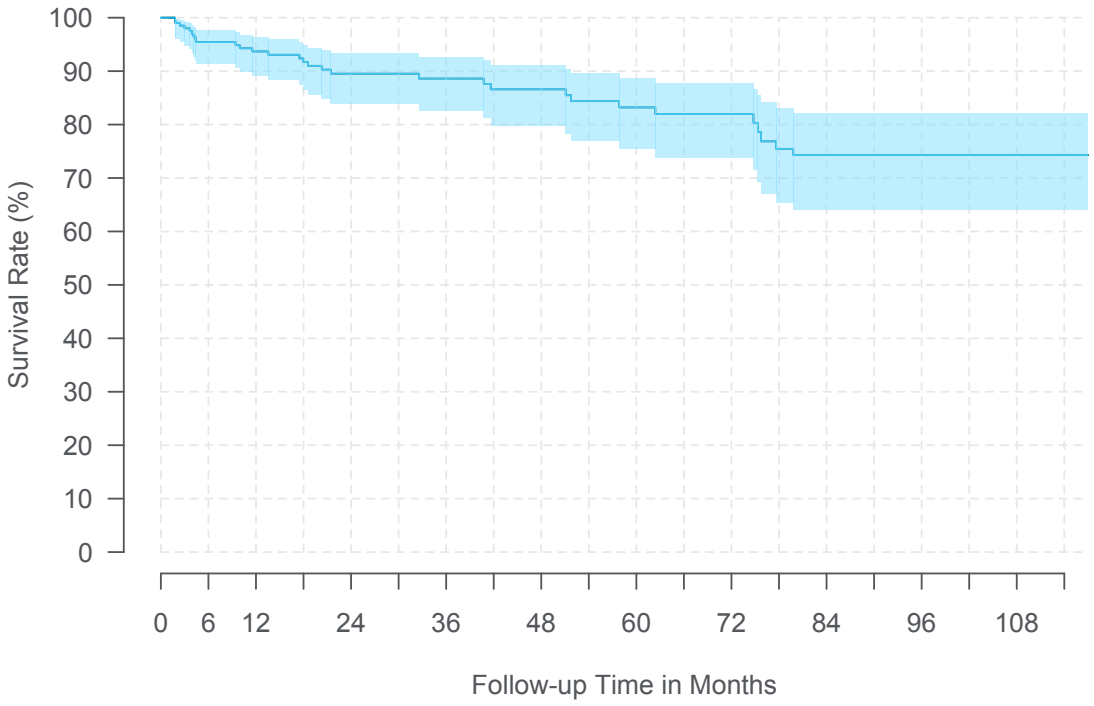
Specification: 8731	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed tip, radiopaque, titanium with 6 side holes
Catheter Volume	2.22 mL/cm
Trimmable Segments	Spinal end

Catheter Event Summary: 8731	N
Catheter Occlusion	23
Catheter Dislodgement	19
Catheter Kink	4
Catheter Related Complication	4
Catheter Break/Cut	3
Catheter Disconnection At Pump	3
Other[a]	4
Total	**60**

[a] Composed of event codes with 1 event each.

3.5.2.5 Model 8731SC

Model/Name	8731SC
FDA Approval Date	March 2006
Catheters Enrolled	278
Catheters Currently Active in Study	93
Device Events	30
Median Follow-up Time (Months)	27.1
Cumulative Follow-up Time (Months)	10,115



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.7% (89.1%, 96.4%)	89.5% (83.8%, 93.3%)	88.6% (82.6%, 92.7%)	86.6% (79.9%, 91.2%)	83.2% (75.4%, 88.7%)
Sample Size	153	113	94	81	68

Time Interval	6 Years	7 Years	8 Years	9 Years	At 117 Months
Survival (95% CI)	82.0% (73.9%, 87.8%)	74.3% (64.0%, 82.0%)	74.3% (64.0%, 82.0%)	74.3% (64.0%, 82.0%)	74.3% (64.0%, 82.0%)
Sample Size	51	63	39	29	21

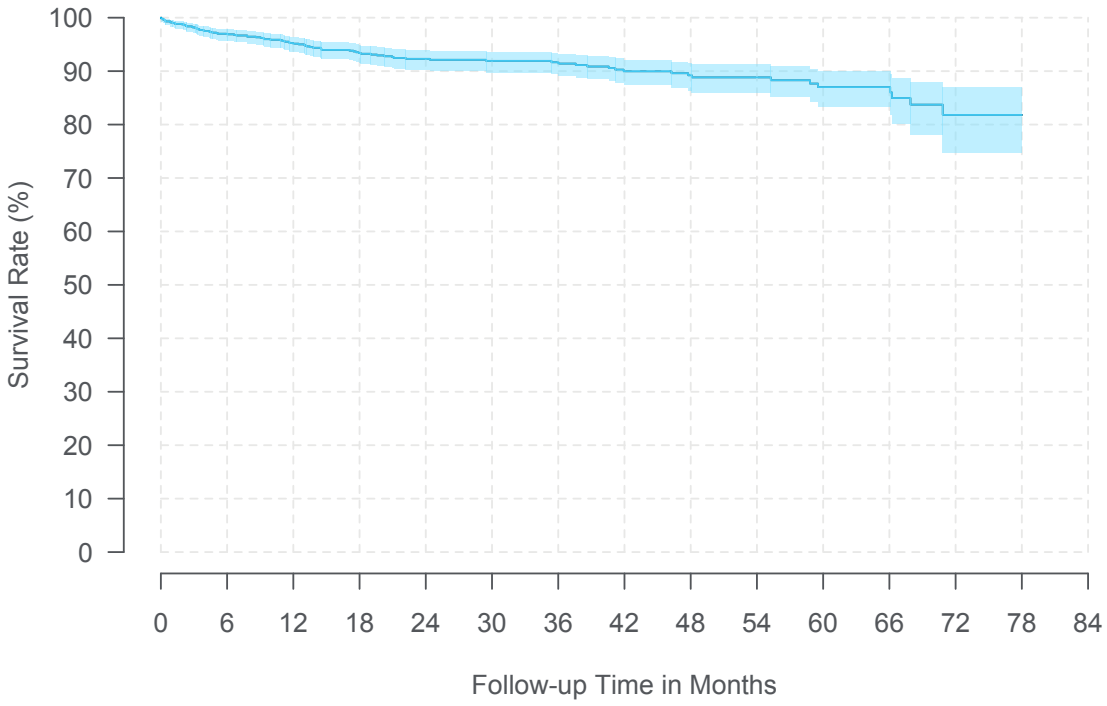
Specification: 8731SC	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Spinal and pump ends

Catheter Event Summary: 8731SC	N
Catheter Occlusion	11
Catheter Dislodgement	8
Catheter Kink	3
Catheter Related Complication	3
Pump Unable To Enter/Withdraw From Catheter Access Port	2
Other[a]	3
Total	**30**

[a] Composed of event codes with 1 event each.

3.5.2.6 Model 8780

Model/Name	8780/Ascenda
FDA Approval Date	May 2012
Catheters Enrolled	1,256
Catheters Currently Active in Study	746
Device Events	88
Median Follow-up Time (Months)	19.7
Cumulative Follow-up Time (Months)	32,055



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	95.1% (93.6%, 96.3%)	92.3% (90.3%, 93.9%)	91.7% (89.5%, 93.4%)	89.2% (86.4%, 91.5%)	87.0% (83.3%, 89.9%)
Sample Size	764	524	354	226	126

Time Interval	6 Years	At 78 Months			
Survival (95% CI)	81.8% (74.8%, 87.0%)	81.8% (74.8%, 87.0%)			
Sample Size	36	27			

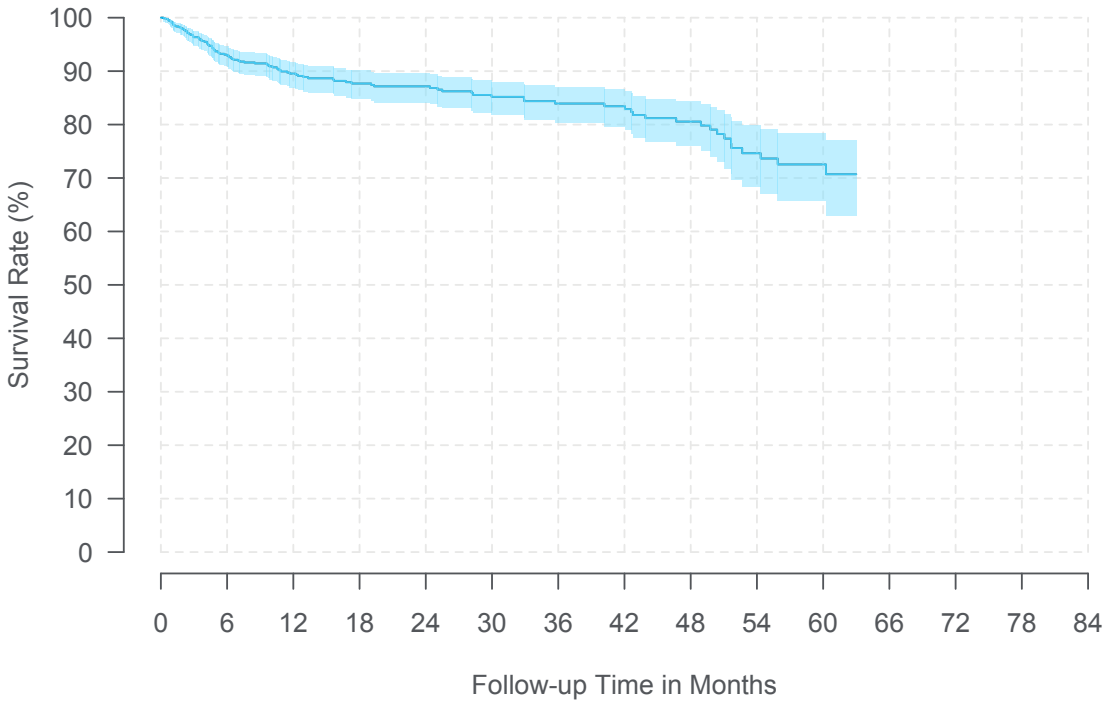
Specification: 8780	
Total Length	114 cm
Outer Diameter (spinal segment)	1.2 mm (4.0 French)
Inner Diameter (spinal segment)	0.5 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Connector end of the spinal segment

Catheter Event Summary: 8780	N
Catheter Occlusion	38
Catheter Dislodgement	19
Catheter Kink	16
Catheter Break/Cut	7
Catheter Leakage	3
Catheter Disconnection At Pump	2
Catheter Related Complication	2
Other[a]	1
Total	**88**

[a] Composed of event codes with 1 event each.

3.5.2.7 Model 8781

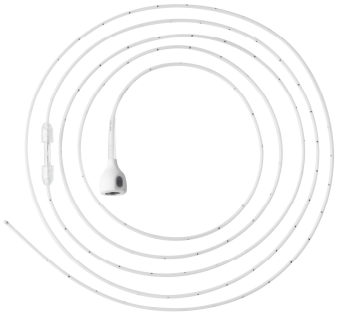
Model/Name	8781/Ascenda
FDA Approval Date	May 2012
Catheters Enrolled	995
Catheters Currently Active in Study	404
Device Events	117
Median Follow-up Time (Months)	11.1
Cumulative Follow-up Time (Months)	18,948



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	89.5% (86.9%, 91.6%)	87.1% (84.2%, 89.6%)	83.9% (80.3%, 87.0%)	80.6% (76.0%, 84.3%)	72.5% (65.7%, 78.3%)
Sample Size	421	288	186	115	39

Time Interval	At 63 Months
Survival (95% CI)	70.7% (63.0%, 77.1%)
Sample Size	31

Specification: 8781	
Total Length	140 cm
Outer Diameter (spinal segment)	1.2 mm (4.0 French)
Inner Diameter (spinal segment)	0.5 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Catheter connector ends of the spinal and pump segments

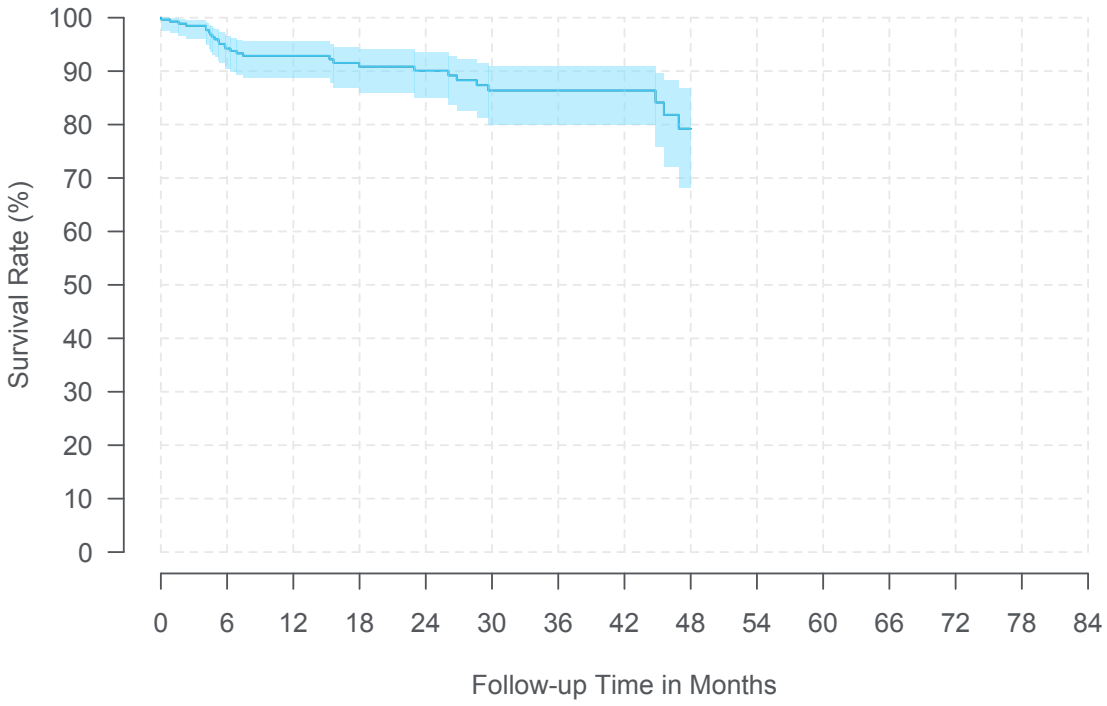


Catheter Event Summary: 8781	N
Catheter Kink	47
Catheter Dislodgement	32
Catheter Occlusion	20
Catheter Break/Cut	5
Catheter Related Complication	4
Catheter Disconnection At Pump	3
Catheter Leakage	3
Other[a]	3
Total	**117**

[a] Composed of event codes with 1 event each.

3.5.2.8 Ascenda Revised As Designed

Model/Name	Ascenda Revised As Designed
FDA Approval Date	May 2012
Catheters Enrolled	317
Catheters Currently Active in Study	156
Device Events	30
Median Follow-up Time (Months)	12.7
Cumulative Follow-up Time (Months)	6,079



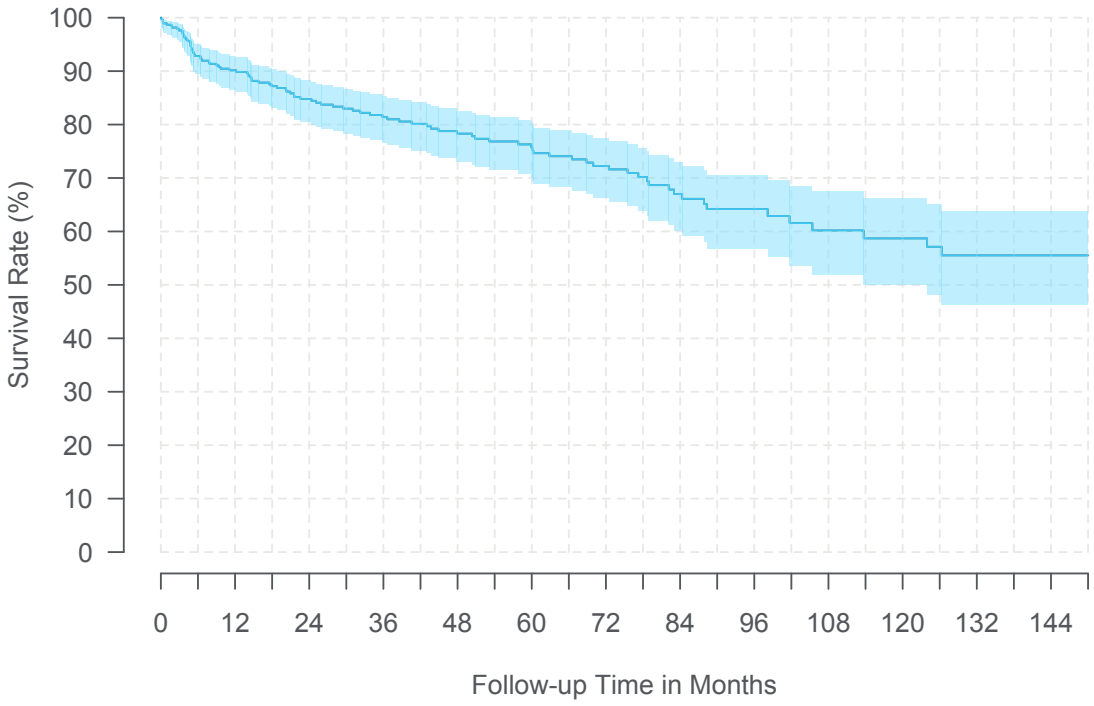
Time Interval	1 Year	2 Years	3 Years	4 Years
Survival (95% CI)	92.9% (88.7%, 95.5%)	90.1% (85.0%, 93.5%)	86.4% (80.0%, 90.8%)	79.2% (68.2%, 86.8%)
Sample Size	165	109	63	27

Catheter Event Summary: Ascenda RAD	N
Catheter Dislodgement	9
Catheter Occlusion	9
Catheter Kink	7
Other[a]	5
Total	**30**

[a] Composed of event codes with 1 event each.

3.5.2.9 Grafted Not As Designed

Model/Name	Grafted Not As Designed
FDA Approval Date	NA
Catheters Enrolled	485
Catheters Currently Active in Study	138
Device Events	99
Median Follow-up Time (Months)	32.2
Cumulative Follow-up Time (Months)	20,626



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	90.1% (86.5%, 92.8%)	84.8% (80.5%, 88.3%)	81.4% (76.6%, 85.3%)	78.3% (73.1%, 82.6%)	75.7% (70.2%, 80.4%)
Sample Size	287	238	199	166	137

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	72.3% (66.3%, 77.4%)	67.0% (60.2%, 72.9%)	64.2% (56.9%, 70.6%)	60.2% (51.9%, 67.5%)	58.7% (50.1%, 66.3%)
Sample Size	112	75	49	42	37

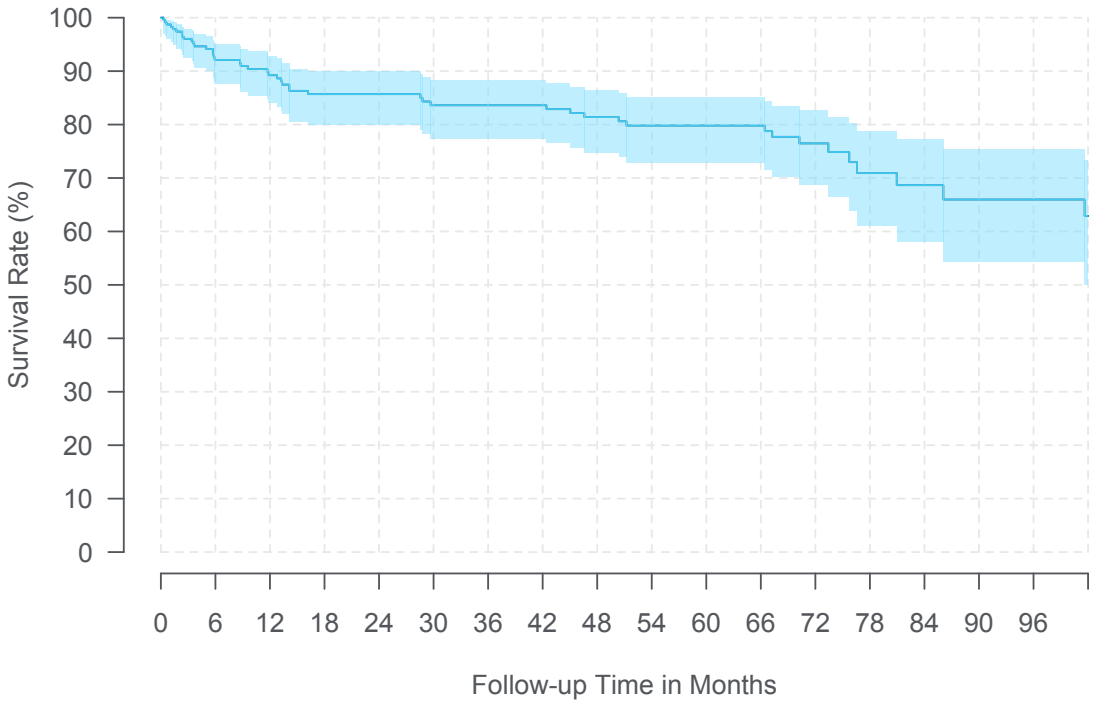
Time Interval	11 Years	12 Years	At 150 Months		
Survival (95% CI)	55.5% (46.3%, 63.8%)	55.5% (46.3%, 63.8%)	55.5% (46.3%, 63.8%)		
Sample Size	29	22	21		

Catheter Event Summary: Grafted Not As Designed	N
Catheter Occlusion	31
Catheter Dislodgement	26
Catheter Break/Cut	12
Catheter Kink	7
Catheter Related Complication	7
Catheter Leakage	6
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Other[a]	6
Total	**99**

[a] Composed of event codes with 1 event each.

3.5.2.10 Revised As Designed

Model/Name	Revised As Designed
FDA Approval Date	October 2002
Catheters Enrolled	396
Catheters Currently Active in Study	203
Device Events	48
Median Follow-up Time (Months)	9.0
Cumulative Follow-up Time (Months)	10,523



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	89.2% (84.1%, 92.8%)	85.7% (79.9%, 89.9%)	83.6% (77.4%, 88.3%)	81.4% (74.8%, 86.4%)	79.8% (72.9%, 85.1%)
Sample Size	155	129	117	104	87

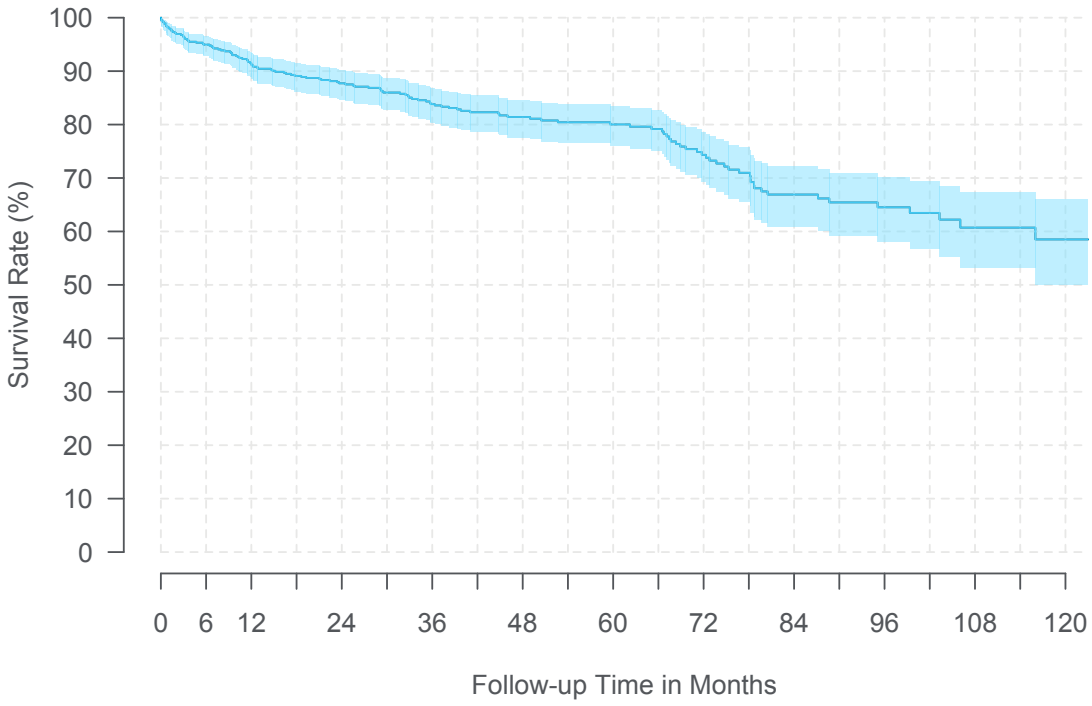
Time Interval	6 Years	7 Years	8 Years	At 102 Months	
Survival (95% CI)	76.5% (68.7%, 82.6%)	68.7% (58.0%, 77.2%)	66.0% (54.3%, 75.4%)	62.9% (50.1%, 73.3%)	
Sample Size	52	26	21	20	

Catheter Event Summary: Revised As Designed	N
Catheter Dislodgement	19
Catheter Occlusion	16
Catheter Kink	4
Catheter Break/Cut	3
Catheter Related Complication	3
Other[a]	3
Total	**48**

[a] Composed of event codes with 1 event each.

3.5.2.11 Revised Not As Designed

Model/Name	Revised Not As Designed
FDA Approval Date	NA
Catheters Enrolled	708
Catheters Currently Active in Study	180
Device Events	130
Median Follow-up Time (Months)	37.1
Cumulative Follow-up Time (Months)	29,816



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.2% (88.5%, 93.3%)	87.7% (84.7%, 90.2%)	83.8% (80.3%, 86.8%)	81.4% (77.6%, 84.6%)	80.0% (76.0%, 83.4%)
Sample Size	498	428	342	262	199

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	74.3% (69.4%, 78.6%)	66.9% (60.9%, 72.2%)	64.5% (58.1%, 70.2%)	60.7% (53.2%, 67.4%)	58.5% (50.0%, 66.1%)
Sample Size	137	102	67	38	22

Time Interval	At 123 Months
Survival (95% CI)	58.5% (50.0%, 66.1%)
Sample Size	22

Catheter Event Summary: Revised Not As Designed	N
Catheter Occlusion	48
Catheter Dislodgement	24
Catheter Break/Cut	16
Catheter Kink	14
Catheter Leakage	6
Catheter Related Complication	6
Pump Unable To Enter/Withdraw From Catheter Access Port	5
Catheter Disconnection At Pump	4
Other[a]	7
Total	**130**

[a] Composed of event codes with 1 event each.

3.5.3 Catheter Summary

Table 3.25: Targeted Drug Delivery Catheter Characteristics

Model/Name	FDA Approval Date	Catheters Enrolled	Catheters Active	Catheter Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
8709	May 1998	2,888	178	356	17.4	94,664
8709SC	March 2006	1,090	208	151	25.4	42,063
8711	October 1999	655	87	94	31.0	29,460
8731	October 2002	526	48	60	31.6	22,797
8731SC	March 2006	278	93	30	27.1	10,115
8780	May 2012	1,256	746	88	19.7	32,055
8781	May 2012	995	404	117	11.1	18,948
Ascenda Revised As Designed	May 2012	317	156	30	12.7	6,079
Grafted Not As Designed	NA	485	138	99	32.2	20,626
Revised As Designed	October 2002	396	203	48	9.0	10,523
Revised Not As Designed	NA	708	180	130	37.1	29,816

Table 3.26: Targeted Drug Delivery Catheter Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
8709	91.8% (90.0%, 93.2%)	89.0% (87.1%, 90.7%)	85.5% (83.2%, 87.4%)	82.5% (80.1%, 84.7%)	79.9% (77.3%, 82.2%)
8709SC	93.9% (92.0%, 95.4%)	89.5% (87.0%, 91.5%)	87.0% (84.2%, 89.3%)	84.1% (81.0%, 86.8%)	82.1% (78.7%, 85.0%)
8711	92.4% (88.8%, 94.9%)	90.0% (86.0%, 92.9%)	84.9% (80.4%, 88.4%)	82.5% (77.7%, 86.3%)	80.7% (75.8%, 84.7%)
8731	93.6% (88.9%, 96.3%)	92.3% (87.5%, 95.3%)	91.3% (86.5%, 94.5%)	89.4% (84.4%, 92.8%)	87.8% (82.5%, 91.6%)
8731SC	93.7% (89.1%, 96.4%)	89.5% (83.8%, 93.3%)	88.6% (82.6%, 92.7%)	86.6% (79.9%, 91.2%)	83.2% (75.4%, 88.7%)
8780	95.1% (93.6%, 96.3%)	92.3% (90.3%, 93.9%)	91.7% (89.5%, 93.4%)	89.2% (86.4%, 91.5%)	87.0% (83.3%, 89.9%)
8781	89.5% (86.9%, 91.6%)	87.1% (84.2%, 89.6%)	83.9% (80.3%, 87.0%)	80.6% (76.0%, 84.3%)	72.5% (65.7%, 78.3%)
Ascenda Revised As Designed	92.9% (88.7%, 95.5%)	90.1% (85.0%, 93.5%)	86.4% (80.0%, 90.8%)	79.2% (68.2%, 86.8%)	
Grafted Not As Designed	90.1% (86.5%, 92.8%)	84.8% (80.5%, 88.3%)	81.4% (76.6%, 85.3%)	78.3% (73.1%, 82.6%)	75.7% (70.2%, 80.4%)
Revised As Designed	89.2% (84.1%, 92.8%)	85.7% (79.9%, 89.9%)	83.6% (77.4%, 88.3%)	81.4% (74.8%, 86.4%)	79.8% (72.9%, 85.1%)
Revised Not As Designed	91.2% (88.5%, 93.3%)	87.7% (84.7%, 90.2%)	83.8% (80.3%, 86.8%)	81.4% (77.6%, 84.6%)	80.0% (76.0%, 83.4%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
8709	74.7% (71.8%, 77.3%)	70.1% (67.0%, 73.0%)	67.8% (64.6%, 70.8%)	66.2% (62.9%, 69.3%)	63.5% (60.0%, 66.8%)
8709SC	79.4% (75.7%, 82.7%)	73.4% (69.0%, 77.3%)	70.5% (65.8%, 74.8%)	69.3% (64.2%, 73.7%)	66.2% (60.1%, 71.6%)
8711	77.2% (72.0%, 81.6%)	74.0% (68.5%, 78.7%)	72.1% (66.4%, 77.0%)	71.0% (65.1%, 76.0%)	68.2% (61.9%, 73.6%)
8731	82.4% (76.3%, 87.1%)	79.1% (72.5%, 84.3%)	75.8% (68.5%, 81.6%)	73.8% (66.2%, 80.0%)	72.7% (64.9%, 79.1%)
8731SC	82.0% (73.9%, 87.8%)	74.3% (64.0%, 82.0%)	74.3% (64.0%, 82.0%)	74.3% (64.0%, 82.0%)	
8780	81.8% (74.8%, 87.0%)				
8781					
Ascenda Revised As Designed					
Grafted Not As Designed	72.3% (66.3%, 77.4%)	67.0% (60.2%, 72.9%)	64.2% (56.9%, 70.6%)	60.2% (51.9%, 67.5%)	58.7% (50.1%, 66.3%)
Revised As Designed	76.5% (68.7%, 82.6%)	68.7% (58.0%, 77.2%)	66.0% (54.3%, 75.4%)		
Revised Not As Designed	74.3% (69.4%, 78.6%)	66.9% (60.9%, 72.2%)	64.5% (58.1%, 70.2%)	60.7% (53.2%, 67.4%)	58.5% (50.0%, 66.1%)

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
8709	61.3% (57.6%, 64.8%)	59.0% (55.1%, 62.8%)	56.1% (51.7%, 60.2%)	54.0% (49.3%, 58.4%)	53.3% (48.5%, 57.9%)
8709SC					
8711	65.6% (58.9%, 71.5%)	64.2% (57.0%, 70.5%)	60.9% (52.6%, 68.2%)	59.0% (50.0%, 66.9%)	59.0% (50.0%, 66.9%)
8731	71.5% (63.4%, 78.1%)	69.0% (60.4%, 76.2%)	65.1% (55.7%, 72.9%)	60.3% (50.1%, 69.1%)	
8731SC					
8780					
8781					
Ascenda Revised As Designed					
Grafted Not As Designed	55.5% (46.3%, 63.8%)	55.5% (46.3%, 63.8%)			
Revised As Designed					
Revised Not As Designed					

Model Name	16 Years	17 Years			
8709	53.3% (48.5%, 57.9%)	52.2% (47.0%, 57.1%)			
8709SC					
8711					
8731					
8731SC					
8780					
8781					
Ascenda Revised As Designed					
Grafted Not As Designed					
Revised As Designed					
Revised Not As Designed					

4 Spinal Cord Stimulation Systems

4.1 Study Participants

4.1.1 Centers

The spinal cord stimulation tables and graphs were generated based on data collected between June 2004 and the report cut-off date of October 31, 2019. Eighty-four centers spanning 9 countries in North America, Europe and South America, enrolled patients and contributed patient data to the spinal cord stimulation systems section of this report. Figure 4.1 shows a World Map, in which the countries that enrolled PSTM patients are highlighted.

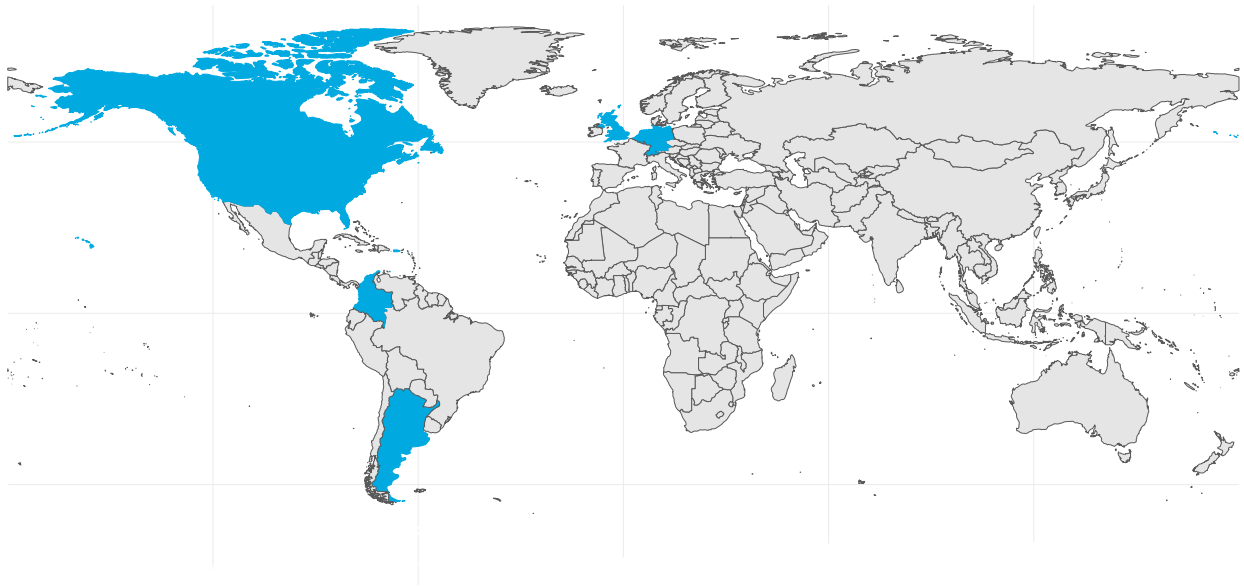


Figure 4.1: Countries with Spinal Cord Stimulation Therapy Patients in Registry (Highlighted)

4.1.2 Patients

Of the 5,712 spinal cord stimulation patients enrolled, 45.7% were implanted for the treatment of failed back pain, 25.5% were implanted for the treatment of other primary indications, 17.9% were implanted for the treatment of trunk and limb pain, 10.3% were implanted for the treatment

of CRPS, and 0.6% were implanted for indications that were not specified in the database (see Figure 4.2 and Table 4.1).

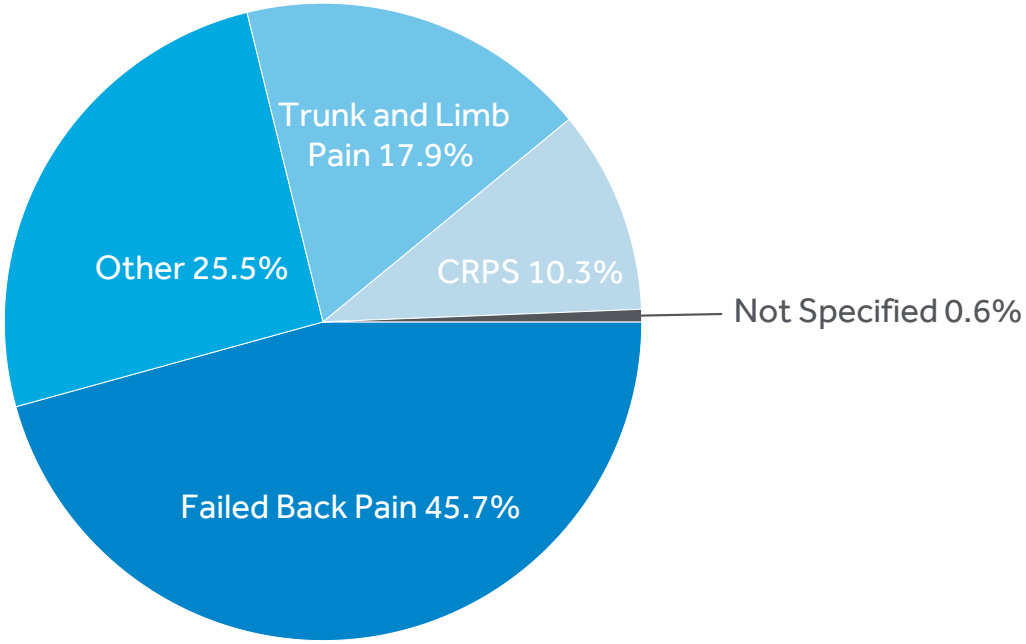


Figure 4.2: Spinal Cord Stimulation Primary Treatment Indications

Table 4.1: Spinal Cord Stimulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Failed Back Pain	**2,611 (45.71%)**
Failed Back Surgery Syndrome (FBSS)	902 (15.79%)
Post Laminectomy Pain	891 (15.60%)
Combination Back and Leg Pain	698 (12.22%)
Multiple Back Operations	86 (1.51%)
Arachnoiditis	22 (0.39%)
Unsuccessful Disc Surgery	12 (0.21%)
Other Primary Indication	**1,454 (25.46%)**
Other Chronic Pain	836 (14.64%)
Cervical Pain	74 (1.30%)
Traumatic Nerve Injury	45 (0.79%)
Chronic Cluster Headache	35 (0.61%)
Diabetic Neuropathy	33 (0.58%)
Post Herpetic Neuralgia	18 (0.32%)
Facial Pain	8 (0.14%)
Angina	6 (0.11%)
Epidural Fibrosis	4 (0.07%)
Post Herniorrhaphy Pain	3 (0.05%)
Other Secondary Indication	392 (6.86%)
Trunk and Limb Pain	**1,021 (17.87%)**
Radicular Pain Syndrome	772 (13.52%)
Degenerative Disc Disease	249 (4.36%)
CRPS	**590 (10.33%)**
CRPS I	457 (8.00%)
CRPS II	133 (2.33%)
Not Specified	**36 (0.63%)**
Total Patients	**5712 (100%)**

[a] For approved indications refer to product labeling for your geography.

It is recognized that healthcare providers prescribe therapies to meet specific patient needs; however, Medtronic only directs the use of its products based on approved regulatory labeling. Product labeling varies by geography. Contact a local Medtronic representative (http://www.medtronic.com/us-en/about/locations.html) for region-specific product labeling.

4.2 Event Summary

There were 1,607 product performance events reported between June 2004 and October 31, 2019, in patients with spinal cord stimulation systems. These events represent 35.6% of the

total reported events (1,607/4,520), occured in 771 (13.5%) of the 5,712 total patients enrolled, and are presented graphically within this report (e.g. events per patient years as well as survival curves). In addition, there were 2,879 non-product performance events that were collected to understand patient experience (clinical signs and symptoms) with the spinal cord stimulation systems. As an ongoing registry, events not coded at the time of the data snapshot (waiting on further information) will be included in future reports (n=34).

All registry devices that are returned to Medtronic are analyzed via a Returned Product Analysis (RPA) process. If available, RPA findings assist in the classification of the events. Within this report, Table 4.2 differentiates the events by those determined by the RPA process versus those determined by the physician. Please refer to the Methodology section for more information.

There were 199 deaths reported for patients followed in the PSR with spinal cord stimulation systems, none of which were reported as a direct result of a product performance event.

4.2.1 Product Performance Events

Table 4.2: Spinal Cord Stimulation System Product Performance Events

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=5,712[b]
RPA Determination	**4**	**0.03**	**4 (0.07%)**
Broken Bond Wire	1	0.01	1 (0.02%)
Grommet Loose	1	0.01	1 (0.02%)
Medical Device Complication[c]	1	0.01	1 (0.02%)
No Anomaly Found By RPA	1	0.01	1 (0.02%)
Physician's Determination	**1,603**	**13.05**	**768 (13.45%)**
Lead Migration/Dislodgement	707	5.75	373 (6.53%)
High Impedance	414	3.37	186 (3.26%)
Lead Fracture	87	0.71	58 (1.02%)
Neurostimulator Unable To Recharge[d]	82	0.67	76 (1.33%)
Device Malfunction[e]	71	0.58	65 (1.14%)
Device Stimulation Issue[f]	50	0.41	29 (0.51%)
Low Impedance	47	0.38	20 (0.35%)
Device Breakage[g]	32	0.26	29 (0.51%)
Extension Fracture	18	0.15	12 (0.21%)
Medical Device Complication[h]	16	0.13	10 (0.18%)
Device Electrical Impedance Issue	12	0.10	8 (0.14%)
Extension Migration	8	0.07	6 (0.11%)
Device Lead Damage	7	0.06	5 (0.09%)
Device Battery Issue	6	0.05	5 (0.09%)
Antenna Cable Breakage	5	0.04	5 (0.09%)
Device Connection Issue	5	0.04	3 (0.05%)
Device Difficult To Use	5	0.04	4 (0.07%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=5,712[b]
Device Telemetry Issue	5	0.04	5 (0.09%)
Therapeutic Product Ineffective	5	0.04	4 (0.07%)
Device Failure[i]	4	0.03	3 (0.05%)
Neurostimulator Migration	3	0.02	3 (0.05%)
Device Loosening	2	0.02	2 (0.04%)
Inadequate Lead Connection	2	0.02	1 (0.02%)
Medical Device Site Erosion	2	0.02	1 (0.02%)
Paraesthesia	2	0.02	1 (0.02%)
Device Kink	1	0.01	1 (0.02%)
Device Material Deterioration	1	0.01	1 (0.02%)
Lead Insulation Failure	1	0.01	1 (0.02%)
Medical Device Site Erythema	1	0.01	1 (0.02%)
Medical Device Site Warmth	1	0.01	1 (0.02%)
Sensory Disturbance	1	0.01	1 (0.02%)
Total	**1,607**	**13.08**	**771 (13.50%)**

[a] Medical Dictionary for Regulatory Activities (MedDRA) Lower-Level Term or Medtronic's coding system term for events that do not exist in the MedDRA dictionary.

[b] The total number of patients with events may not represent the sum of all rows, as a patient may have experienced more than one type of event.

[c] 1 event without a device diagnosis but has RPA finding. RPA finding is described as a problem with the functionality of the INS that appears to be related to the hybrid; however, the exact cause of the problem could not be determined.

[d] There were a total of 3,791 patients that used rechargeable SCS neurostimulators in the registry. A total of 2.0% (76/3,791) of patients with a rechargeable SCS neurostimulator experienced a neurostimulator unable to recharge product performance event.

[e] Device malfunction includes 14 malfunctioning programmer, 13 recharging malfunctions, 6 antenna malfunctions, 5 stimulator turning off and on, 4 suspected dysfunction, 4 neurostimulator malfunctions, 3 contacts not working, 3 device shut off, 2 inability to turn neurostimulator on, 2 events for non-functional lead electrodes, 2 recharging cable malfunction, 2 stimulator error message, 2 lead malfucntions described as lead migration, 1 programmer reporting error message, 1 issue with INS clock, 1 SCS stopped abruptly, 1 SCS turned on involuntary, 1 extension stuck in neurostimulator, 1 power cord defective, 1 patient reported warming of neurostimulator during MRI, 1 generator reporting inconsistent time usage, and 1 problem with handset.

[f] Device stimulation issue reported by physician as being caused by neurostimulator (n=2), lead (n=45) or programming (n=3).

[g] Device breakage includes 13 broken charger belts, 11 broken charger, 4 broken patient programmers, 1 broken recharger cord, 1 frayed cord to charger antenna, 1 broken recharger strap, and 1 frayed wire to charger.

[h] Medical device complication includes 4 leads no longer providing stimulation, 3 error messages on patient programmer, 2 unable to pass stylet into lead, 2 unable to communicate with controller to switch device on, 2 leads with open circuits, 1 unknown problem with extension, 1 excessive heating of charging unit, and 1 unknown programmer error message.

[i] Device failure includes 3 events for lead failure, and 1 extension failure.

A total of 1,236 (76.9%) of the 1,607 product performance events were related to the lead, 129 (8.0%) were related to "other component", 81 (5.0%) were related to the neurostimulator, 50 (3.1%) were related to "multiple etiologies" (which includes events where at least one device and one non-device etiology was indicated), 41 (2.6%) were related to recharging process, 38 (2.4%) were related to the extension, 14 (0.9%) were related to programming/stimulation, 8 (0.5%) were related to incisional site/device tract, 5 (0.3%) were related to surgery/anesthesia, 4 (0.2%) were related to "other etiology", and 1 (0.1%) was related to MRI. Relatedness is reported by the physician.

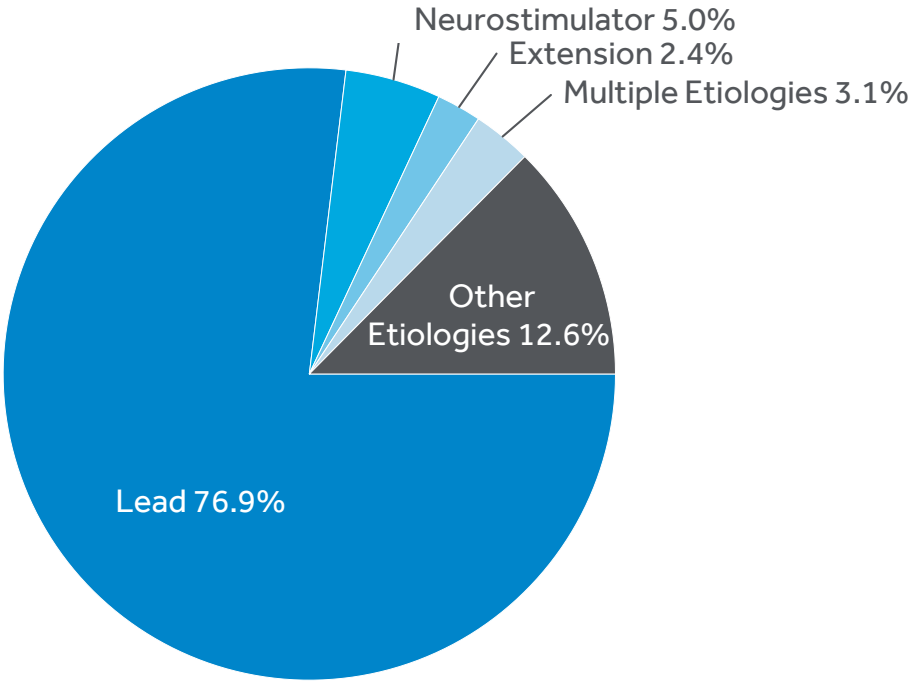


Figure 4.3: Spinal Cord Stimulation System Product Performance Events by Relatedness

Table 4.3 and Table 4.4 describe the interventions taken for reported impedance events. In 23.4% and 17.0% of the high and low impedance events, the action taken was a surgical intervention. However, impedance could be used as a diagnostic measurement and may not result in any intervention or clinical impact. The majority of events required no intervention or device reprogramming only (73.4% for high impedance and 80.9% for low impedance).

Table 4.3: Spinal Cord Stimulation System High Impedance Events by Intervention

Intervention	N (%) of High Impedance Events
Reprogrammed	193 (46.6%)
Device Surgical Intervention	96 (23.2%)
Therapy Suspended	8 (1.9%)
Other intervention	5 (1.2%)
Other Surgical Intervention	1 (0.2%)
No Action Taken	111 (26.8%)
Total	**414 (100%)**

Table 4.4: Spinal Cord Stimulation System Low Impedance Events by Intervention

Intervention	N (%) of Low Impedance Events
Reprogrammed	25 (53.2%)
Device Surgical Intervention	7 (14.9%)
Other Surgical Intervention	1 (2.1%)
Other intervention	1 (2.1%)
No Action Taken	13 (27.7%)
Total	**47 (100%)**

Table 4.5 describes the interventions taken for reported lead migration/dislodgement events; 78.5% of them led to a surgical intervention, and 11.3% were reprogramming.

Table 4.5: Spinal Cord Stimulation System Lead Migration/Dislodgement Events by Intervention

Intervention	N (%) of Lead Migration/Dislodgement Events
Device Surgical Intervention	515 (72.8%)
Reprogrammed	80 (11.3%)
Other Surgical Intervention	40 (5.7%)
Therapy Suspended	16 (2.3%)
Other intervention	12 (1.7%)
Medical or non-sugical Therapy	3 (0.4%)
No Action Taken	41 (5.8%)
Total	**707 (100%)**

4.2.2 Clinical Events Not Related To Product Performance

The clinical events not related to product performance are summarized if:

- The patient was enrolled in the PSR at the time in which the clinical event collection was initiated (N=2,821)
- Categorized as serious adverse events
- Occurred with a System Organ Class (SOC) threshold $\geq$1% of patients
- Other Considerations
  - Some events are described in high level group terms (HLGT) to provide more specificity, if needed

Table 4.6: Spinal Cord Stimulation Clinical Events Not Related To Product Performance

Event Type	Number of SAE	Patients with SAE n (%) N=2,821	SAE Per 100 Patient Months	Patient with SAE Requiring Surgical Intervention n (%) N=2,821
Infections and infestations	**46**	**46 (1.63%)**	**0.08**	**32 (1.13%)**
Infections - pathogen unspecified	38	38 (1.35%)	0.07	28 (0.99%)
Bacterial infectious disorders	8	8 (0.28%)	0.01	4 (0.14%)
Other SOC Terms (<1.0% Threshold)	**38**	**33 (1.17%)**	**0.07**	**20 (0.71%)**
Total	**84**	**76 (2.69%)**	**1.54**	**49 (1.74%)**

[a] Composed of high level group term event codes with fewer than 5 events each.

4.2.3 Patient Deaths

In earlier versions of the protocol, deaths were only assessed for the relatedness to the device product performance. After 2010, death assessments were expanded to also include the relationship to the implant procedure and/or therapy. As of the report cut-off, a total of 199 patients in the registry had expired. As with previous reports, no deaths were reported as a direct result of a product performance event.

Since 2010, a total of 41 (20.6%) deaths have been reported in this patient registry study based upon patients receiving therapy for other chronic pain, 32 (16.1%) for radicular pain syndrome, 28 (14.1%) for failed back surgery syndrome (FBSS), 28 (14.1%) for post laminectomy pain, 18 (9.0%) for combination back and leg pain, 12 (6.0%) for CRPS I, 9 (4.5%) for degenerative disc disease, 7 (3.5%) for multiple back operations, 3 (1.5%) for CRPS II, 2 (1.0%) for diabetic neuropathy, 2 (1.0%) for post herpetic neuralgia, 1 (0.5%) for angina, 1 (0.5%) for cervical pain, 1 (0.5%) for traumatic nerve injury, and 14 (7.0%) for other indications. The percentage is based upon the total patient death events and not based upon the rate of occurrence. **All tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 4.7: Spinal Cord Stimulation System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Other Chronic Pain	41 (20.6%)
Radicular Pain Syndrome	32 (16.1%)
Failed Back Surgery Syndrome (FBSS)	28 (14.1%)
Post Laminectomy Pain	28 (14.1%)
Combination Back and Leg Pain	18 (9.0%)
CRPS I	12 (6.0%)
Degenerative Disc Disease	9 (4.5%)
Multiple Back Operations	7 (3.5%)
CRPS II	3 (1.5%)
Diabetic Neuropathy	2 (1.0%)
Post Herpetic Neuralgia	2 (1.0%)
Angina	1 (0.5%)
Cervical Pain	1 (0.5%)
Traumatic Nerve Injury	1 (0.5%)
Other	14 (7.0%)
Total	**199 (100%)**

[a] For approved indications refer to product labeling for your geography.

4.3 Neurostimulators

From June 2004 to the report cut-off date of October 31, 2019, there were 6,252 neurostimulators followed in the registry. The difference between the total number of patients (n=5,712) versus neurostimulators is due to the fact that some patients were subsequently re-implanted. The aggregate prospective follow-up time for all spinal cord neurostimulators was 142,784 months (11,899 years). Table 4.8 provides the number and percentage of neurostimulators by model.

Table 4.8: Spinal Cord Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**4,526 (72.4%)**
RestoreSensor SureScan MRI (97714)	1,371 (22.0%)
Intellis with AdaptiveStim (97715)	719 (11.5%)
PrimeAdvanced SureScan MRI (97702)	702 (11.2%)
PrimeAdvanced (37702)	670 (10.7%)
RestoreSensor (37714)	380 (6.1%)
RestoreAdvanced (37713)	357 (5.7%)
Itrel 4 (37703)	118 (1.9%)
RestoreAdvanced SureScan MRI (97713)	117 (1.9%)
RestoreUltra SureScan MRI (97712)	92 (1.5%)
No longer manufactured	**1,718 (27.5%)**
RestoreULTRA (37712)	581 (9.3%)
Synergy (7427)	461 (7.4%)
Restore (37711)	447 (7.2%)
Itrel 3 (7425)	96 (1.5%)
RestorePrime (37701)	56 (0.9%)
Synergy Versitrel (7427V)	53 (0.8%)
SynergyPlus (7479)	16 (0.3%)
SynergyCompact (7479B)	8 (0.1%)
Other/Unspecified	**8 (0.1%)**
Total	**6,252 (100%)**

4.3.1 Neurostimulator Events

There were 92 product performance-related events with an underlying reported etiology related to spinal cord neurostimulator function. This includes 81 events with a neurostimulator etiology and 11 events with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 84 were the initial product performance event that affected neurostimulator survival estimates. For spinal cord neurostimulators in the registry, the current return rate to Medtronic Returned Product Analysis (RPA) was 21.0% (358/1,701). The proportion was based upon the number of registry spinal cord neurostimulators received by RPA, divided by the sum of the total number of explanted devices and the total number of neurostimulators in patients who have expired. In the 92 spinal cord neurostimulator events, 95.7 % (88/92) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 4.9).

Table 4.9: Spinal Cord Stimulation Neurostimulator Product Performance Events by Determination

Product Performance Events	N (%)
RPA Determination	**4 (4.3%)**
Broken Bond Wire	1 (1.1%)
Grommet Loose	1 (1.1%)
Medical Device Complication	1 (1.1%)
No Anomaly Found By RPA	1 (1.1%)
Physician's Determination	**88 (95.7%)**
High Impedance	25 (27.2%)
Neurostimulator Unable To Recharge	22 (23.9%)
Device Malfunction	18 (19.6%)
Lead Migration/Dislodgement	7 (7.6%)
Low Impedance	3 (3.3%)
Medical Device Complication	3 (3.3%)
Device Battery Issue	2 (2.2%)
Device Stimulation Issue	2 (2.2%)
Device Difficult To Use	1 (1.1%)
Device Telemetry Issue	1 (1.1%)
Extension Migration	1 (1.1%)
Medical Device Site Warmth	1 (1.1%)
Neurostimulator Migration	1 (1.1%)
Therapeutic Product Ineffective	1 (1.1%)
Total	**92 (100%)**

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For neurostimulators:

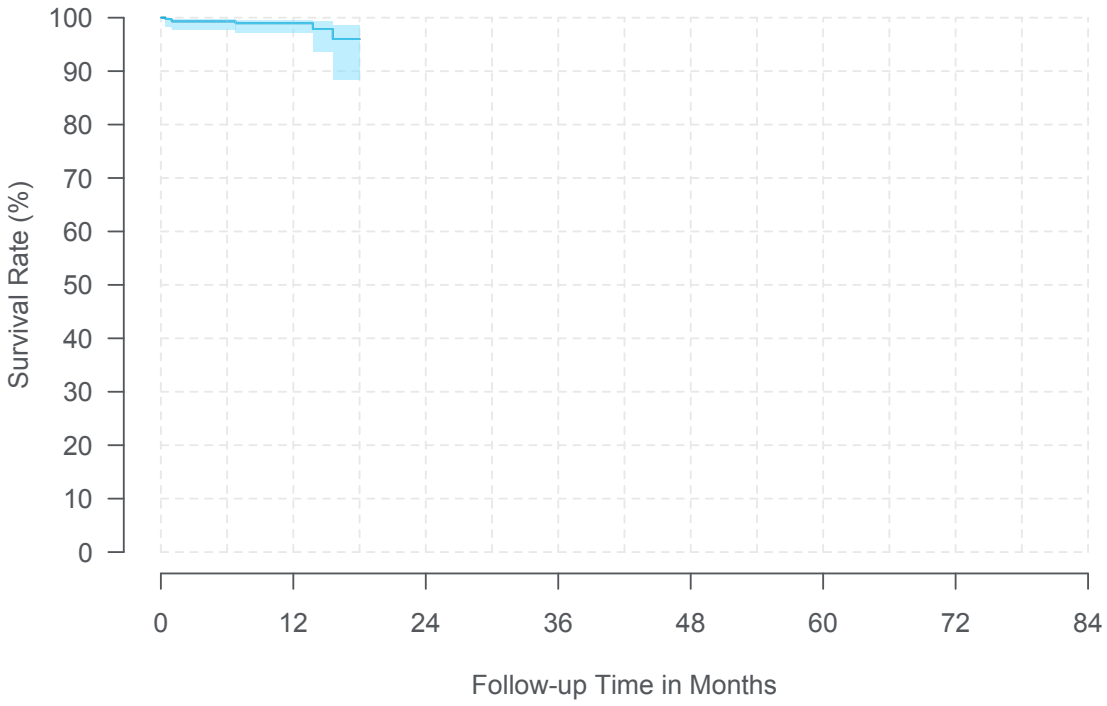
- 84 had follow-up time cut-off due to product performance-related events.
- 4,347 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 1,821 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

4.3.2 Neurostimulator Models

The following figures and tables represent spinal cord neurostimulator survival and 95% confidence intervals where at least 20 spinal cord neurostimulators contributed to each 3-month interval.

4.3.2.1 Intellis with AdaptiveStim

Model Name	Intellis with AdaptiveStim (model 97715)
FDA Approval Date	July 2017
Neurostimulators Enrolled	719
Neurostimulators Currently Active in Study	646
Device Events	7
Median Follow-up Time (Months)	4.4
Cumulative Follow-up Time (Months)	4,099



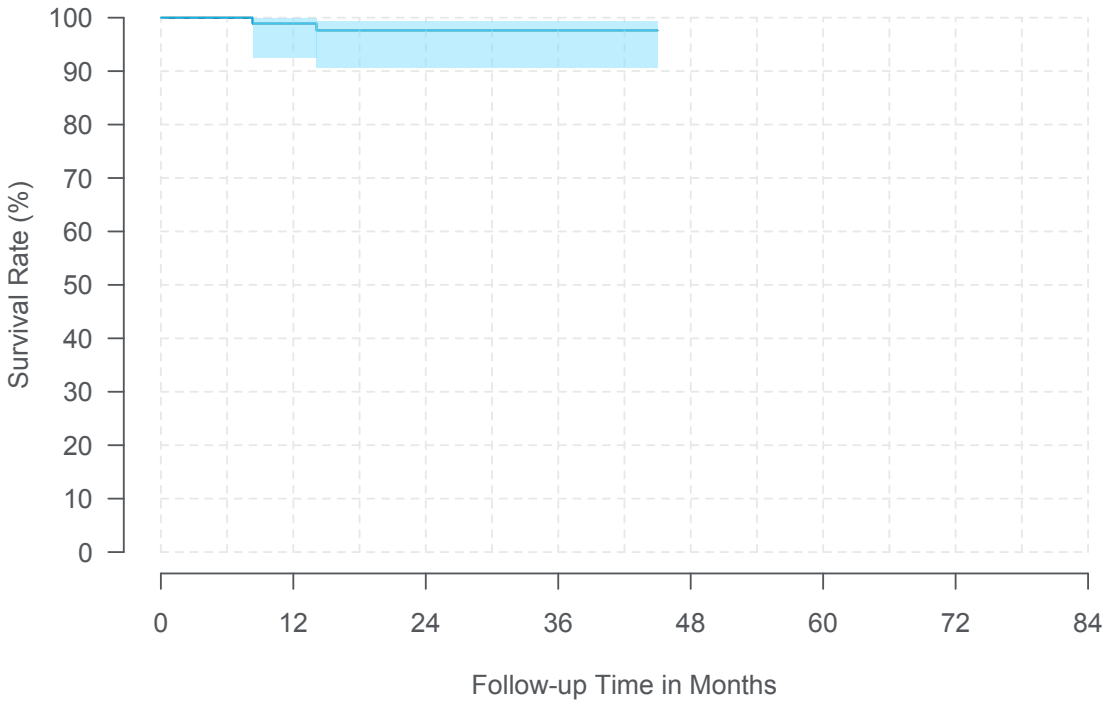
Time Interval	1 Year	At 18 Months
Survival	99.0%	96.0%
(95% CI)	(97.2%, 99.6%)	(88.5%, 98.6%)
Sample Size	123	26

Specification: Intellis with AdaptiveStim	
Height	57.1mm (2.2in)
Width	47.2mm (1.9in)
Thickness Case	6.3 mm (0.2 in)
Thickness Connector	9.1 mm (0.4 in)
Volume	13.9 cc
Battery Type	Rechargeable
Expected Battery Life	9 years before ERI
Maximum Electrodes	16
Amplitude	0 - 100 mA
Rate Range	40 - 1200 Hz
Pulse Width	60 - 1000 µsec
Groups	1 - 3
Programs	12
Implant Depth	≤ 3 cm

Neurostimulator Event Summary: Intellis with AdaptiveStim	N
High impedance	5
Device malfunction	1
Lead migration/dislodgement	1
Total	**7**

4.3.2.2 Model Itrel 4

Model Name	Itrel 4 (model 37703)
FDA Approval Date	May 2012
Neurostimulators Enrolled	118
Neurostimulators Currently Active in Study	61
Device Events	2
Median Follow-up Time (Months)	23.4
Cumulative Follow-up Time (Months)	3,031



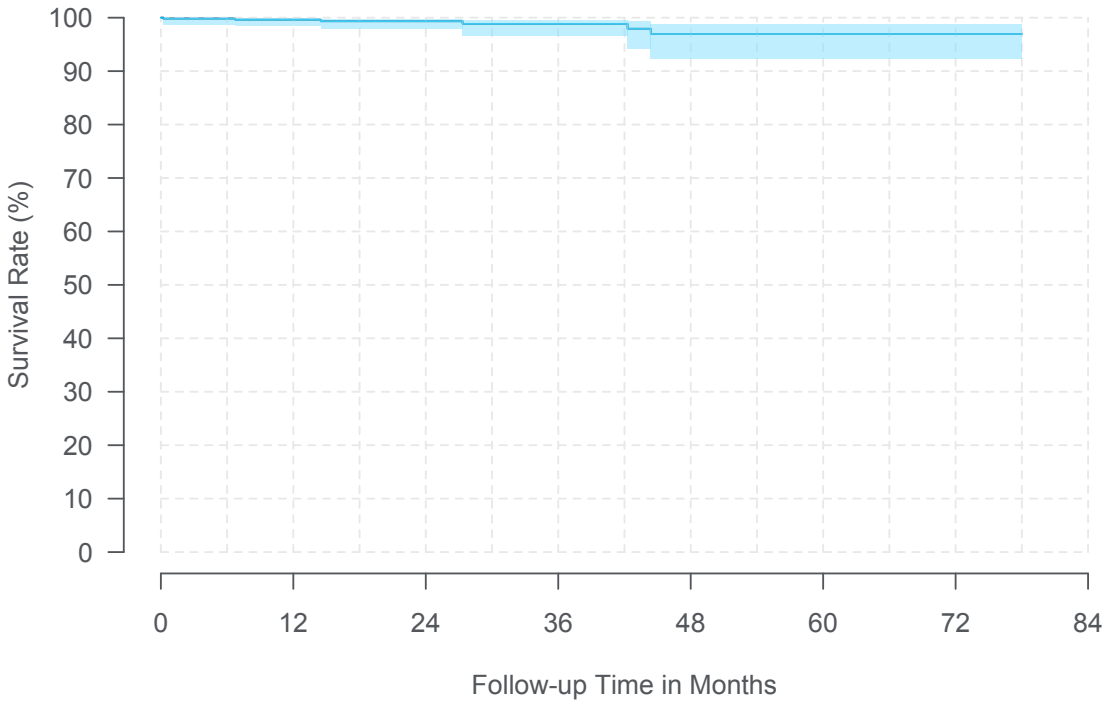
Time Interval	1 Year	2 Years	3 Years	At 45 Months
Survival (95% CI)	98.9% (92.5%, 99.8%)	97.6% (90.7%, 99.4%)	97.6% (90.7%, 99.4%)	97.6% (90.7%, 99.4%)
Sample Size	84	55	38	24

Specification: Itrel 4	
Height	2.2 in (55 mm)
Width	2.4 in (60 mm)
Thickness	0.4 in (11 mm)
Volume	28 cc
Battery type	Non-Rechargeable
Expected Battery life	Depends on settings and use
Maximum Electrodes	4
Amplitude	0 - 10.5 V
Rate	2 - 130 Hz
Pulse Width	60 - 450 µsec
Groups	1
Programs	1
Implant Depth	≤ 4 cm

Neurostimulator Event Summary: Itrel 4	N
Device malfunction	1
High impedance	1
Total	**2**

4.3.2.3 Model PrimeAdvanced

Model Name	PrimeAdvanced (model 37702)
FDA Approval Date	July 2006
Neurostimulators Enrolled	670
Neurostimulators Currently Active in Study	36
Device Events	7
Median Follow-up Time (Months)	16.0
Cumulative Follow-up Time (Months)	14,930



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (98.5%, 99.9%)	99.3% (97.9%, 99.8%)	98.8% (96.6%, 99.6%)	97.0% (92.3%, 98.8%)	97.0% (92.3%, 98.8%)
Sample Size	392	237	138	88	57

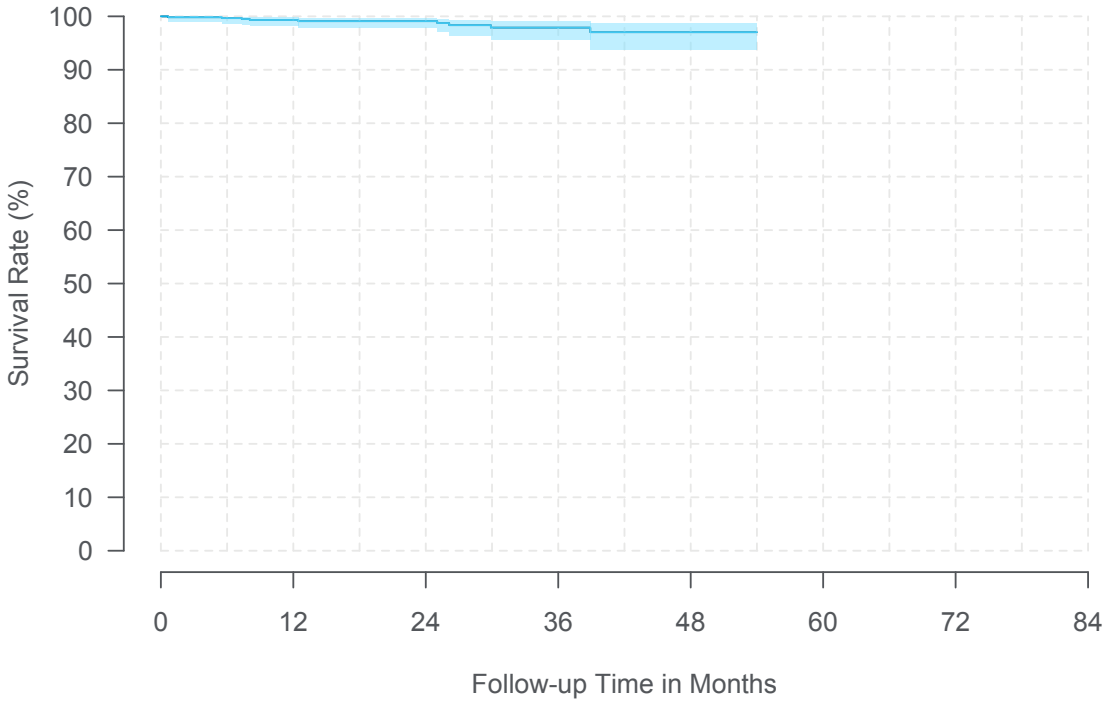
Time Interval	6 Years	At 78 Months			
Survival (95% CI)	97.0% (92.3%, 98.8%)	97.0% (92.3%, 98.8%)			
Sample Size	28	21			

Specification: PrimeAdvanced	
Height	2.6 in (65 mm)
Width	1.9 in (49 mm)
Thickness	0.6 in (15 mm)
Volume	39 cc
Battery type	Non-Rechargeable
Expected Battery life	Depends on settings and use
Maximum Electrodes	16
Amplitude	0 - 10.5 V
Rate	2 - 130 Hz
Pulse Width	60 - 450 µsec
Groups	26
Programs	32
Implant Depth	≤ 4 cm

Neurostimulator Event Summary: PrimeAdvanced	N
High impedance	3
Device malfunction	2
Device stimulation issue	1
Low impedance	1
Total	**7**

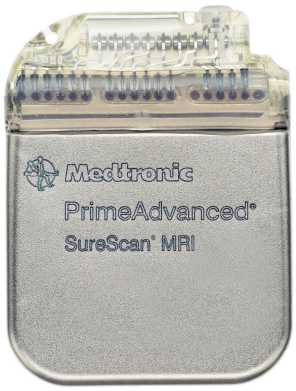
4.3.2.4 Model PrimeAdvanced SureScan MRI

Model Name	PrimeAdvanced SureScan MRI (model 97702)
FDA Approval Date	March 2013
Neurostimulators Enrolled	702
Neurostimulators Currently Active in Study	334
Device Events	9
Median Follow-up Time (Months)	21.4
Cumulative Follow-up Time (Months)	15,785



Time Interval	1 Year	2 Years	3 Years	4 Years	At 54 Months
Survival (95% CI)	99.3% (98.2%, 99.7%)	99.1% (97.9%, 99.6%)	97.9% (95.5%, 99.0%)	97.0% (93.7%, 98.6%)	97.0% (93.7%, 98.6%)
Sample Size	488	302	146	56	26

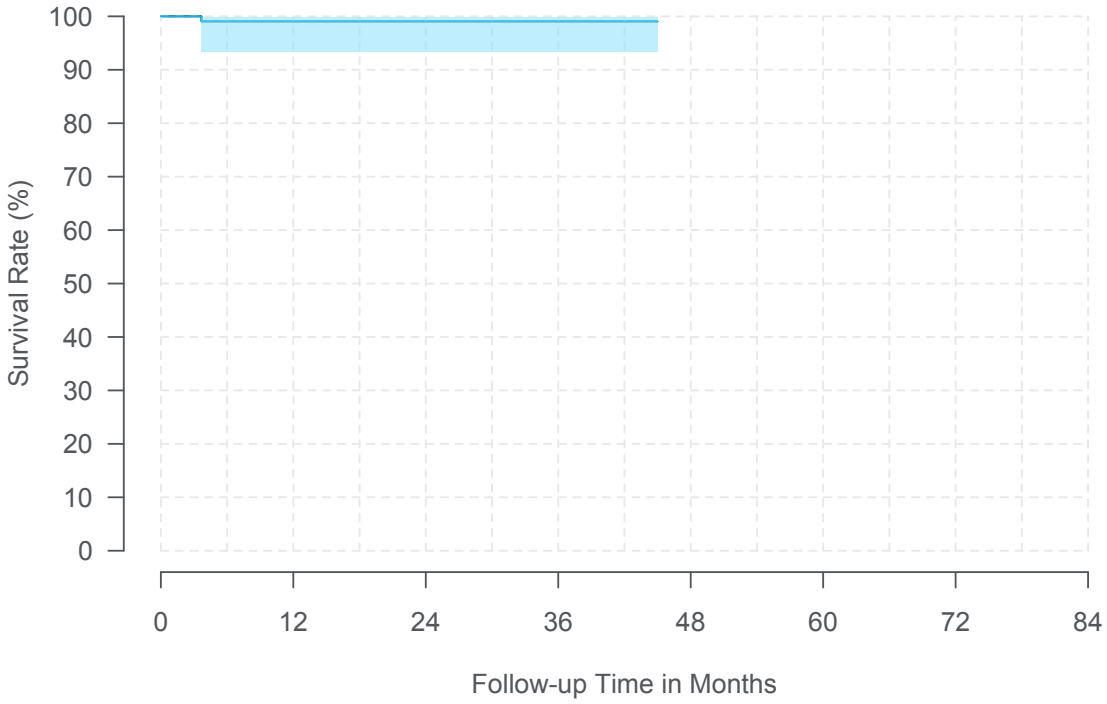
Specification: PrimeAdvanced SureScan MRI	
Height	2.6 in (65 mm)
Width	1.9 in (49 mm)
Thickness	0.6 in (15 mm)
Volume	39 cc
Battery type	Non-Rechargeable
Expected Battery life	Depends on settings and use
Maximum Electrodes	16
Amplitude	0 - 10.5 V
Rate	3 - 130 Hz
Pulse Width	60 - 450 µsec
Groups	26
Programs	32
Implant Depth	≤ 4 cm



Neurostimulator Event Summary: PrimeAdvanced SureScan MRI	N
High impedance	5
Lead migration/dislodgement	2
Device battery issue	1
Neurostimulator unable to recharge	1
Total	**9**

4.3.2.5 Model RestoreAdvanced SureScan MRI

Model Name	RestoreAdvanced SureScan MRI (model 97713)
FDA Approval Date	March 2013
Neurostimulators Enrolled	117
Neurostimulators Currently Active in Study	48
Device Events	1
Median Follow-up Time (Months)	27.5
Cumulative Follow-up Time (Months)	3,251



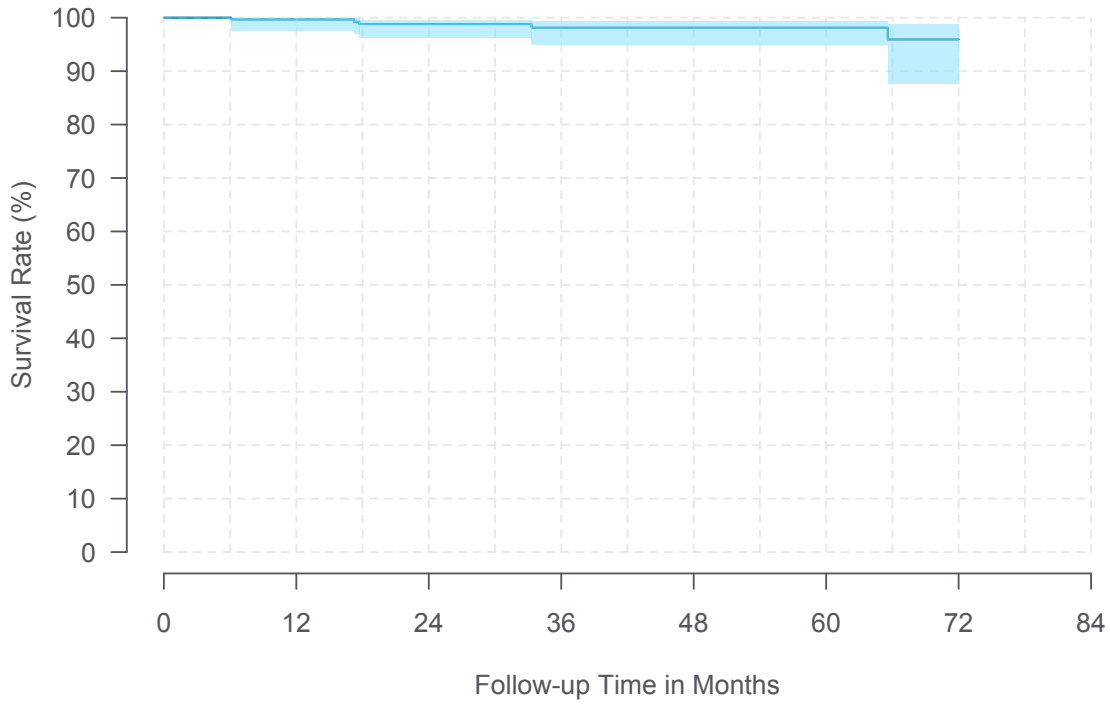
Time Interval	1 Year	2 Years	3 Years	At 45 Months
Survival (95% CI)	99.1% (93.5%, 99.9%)	99.1% (93.5%, 99.9%)	99.1% (93.5%, 99.9%)	99.1% (93.5%, 99.9%)
Sample Size	88	67	38	20

Specification: RestoreAdvanced SureScan MRI	
Height	2.6 in (65 mm)
Width	1.9 in (49 mm)
Thickness	0.6 in (15 mm)
Volume	39 cc
Battery type	Rechargeable
Expected Battery life	9 years
Maximum Electrodes	16
Amplitude	0 - 10.5 V
Rate	2 - 130 Hz
Pulse Width	60 - 450 µsec
Groups	26
Programs	32
Implant Depth	≤ 1 cm

Neurostimulator Event Summary: RestoreAdvanced SureScan MRI	N
Device malfunction	1
Total	**1**

4.3.2.6 Model RestoreSensor

Model Name	RestoreSensor (model 37714)
FDA Approval Date	November 2011
Neurostimulators Enrolled	380
Neurostimulators Currently Active in Study	56
Device Events	5
Median Follow-up Time (Months)	23.2
Cumulative Follow-up Time (Months)	11,119



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.7% (97.7%, 100%)	98.8% (96.3%, 99.6%)	98.1% (94.9%, 99.3%)	98.1% (94.9%, 99.3%)	98.1% (94.9%, 99.3%)
Sample Size	260	187	137	87	56

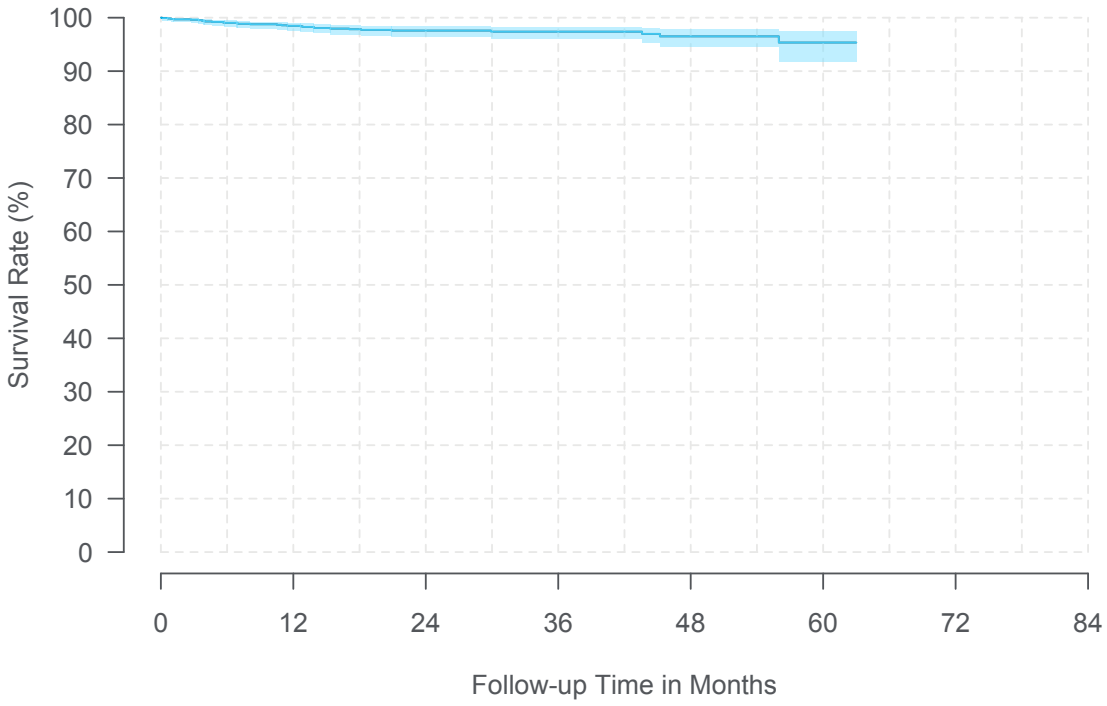
Time Interval	6 Years
Survival (95% CI)	95.9% (87.5%, 98.7%)
Sample Size	24

Specification: RestoreSensor	
Height	2.1 in (54 mm)
Width	2.1 in (54 mm)
Thickness	0.4 in (9 mm)
Volume	22 cc
Battery type	Rechargeable
Expected Battery life	9 years
Maximum Electrodes	16
Amplitude	0 - 10.5 V
Rate	2 - 1200 Hz
Pulse Width	60 - 1000 µsec
Groups	8
Programs	16
Implant Depth	≤ 1 cm

Neurostimulator Event Summary: RestoreSensor	N
Neurostimulator unable to recharge	3
Device difficult to use	1
Device malfunction	1
Total	**5**

4.3.2.7 Model RestoreSensor SureScan MRI

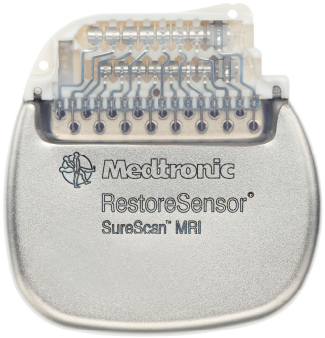
Model Name	RestoreSensor SureScan MRI (model 97714)
FDA Approval Date	March 2013
Neurostimulators Enrolled	1,371
Neurostimulators Currently Active in Study	591
Device Events	31
Median Follow-up Time (Months)	23.0
Cumulative Follow-up Time (Months)	34,462



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.5% (97.6%, 99.0%)	97.6% (96.5%, 98.4%)	97.4% (96.2%, 98.2%)	96.5% (94.5%, 97.8%)	95.3% (91.7%, 97.4%)
Sample Size	989	636	362	169	48

Time Interval	At 63 Months
Survival (95% CI)	95.3% (91.7%, 97.4%)
Sample Size	33

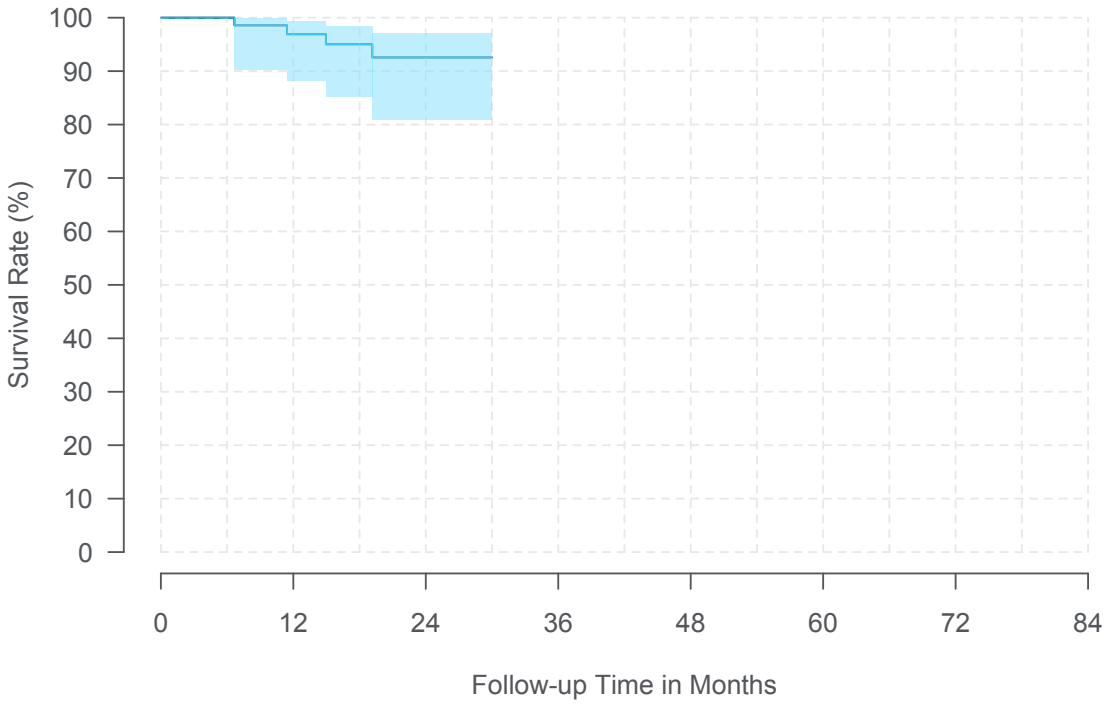
Specification: RestoreSensor SureScan MRI	
Height	54 mm (2.1 in)
Width	54 mm (2.1 in)
Thickness	9 mm (0.4 in)
Volume	22 cc
Battery type	Rechargeable
Expected Battery life	9 years
Maximum Electrodes	16
Amplitude	0 - 10.5 V
Rate	2 - 1200 Hz
Pulse Width	60 - 1000 µsec
Groups	8
Programs	16
Implant Depth	≤ 1 cm



Neurostimulator Event Summary: RestoreSensor SureScan MRI	N
Device malfunction	9
Neurostimulator unable to recharge	8
High impedance	5
Lead migration/dislodgement	3
Low impedance	2
Device telemetry issue	1
Grommet loose	1
Medical device site warmth	1
Neurostimulator migration	1
Total	**31**

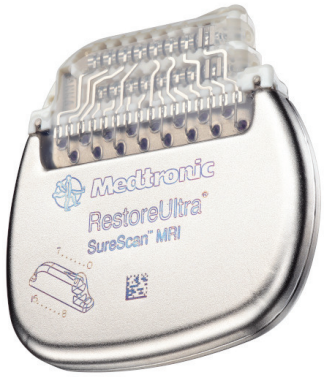
4.3.2.8 Model RestoreUltra SureScan MRI

Model Name	RestoreUltra SureScan MRI (model 97712)
FDA Approval Date	March 2013
Neurostimulators Enrolled	92
Neurostimulators Currently Active in Study	46
Device Events	4
Median Follow-up Time (Months)	17.2
Cumulative Follow-up Time (Months)	1,686



Time Interval	1 Year	2 Years	At 30 Months
Survival (95% CI)	96.9% (88.1%, 99.2%)	92.6% (80.9%, 97.2%)	92.6% (80.9%, 97.2%)
Sample Size	56	30	20

Specification: RestoreUltra SureScan MRI	
Height	2.1 in (54 mm)
Width	2.1 in (54 mm)
Thickness	0.4 in (10 mm)
Volume	22 cc
Battery type	Rechargeable
Expected Battery life	9 years
Maximum Electrodes	16
Amplitude	0 - 10.5 V
Rate	2 - 1200 Hz
Pulse Width	60 - 1000 µsec
Groups	8
Programs	16
Implant Depth	≤ 1 cm



Neurostimulator Event Summary: RestoreUltra SureScan MRI	N
Extension migration	1
Neurostimulator unable to recharge	1
No anomaly found by rpa	1
Therapeutic product ineffective	1
Total	**4**

4.3.3 Neurostimulator Summary

Table 4.10: Spinal Cord Stimulation Primary Cell Neurostimulator Characteristics

Model/Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Neurostimulator Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Itrel 4 (model 37703)	May 2012	118	61	2	23.4	3,031
PrimeAdvanced (model 37702)	July 2006	670	36	7	16.0	14,930
PrimeAdvanced SureScan MRI (model 97702)	March 2013	702	334	9	21.4	15,785

Table 4.11: Spinal Cord Stimulation Primary Cell Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Itrel 4 (model 37703)	98.9% (92.5%, 99.8%)	97.6% (90.7%, 99.4%)	97.6% (90.7%, 99.4%)		
PrimeAdvanced (model 37702)	99.6% (98.5%, 99.9%)	99.3% (97.9%, 99.8%)	98.8% (96.6%, 99.6%)	97.0% (92.3%, 98.8%)	97.0% (92.3%, 98.8%)
PrimeAdvanced SureScan MRI (model 97702)	99.3% (98.2%, 99.7%)	99.1% (97.9%, 99.6%)	97.9% (95.5%, 99.0%)	97.0% (93.7%, 98.6%)	

Model Name	6 Years				
Itrel 4 (model 37703)					
PrimeAdvanced (model 37702)	97.0% (92.3%, 98.8%)				
PrimeAdvanced SureScan MRI (model 97702)					

Table 4.12: Spinal Cord Stimulation Rechargeable Neurostimulator Characteristics

Model/Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Neurostimulator Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Intellis with AdaptiveStim	July 2017	719	646	7	4.4	4,099
RestoreAdvanced SureScan MRI (model 97713)	March 2013	117	48	1	27.5	3,251
RestoreSensor (model 37714)	November 2011	380	56	5	23.2	11,119
RestoreSensor SureScan MRI (model 97714)	March 2013	1,371	591	31	23.0	34,462
RestoreUltra SureScan MRI (model 97712)	March 2013	92	46	4	17.2	1,686

Table 4.13: Spinal Cord Stimulation Rechargeable Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Intellis with AdaptiveStim	99.0% (97.2%, 99.6%)				
RestoreAdvanced SureScan MRI (model 97713)	99.1% (93.5%, 99.9%)	99.1% (93.5%, 99.9%)	99.1% (93.5%, 99.9%)		
RestoreSensor (model 37714)	99.7% (97.7%, 100%)	98.8% (96.3%, 99.6%)	98.1% (94.9%, 99.3%)	98.1% (94.9%, 99.3%)	98.1% (94.9%, 99.3%)
RestoreSensor SureScan MRI (model 97714)	98.5% (97.6%, 99.0%)	97.6% (96.5%, 98.4%)	97.4% (96.2%, 98.2%)	96.5% (94.5%, 97.8%)	95.3% (91.7%, 97.4%)
RestoreUltra SureScan MRI (model 97712)	96.9% (88.1%, 99.2%)	92.6% (80.9%, 97.2%)			

Model Name	6 Years
Intellis with AdaptiveStim	
RestoreAdvanced SureScan MRI (model 97713)	
RestoreSensor (model 37714)	95.9% (87.5%, 98.7%)
RestoreSensor SureScan MRI (model 97714)	
RestoreUltra SureScan MRI (model 97712)	

4.4 Leads

From June 2004 to the report cut-off date of October 31, 2019, there were 10,152 leads followed in the registry. The difference between the total number of leads (n=10,152) versus the number of neurostimulators (n=6,252) is due to the fact that some patients were subsequently re-implanted with a lead or were implanted with more than one lead. The aggregate prospective follow-up time for all leads was 262,376 months (21,865 years). A lead is a set of thin wires with a protective coating and electrodes near the tip (percutaneous lead) or on a paddle (surgical lead). Table 4.14 provides the number and percentage of leads by model.

Table 4.14: Spinal Cord Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**9,214 (90.8%)**
Vectris SureScan MRI 1x8 Compact (977A2)	3,771 (37.2%)
1x8 Compact (3778)	2,167 (21.4%)
Pisces Standard (3487A)	988 (9.7%)
1x8 Standard (3777)	837 (8.2%)
Pisces Plus (3888)	453 (4.5%)
Specify 5-6-5 (39565)	291 (2.9%)
Pisces Compact (3887)	200 (2.0%)
1x8 SC (3776)	188 (1.9%)
Vectris SureScan MRI 1x8 Subcompact (977A1)	137 (1.4%)
AnkerStim Lead (Approved in Europe): 09100	67 (0.7%)
Specify SureScan MRI 5-6-5 (977C1)	54 (0.5%)
Specify 2x8 (39286)	32 (0.3%)
Specify SureScan MRI 2x8 (977C2)	29 (0.3%)
No longer manufactured	**686 (6.8%)**
Specify (3998)	157 (1.5%)
Pisces Z Standard (3890)	143 (1.4%)
Pisces Z Compact (3891)	130 (1.3%)
Resume TL (3986A)	108 (1.1%)
Resume II (3587A)	58 (0.6%)
2x4 Hinged Specify (3999)	54 (0.5%)
Pisces Z Plus (3892)	25 (0.2%)
On-Point (3987A)	9 (0.1%)
SymMix (3982A)	2 (0.0%)
Other/Unspecified	**252 (2.5%)**
Total	**10,152 (100%)**

Percutaneous leads composed 89.0% (9,039/10,152) of leads in the registry, including 38.5% (3,908/10,152) in the Vectris SureScan lead family, 31.4% (3,192/10,152) in the Pisces-Octad lead family, 16.2% (1,641/10,152) in the Pisces-Quad lead family, and 2.9% (298/10,152) in the Pisces-

Quad LZ lead family; 7.8% (794/10,152) of leads were surgical leads; and 3.1% (319/10,152) of leads were designated as "Other" or were unspecified in the database.

4.4.1 Lead Events

There were 1,262 product performance-related events with an underlying reported etiology related to lead function. This includes 1,236 events with a lead etiology and 26 events with both a lead and other etiology (including device and non-device etiologies). Of these, 1,041 were the initial product performance event that affected lead survival estimates; the majority were lead migration/dislodgement (n=585), high impedance (n=270), lead fracture (n=76), device stimulation issue (n=42), and low impedance (n=36). There were 950 events in 9,039 (10.5%) percutaneous leads, 48 events in 794 (6.0%) surgical leads, and 43 events occurred in leads with unknown/other model numbers.

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For leads:

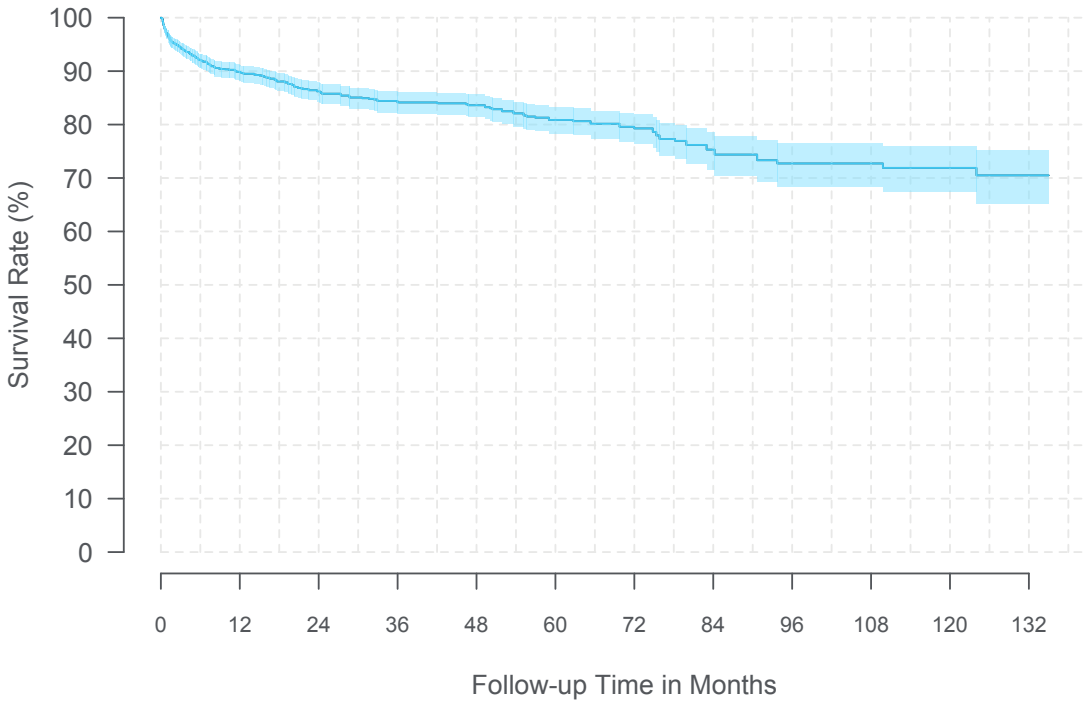
- 1,041 had follow-up time cut-off due to product performance-related events.
- 6,164 were censored in the survival analysis for the following reasons: patient expired, lead explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,947 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

4.4.2 Lead Models

The following figures and tables represent spinal cord lead survival and 95% confidence intervals where at least 20 spinal cord leads contributed to each 3-month interval.

4.4.2.1 Model 1x8 Compact

Model Name	1x8 Compact (model 3778)
FDA Approval Date	April 2005
Leads Enrolled	2,167
Leads Currently Active in Study	213
Device Events	281
Median Follow-up Time (Months)	17.7
Cumulative Follow-up Time (Months)	63,823



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	89.8% (88.2%, 91.2%)	86.2% (84.3%, 87.9%)	84.1% (82.0%, 86.0%)	83.6% (81.4%, 85.6%)	80.9% (78.3%, 83.2%)
Sample Size	1,202	793	594	453	373

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	79.3% (76.4%, 81.8%)	75.3% (71.6%, 78.6%)	72.7% (68.5%, 76.5%)	72.7% (68.5%, 76.5%)	71.9% (67.3%, 75.9%)
Sample Size	262	161	120	91	68

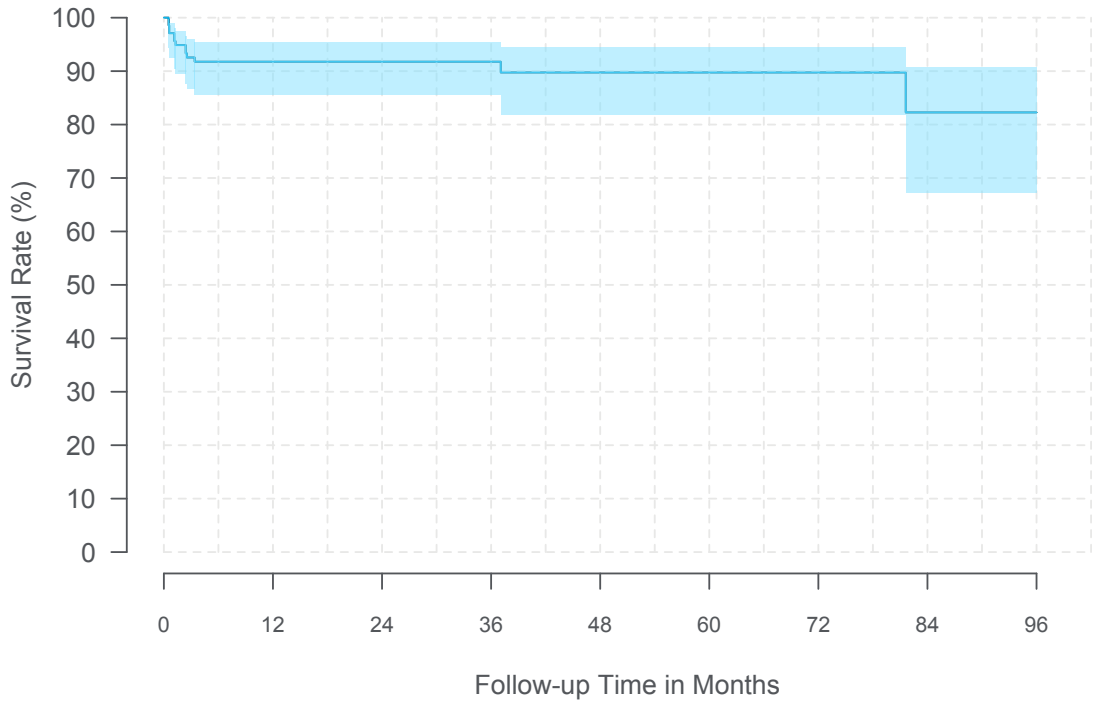
Time Interval	11 Years	At 135 Months			
Survival (95% CI)	70.5% (65.2%, 75.2%)	70.5% (65.2%, 75.2%)			
Sample Size	23	23			

Specification: 1x8 Compact	
Lead Type	Percutaneous
Lead	
Length (cm)	45, 60, 75
Diameter (mm)	1.3
Electrode	
Number	8
Shape	Cylindrical
Length (mm)	3.0
Individual Surface Area (mm^2)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	4.0
Array Length (mm)	52.0

Lead Event Summary: 1x8 Compact	N
Lead migration/dislodgement	208
High impedance	38
Lead fracture	19
Device stimulation issue	6
Medical device complication	4
Device malfunction	3
Medical device site erosion	2
Low impedance	1
Total	**281**

4.4.2.2 Model 1x8 SC

Model Name	1x8 SC (model 3776)
FDA Approval Date	November 2005
Leads Enrolled	188
Leads Currently Active in Study	28
Device Events	15
Median Follow-up Time (Months)	14.1
Cumulative Follow-up Time (Months)	4,946



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.8% (85.6%, 95.4%)	91.8% (85.6%, 95.4%)	91.8% (85.6%, 95.4%)	89.7% (81.8%, 94.3%)	89.7% (81.8%, 94.3%)
Sample Size	84	62	47	34	23

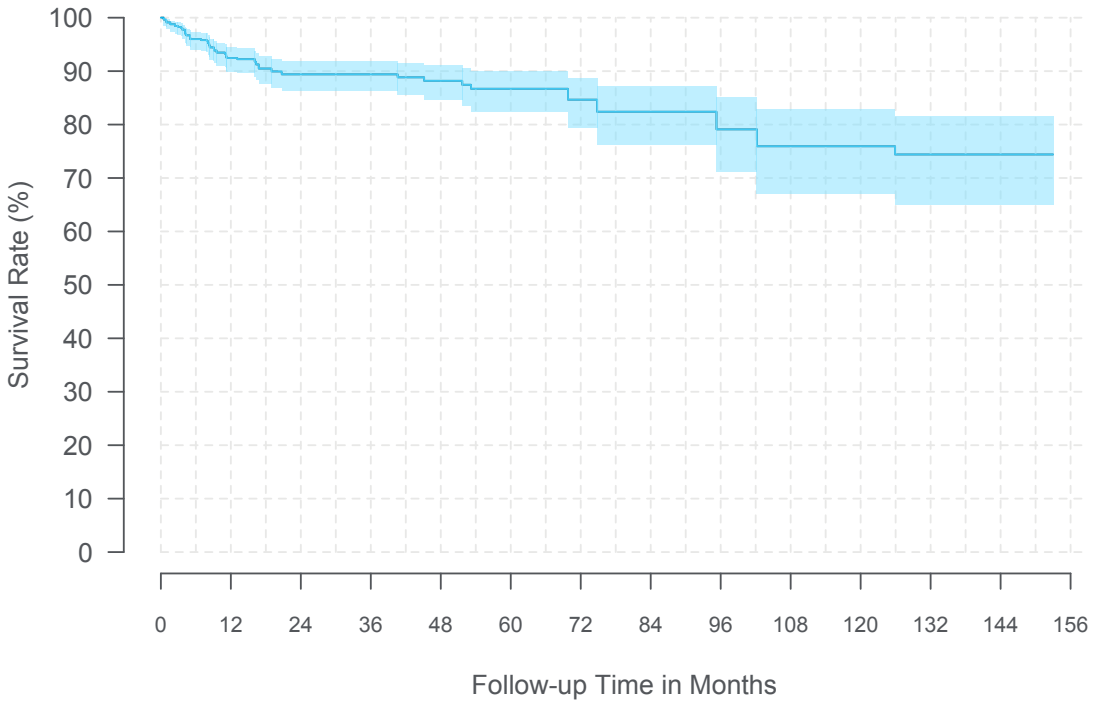
Time Interval	At 69 Months
Survival (95% CI)	89.7% (81.8%, 94.3%)
Sample Size	20

Specification: 1x8 SC	
Lead Type	Percutaneous
Lead	
Length (cm)	45, 60, 75
Diameter (mm)	1.3
Electrode	
Number	8
Shape	Cylindrical
Length (mm)	3.0
Individual Surface Area (mm^2)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	1.5
Array Length (mm)	35.0

Lead Event Summary: 1x8 SC	N
Lead migration/dislodgement	10
High impedance	3
Device stimulation issue	1
Lead fracture	1
Total	**15**

4.4.2.3 Model 1x8 Standard

Model Name	1x8 Standard (model 3777)
FDA Approval Date	April 2005
Leads Enrolled	837
Leads Currently Active in Study	92
Device Events	71
Median Follow-up Time (Months)	16.4
Cumulative Follow-up Time (Months)	22,550



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.5% (89.9%, 94.4%)	89.4% (86.3%, 91.8%)	89.4% (86.3%, 91.8%)	88.2% (84.6%, 91.0%)	86.7% (82.4%, 90.0%)
Sample Size	440	287	185	127	99

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	84.7% (79.4%, 88.7%)	82.4% (76.2%, 87.1%)	79.1% (71.2%, 85.1%)	75.9% (67.0%, 82.8%)	75.9% (67.0%, 82.8%)
Sample Size	78	57	47	61	57

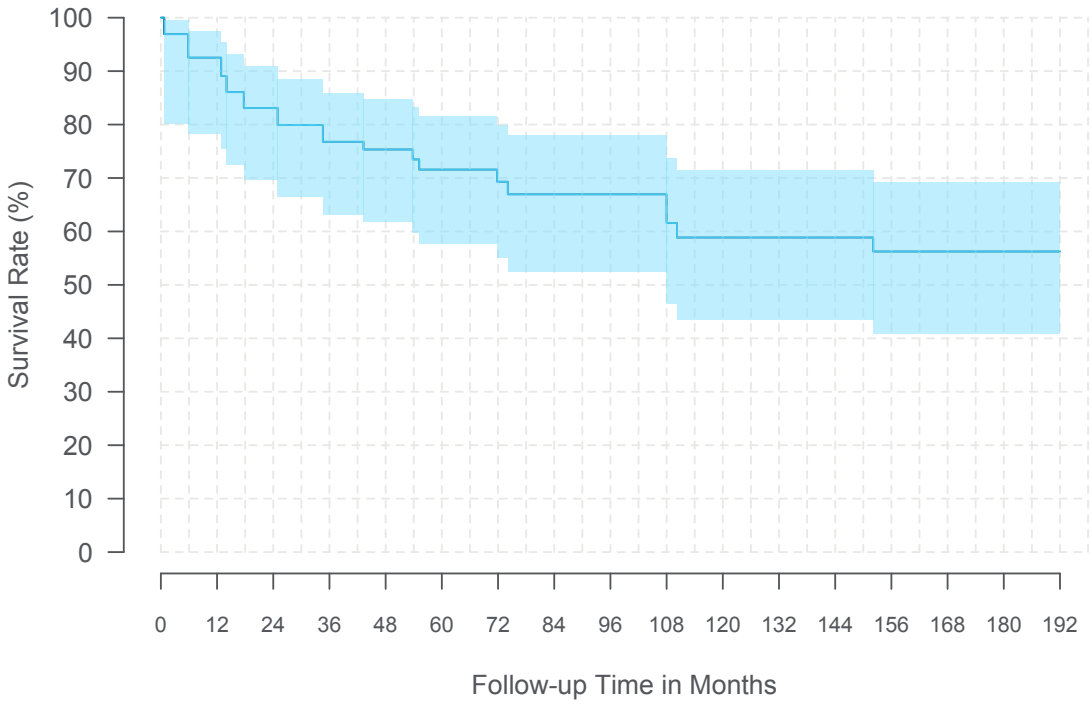
Time Interval	11 Years	12 Years	At 153 Months		
Survival (95% CI)	74.4% (65.0%, 81.6%)	74.4% (65.0%, 81.6%)	74.4% (65.0%, 81.6%)		
Sample Size	47	31	23		

Specification: 1x8 Standard	
Lead Type	Percutaneous
Lead	
Length (cm)	45, 60, 75
Diameter (mm)	1.3
Electrode	
Number	8
Shape	Cylindrical
Length (mm)	3.0
Individual Surface Area (mm^2)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	6.0
Array Length (mm)	66.0

Lead Event Summary: 1x8 Standard	N
Lead migration/dislodgement	43
High impedance	14
Device stimulation issue	7
Lead fracture	3
Device lead damage	2
Low impedance	2
Total	**71**

4.4.2.4 Model Pisces Compact

Model Name	Pisces Compact (model 3887)
FDA Approval Date	January 1997
Leads Enrolled	200
Leads Currently Active in Study	46
Device Events	24
Median Follow-up Time (Months)	19.8
Cumulative Follow-up Time (Months)	6,507



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.5% (78.3%, 97.6%)	83.1% (69.7%, 90.9%)	76.8% (63.2%, 85.9%)	75.3% (61.8%, 84.7%)	71.6% (57.7%, 81.6%)
Sample Size	51	54	49	43	37

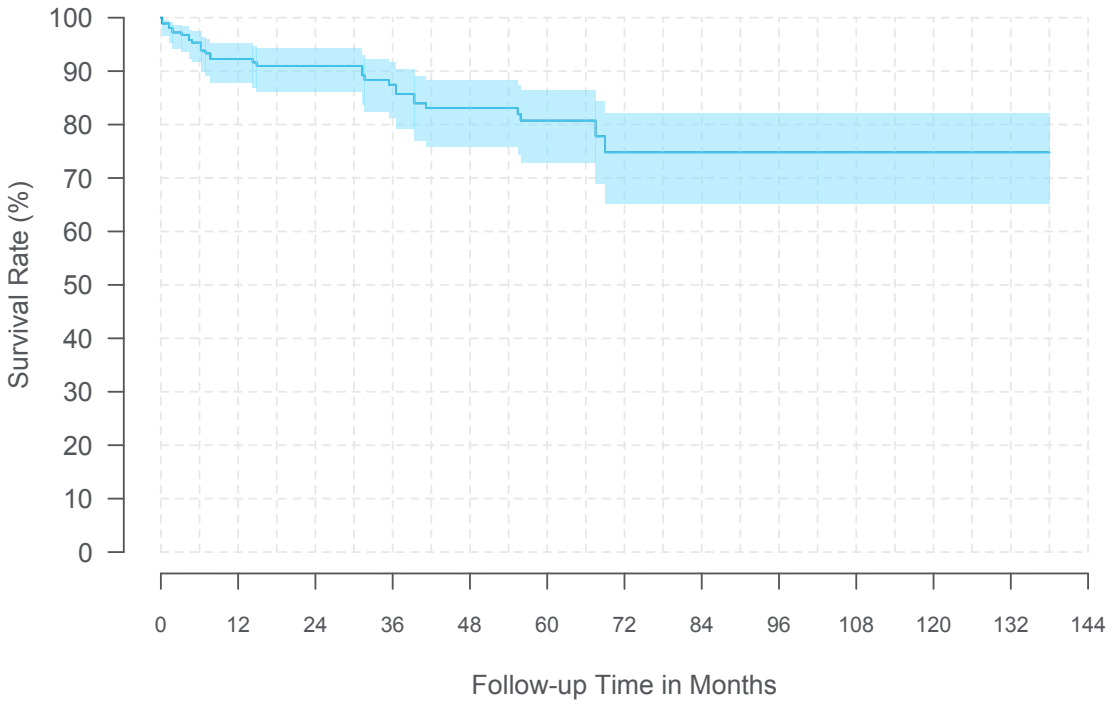
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	69.3% (55.1%, 79.8%)	67.0% (52.5%, 77.9%)	67.0% (52.5%, 77.9%)	61.6% (46.4%, 73.6%)	58.9% (43.5%, 71.4%)
Sample Size	30	25	24	22	21

Specification: Pisces Compact	
Lead Type	Percutaneous
Lead	
Length (cm)	28, 33, 45, 56
Diameter (mm)	1.3
Electrode	
Number	4
Shape	Cylindrical
Length (mm)	3.0
Individual Surface Area (mm^2)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	4.0
Array Length (mm)	24.0

Lead Event Summary: Pisces Compact	N
Lead migration/dislodgement	9
Lead fracture	8
High impedance	4
Device stimulation issue	2
Device lead damage	1
Total	**24**

4.4.2.5 Model Pisces Plus

Model Name	Pisces Plus (model 3888)
FDA Approval Date	November 1992
Leads Enrolled	453
Leads Currently Active in Study	60
Device Events	42
Median Follow-up Time (Months)	14.5
Cumulative Follow-up Time (Months)	10,825



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.3% (87.8%, 95.1%)	91.0% (86.1%, 94.2%)	87.5% (81.3%, 91.7%)	83.1% (75.9%, 88.3%)	80.7% (72.9%, 86.5%)
Sample Size	156	113	101	82	64

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)
Sample Size	42	33	31	32	29

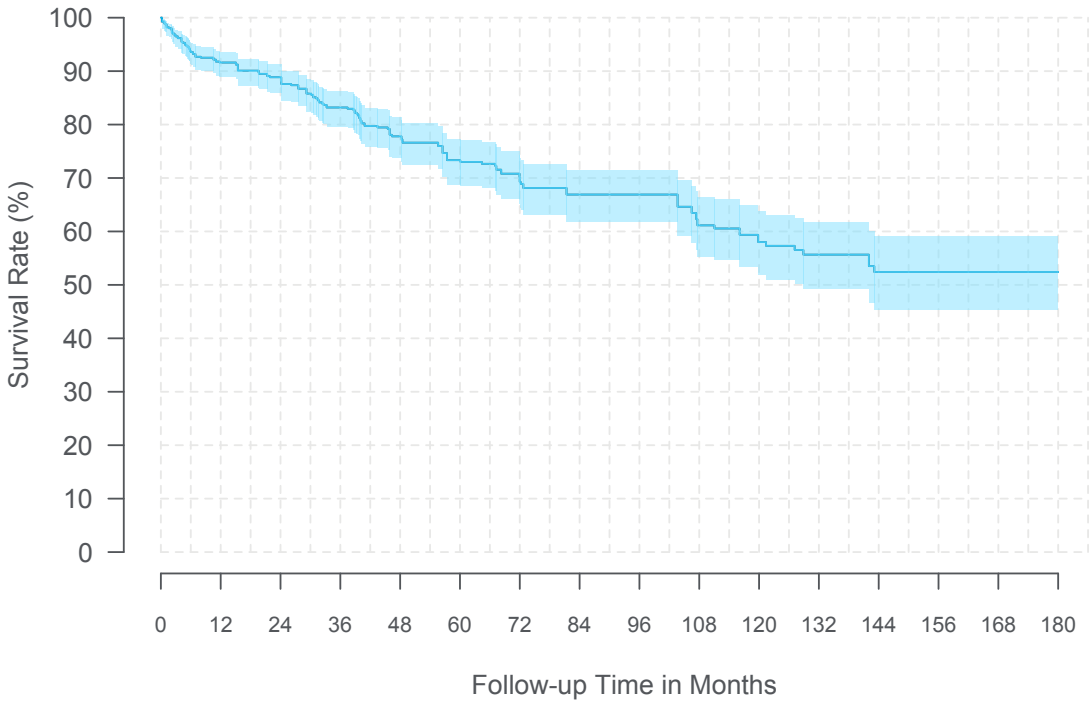
Time Interval	11 Years	At 138 Months			
Survival (95% CI)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)			
Sample Size	24	20			

Specification: Pisces Plus	
Lead Type	Percutaneous
Lead	
Length (cm)	28, 33, 45, 56
Diameter (mm)	1.3
Electrode	
Number	4
Shape	Cylindrical
Length (mm)	6.0
Individual Surface Area (mm^2)	24.0
Inter-Electrode Spacing: Edge to Edge (mm)	12.0
Array Length (mm)	60.0

Lead Event Summary: Pisces Plus	N
Lead migration/dislodgement	26
High impedance	13
Device stimulation issue	2
Lead fracture	1
Total	**42**

4.4.2.6 Model Pisces Standard

Model Name	Pisces Standard (model 3487A)
FDA Approval Date	May 1988
Leads Enrolled	988
Leads Currently Active in Study	91
Device Events	180
Median Follow-up Time (Months)	29.4
Cumulative Follow-up Time (Months)	39,751



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.6% (89.0%, 93.6%)	88.9% (85.9%, 91.2%)	83.2% (79.6%, 86.2%)	77.8% (73.7%, 81.3%)	73.3% (68.8%, 77.3%)
Sample Size	509	417	347	266	216

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	69.3% (64.4%, 73.6%)	66.9% (61.8%, 71.5%)	66.9% (61.8%, 71.5%)	61.1% (55.3%, 66.5%)	58.0% (51.8%, 63.7%)
Sample Size	181	154	121	106	85

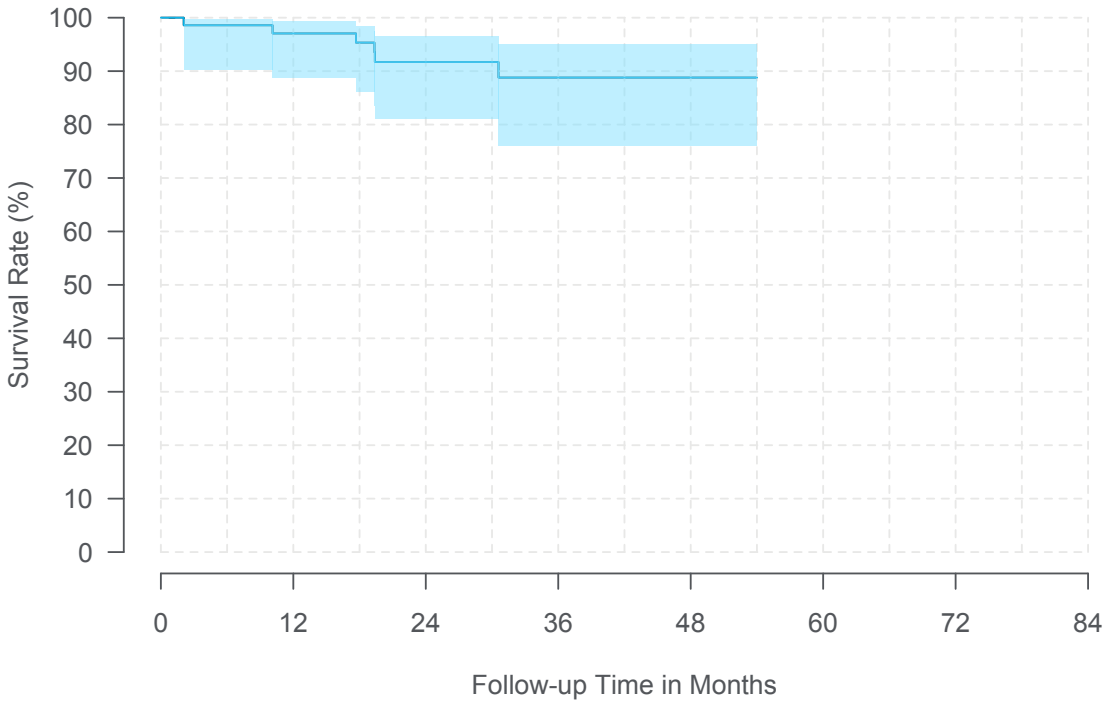
Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	55.7% (49.1%, 61.7%)	52.4% (45.3%, 59.0%)	52.4% (45.3%, 59.0%)	52.4% (45.3%, 59.0%)	52.4% (45.3%, 59.0%)
Sample Size	59	48	43	28	21

Specification: Pisces Standard	
Lead Type	Percutaneous
Lead	
Length (cm)	28, 33, 45, 56
Diameter (mm)	1.3
Electrode	
Number	4
Shape	Cylindrical
Length (mm)	3.0
Individual Surface Area (mm)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	6.0
Array Length (mm)	30.0

Lead Event Summary: Pisces Standard	N
High impedance	80
Lead migration/dislodgement	49
Low impedance	23
Device stimulation issue	17
Lead fracture	8
Inadequate lead connection	2
Device lead damage	1
Total	**180**

4.4.2.7 Model Specify

Model Name	Specify (model 3998)
FDA Approval Date	February 1998
Leads Enrolled	157
Leads Currently Active in Study	23
Device Events	10
Median Follow-up Time (Months)	19.3
Cumulative Follow-up Time (Months)	4,141



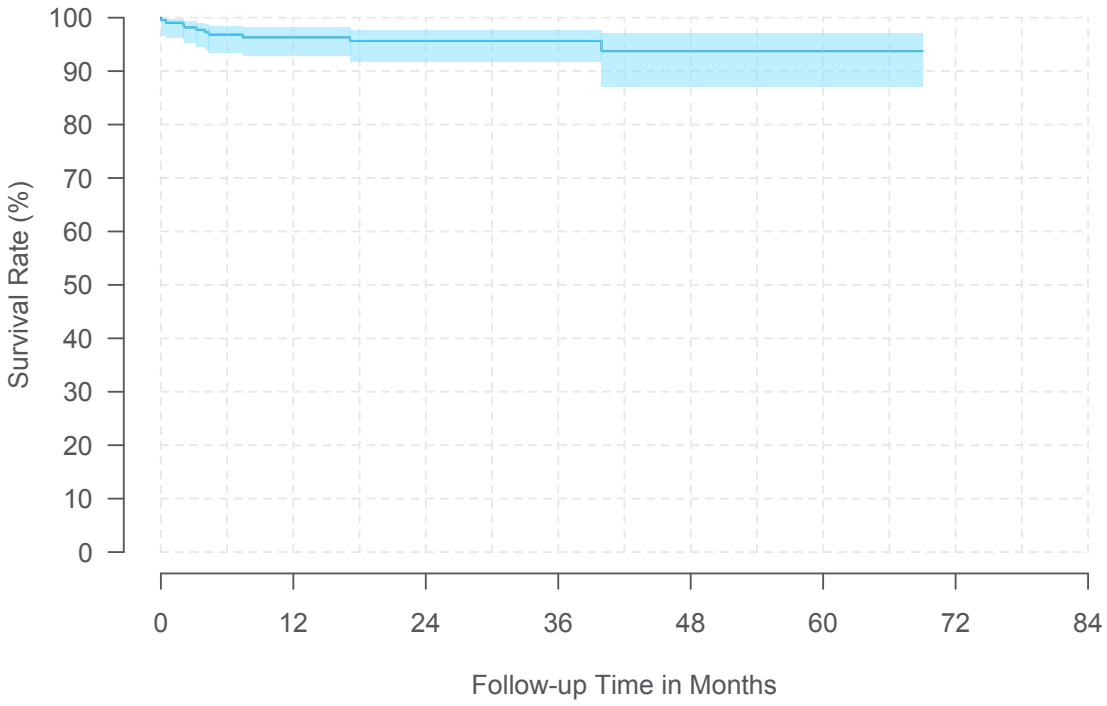
Time Interval	1 Year	2 Years	3 Years
Survival (95% CI)	97.1% (88.7%, 99.3%)	91.7% (81.1%, 96.5%)	88.8% (76.0%, 95.0%)
Sample Size	60	41	22

Specification: Specify	
Lead Type	Surgical
Lead	
Length (cm)	20
Diameter (mm)	1.3
Electrode	
Number	8
Shape	Rectangular
Length (mm)	3.0
Width (mm)	2.0
Individual Surface Area (mm^2)	6.0
Longitudinal Spacing: Edge to Edge (mm)	6.0
Lateral Spacing: Edge to Edge (mm)	2.0
Array Length (mm)	30.0
Array Width (mm)	6.0
Paddle	
Length (mm)	45.0
Width (mm)	7.9
Thickness (mm)	1.8

Lead Event Summary: Specify	N
High impedance	4
Lead fracture	3
Lead migration/dislodgement	2
Device stimulation issue	1
Total	**10**

4.4.2.8 Model Specify 5-6-5

Model Name	Specify 5-6-5 (model 39565)
FDA Approval Date	June 2007
Leads Enrolled	291
Leads Currently Active in Study	40
Device Events	12
Median Follow-up Time (Months)	20.0
Cumulative Follow-up Time (Months)	7,188



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	96.3% (92.8%, 98.1%)	95.7% (91.8%, 97.7%)	95.7% (91.8%, 97.7%)	93.7% (87.0%, 97.0%)	93.7% (87.0%, 97.0%)
Sample Size	162	113	64	38	24

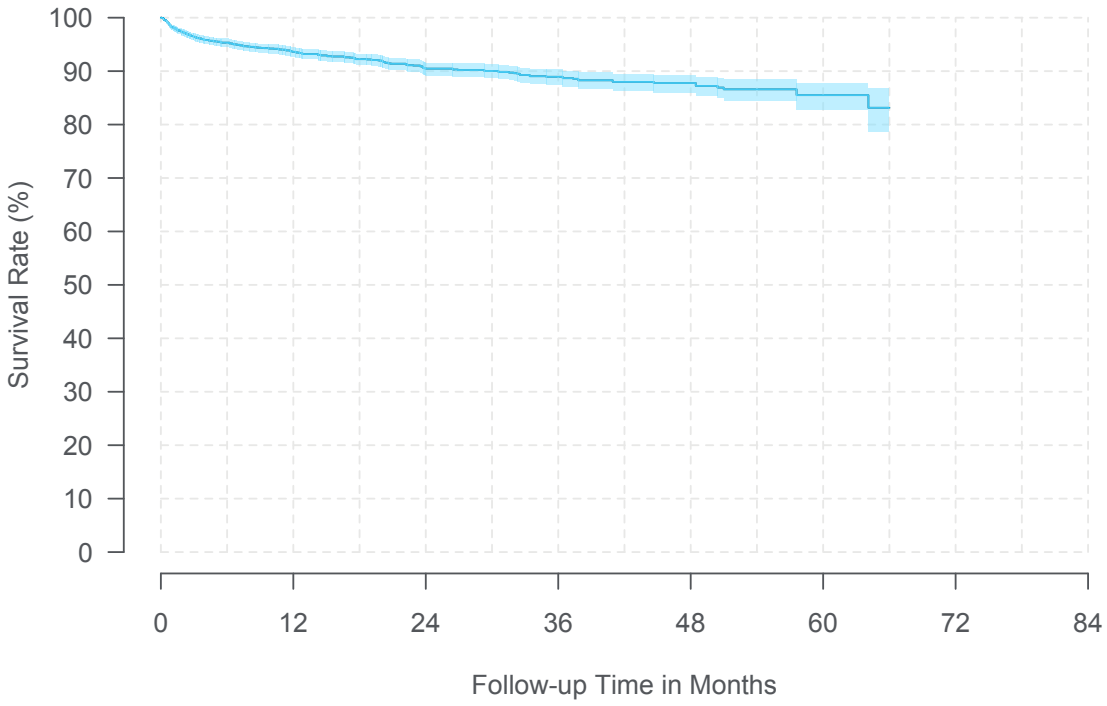
Time Interval	At 69 Months
Survival (95% CI)	93.7% (87.0%, 97.0%)
Sample Size	21

Specification: Specify 5-6-5	
Lead Type	Surgical
Lead	
Length (cm)	30, 65
Diameter (mm)	1.3
Electrode	
Number	16
Shape	Rectangular
Length (mm)	4.0
Width (mm)	1.5
Individual Surface Area (mm^2)	6.0
Longitudinal Spacing: Edge to Edge (mm)	4.5
Lateral Spacing: Edge to Edge (mm)	1.0
Array Length (mm)	49.0
Array Width (mm)	7.5
Paddle	
Length (mm)	64.2
Width (mm)	10.0
Thickness (mm)	7.5

Lead Event Summary: Specify 5-6-5	N
Lead migration/dislodgement	9
High impedance	1
Lead fracture	1
Lead insulation failure	1
Total	**12**

4.4.2.9 Model Vectris SureScan MRI 1x8 Compact

Model Name	Vectris SureScan MRI 1x8 Compact (model 977A2)
FDA Approval Date	March 2013
Leads Enrolled	3,771
Leads Currently Active in Study	2,163
Device Events	284
Median Follow-up Time (Months)	15.4
Cumulative Follow-up Time (Months)	75,253



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.6% (92.6%, 94.4%)	90.5% (89.2%, 91.6%)	88.9% (87.4%, 90.3%)	87.8% (86.1%, 89.3%)	85.5% (82.9%, 87.8%)
Sample Size	2,079	1,224	723	327	121

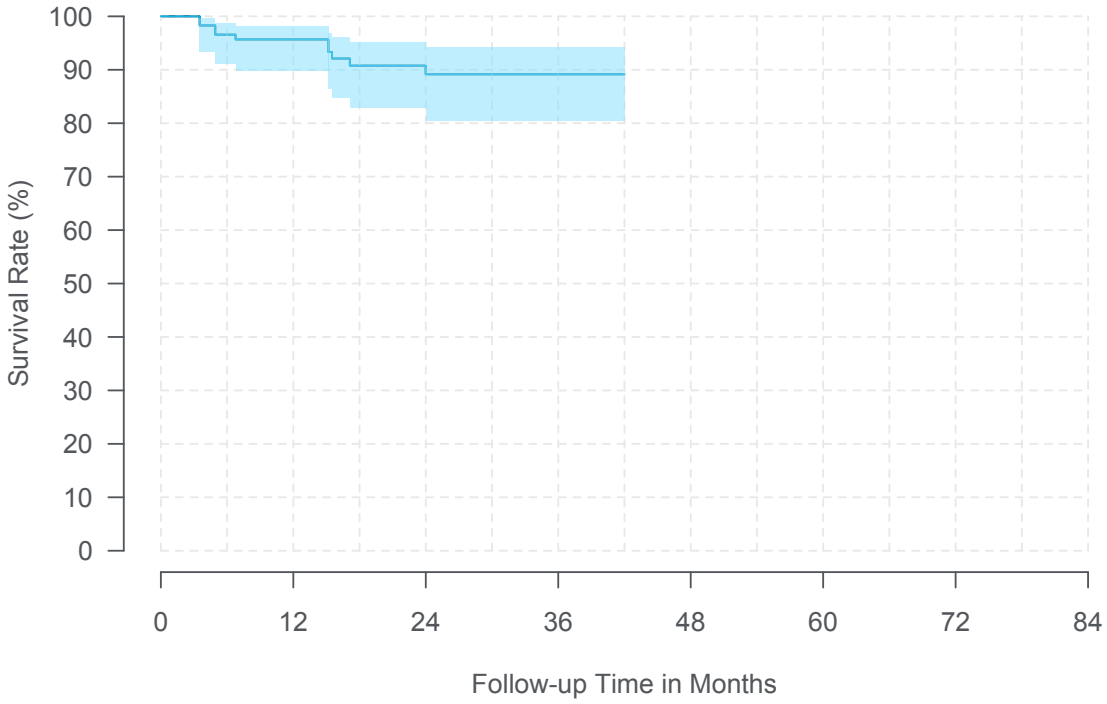
Time Interval	At 66 Months
Survival (95% CI)	83.1% (78.7%, 86.8%)
Sample Size	46

Specification: Vectris SureScan MRI 1x8 Compact	
Lead Type	Percutaneous
Lead	
Length (cm)	60, 75, 90
Diameter (mm)	1.3
Electrode	
Number	8
Shape	Cylindrical
Length (mm)	3.0
Individual Surface Area (mm)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	4.0
Array Length (mm)	52.0

Lead Event Summary: Vectris SureScan MRI 1x8 Compact	N
Lead migration/dislodgement	192
High impedance	61
Lead fracture	18
Device electrical impedance issue	6
Low impedance	3
Device difficult to use	2
Device malfunction	2
Total	**284**

4.4.2.10 Model Vectris SureScan MRI 1x8 Subcompact

Model Name	Vectris SureScan MRI 1x8 Subcompact (model 977A1)
FDA Approval Date	March 2013
Leads Enrolled	137
Leads Currently Active in Study	48
Device Events	10
Median Follow-up Time (Months)	17.9
Cumulative Follow-up Time (Months)	3,076



Time Interval	1 Year	2 Years	3 Years	At 42 Months
Survival (95% CI)	95.7% (89.9%, 98.2%)	89.1% (80.4%, 94.1%)	89.1% (80.4%, 94.1%)	89.1% (80.4%, 94.1%)
Sample Size	82	54	29	20

Specification: Vectris SureScan MRI 1x8 Subcompact	
Lead Type	Percutaneous
Lead	
Length (cm)	60, 75, 90
Diameter (mm)	1.3
Electrode	
Number	8
Shape	Cylindrical
Length (mm)	3.0
Individual Surface Area (mm)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	1.5
Array Length (mm)	34.5

Lead Event Summary: Vectris SureScan MRI 1x8 Subcompact	N
Lead migration/dislodgement	7
Lead fracture	2
High impedance	1
Total	**10**

4.4.3 Lead Summary

Table 4.15: Spinal Cord Stimulation Percutaneous Lead Characteristics

Model/Name	FDA Approval Date	Leads Enrolled	Leads Active	Lead Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
1x8 Compact (model 3778)	April 2005	2,167	213	281	17.7	63,823
1x8 SC (model 3776)	November 2005	188	28	15	14.1	4,946
1x8 Standard (model 3777)	April 2005	837	92	71	16.4	22,550
Pisces Compact (model 3887)	January 1997	200	46	24	19.8	6,507
Pisces Plus (model 3888)	November 1992	453	60	42	14.5	10,825
Pisces Standard (model 3487A)	May 1988	988	91	180	29.4	39,751
Vectris SureScan MRI 1x8 Compact (model 977A2)	March 2013	3,771	2,163	284	15.4	75,253
Vectris SureScan MRI 1x8 Subcompact (model 977A1)	March 2013	137	48	10	17.9	3,076

Table 4.16: Spinal Cord Stimulation Percutaneous Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
1x8 Compact (model 3778)	89.8% (88.2%, 91.2%)	86.2% (84.3%, 87.9%)	84.1% (82.0%, 86.0%)	83.6% (81.4%, 85.6%)	80.9% (78.3%, 83.2%)
1x8 SC (model 3776)	91.8% (85.6%, 95.4%)	91.8% (85.6%, 95.4%)	91.8% (85.6%, 95.4%)	89.7% (81.8%, 94.3%)	89.7% (81.8%, 94.3%)
1x8 Standard (model 3777)	92.5% (89.9%, 94.4%)	89.4% (86.3%, 91.8%)	89.4% (86.3%, 91.8%)	88.2% (84.6%, 91.0%)	86.7% (82.4%, 90.0%)
Pisces Compact (model 3887)	92.5% (78.3%, 97.6%)	83.1% (69.7%, 90.9%)	76.8% (63.2%, 85.9%)	75.3% (61.8%, 84.7%)	71.6% (57.7%, 81.6%)
Pisces Plus (model 3888)	92.3% (87.8%, 95.1%)	91.0% (86.1%, 94.2%)	87.5% (81.3%, 91.7%)	83.1% (75.9%, 88.3%)	80.7% (72.9%, 86.5%)
Pisces Standard (model 3487A)	91.6% (89.0%, 93.6%)	88.9% (85.9%, 91.2%)	83.2% (79.6%, 86.2%)	77.8% (73.7%, 81.3%)	73.3% (68.8%, 77.3%)
Vectris SureScan MRI 1x8 Compact (model 977A2)	93.6% (92.6%, 94.4%)	90.5% (89.2%, 91.6%)	88.9% (87.4%, 90.3%)	87.8% (86.1%, 89.3%)	85.5% (82.9%, 87.8%)
Vectris SureScan MRI 1x8 Subcompact (model 977A1)	95.7% (89.9%, 98.2%)	89.1% (80.4%, 94.1%)	89.1% (80.4%, 94.1%)		

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
1x8 Compact (model 3778)	79.3% (76.4%, 81.8%)	75.3% (71.6%, 78.6%)	72.7% (68.5%, 76.5%)	72.7% (68.5%, 76.5%)	71.9% (67.3%, 75.9%)
1x8 SC (model 3776)					
1x8 Standard (model 3777)	84.7% (79.4%, 88.7%)	82.4% (76.2%, 87.1%)	79.1% (71.2%, 85.1%)	75.9% (67.0%, 82.8%)	75.9% (67.0%, 82.8%)
Pisces Compact (model 3887)	69.3% (55.1%, 79.8%)	67.0% (52.5%, 77.9%)	67.0% (52.5%, 77.9%)	61.6% (46.4%, 73.6%)	58.9% (43.5%, 71.4%)
Pisces Plus (model 3888)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)	74.8% (65.3%, 82.1%)
Pisces Standard (model 3487A)	69.3% (64.4%, 73.6%)	66.9% (61.8%, 71.5%)	66.9% (61.8%, 71.5%)	61.1% (55.3%, 66.5%)	58.0% (51.8%, 63.7%)
Vectris SureScan MRI 1x8 Compact (model 977A2)					
Vectris SureScan MRI 1x8 Subcompact (model 977A1)					

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
1x8 Compact (model 3778)	70.5% (65.2%, 75.2%)				
1x8 SC (model 3776)					
1x8 Standard (model 3777)	74.4% (65.0%, 81.6%)	74.4% (65.0%, 81.6%)			
Pisces Compact (model 3887)					
Pisces Plus (model 3888)	74.8% (65.3%, 82.1%)				
Pisces Standard (model 3487A)	55.7% (49.1%, 61.7%)	52.4% (45.3%, 59.0%)	52.4% (45.3%, 59.0%)	52.4% (45.3%, 59.0%)	52.4% (45.3%, 59.0%)
Vectris SureScan MRI 1x8 Compact (model 977A2)					
Vectris SureScan MRI 1x8 Subcompact (model 977A1)					

Model Name					
1x8 Compact (model 3778)					
1x8 SC (model 3776)					
1x8 Standard (model 3777)					
Pisces Compact (model 3887)					
Pisces Plus (model 3888)					
Pisces Standard (model 3487A)					
Vectris SureScan MRI 1x8 Compact (model 977A2)					
Vectris SureScan MRI 1x8 Subcompact (model 977A1)					

Table 4.17: Spinal Cord Stimulation Surgical Lead Characteristics

Model/Name	FDA Approval Date	Leads Enrolled	Leads Active	Lead Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Specify (model 3998)	February 1998	157	23	10	19.3	4,141
Specify 5-6-5 (model 39565)	June 2007	291	40	12	20.0	7,188

Table 4.18: Spinal Cord Stimulation Surgical Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Specify (model 3998)	97.1%	91.7%	88.8%		
	(88.7%, 99.3%)	(81.1%, 96.5%)	(76.0%, 95.0%)		
Specify 5-6-5 (model 39565)	96.3%	95.7%	95.7%	93.7%	93.7%
	(92.8%, 98.1%)	(91.8%, 97.7%)	(91.8%, 97.7%)	(87.0%, 97.0%)	(87.0%, 97.0%)

4.5 Extensions

From June 2004 to the report cut-off date of October 31, 2019, there were 3,520 extensions followed in the registry. The difference between the total number of extensions (n=3,520) versus neurostimulators (n=6,252) is due to the fact that some systems did not use an extension. The aggregate prospective follow-up time for all extensions was 103,138 months (8,595 years). An extension is a set of thin wires with a protective coating that connects the neurostimulator to the lead. Table 4.19 provides the number and percentage of extensions by model.

Table 4.19: Spinal Cord Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**2,419 (68.7%)**
1x8 (37081)	1,500 (42.7%)
Bifurcated Stretch-Coil (37082)	642 (18.3%)
Single Stretch-Coil (37083)	277 (7.9%)
No longer manufactured	**1,081 (30.7%)**
Low Profile Quad (7489)	758 (21.6%)
Quadripolar in-line (7495)	279 (7.9%)
Synergy bifurcated 1x8 (7472)	26 (0.7%)
Quadripolar (7496)	9 (0.3%)
Synergy 1x8 (7471)	9 (0.3%)
Other/Unspecified	**20 (0.6%)**
Total	**3,520 (100%)**

4.5.1 Extension Events

There were 48 product performance-related events with an underlying reported etiology related to extension function. This includes 38 events with an extension etiology and 10 events with both an extension and other etiology (including device and non-device etiologies). Of these, 39 were the initial product performance event that affected extension survival estimates; the majority were extension fracture (n=17) and high impedance (n=11).

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For extensions:

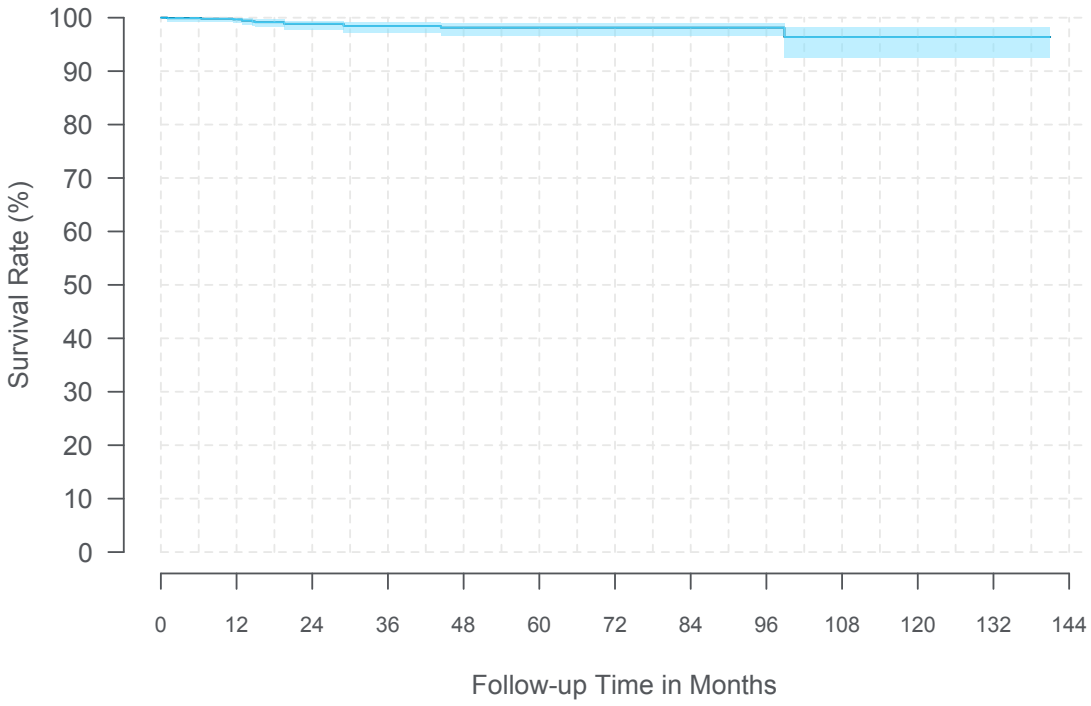
- 39 had follow-up time cut-off due to product performance-related events.
- 2,816 were censored in the survival analysis for the following reasons: patient expired, extension explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 665 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

4.5.2 Extension Models

The following figures and tables represent spinal cord extension survival and 95% confidence intervals where at least 20 spinal cord extensions contributed to each 3-month interval.

4.5.2.1 Model 1x8 Extension

Model Name	1x8 Extension (model 37081)
FDA Approval Date	April 2005
Extensions Enrolled	1,500
Extensions Currently Active in Study	393
Device Events	17
Median Follow-up Time (Months)	19.3
Cumulative Follow-up Time (Months)	42,337



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.7% (99.0%, 99.9%)	98.8% (97.8%, 99.4%)	98.4% (97.2%, 99.1%)	98.1% (96.6%, 99.0%)	98.1% (96.6%, 99.0%)
Sample Size	821	534	371	294	248

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	98.1% (96.6%, 99.0%)	98.1% (96.6%, 99.0%)	98.1% (96.6%, 99.0%)	96.4% (92.5%, 98.3%)	96.4% (92.5%, 98.3%)
Sample Size	192	145	124	90	77

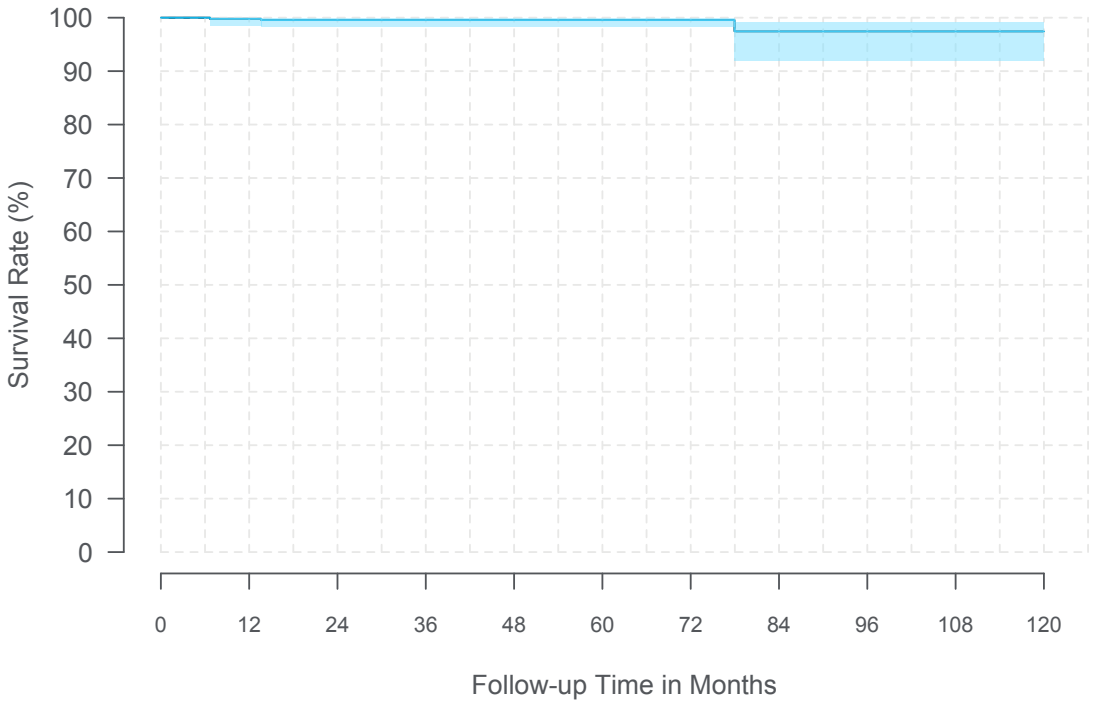
Time Interval	11 Years	At 141 Months			
Survival (95% CI)	96.4% (92.5%, 98.3%)	96.4% (92.5%, 98.3%)			
Sample Size	49	23			

Specification: 1x8 Extension	
Length (cm)	20, 40, 60
Distal End Compatibility	1 Octad Lead
Distal End Set Screws	1
Proximal End INS Compatibility	Restore Family

Extension Event Summary: 1x8 Extension	N
Extension fracture	7
High impedance	7
Extension migration	2
Low impedance	1
Total	**17**

4.5.2.2 Model Bifurcated Stretch-Coil Extension

Model Name	Bifurcated Stretch-Coil Extension (model 37082)
FDA Approval Date	March 2006
Extensions Enrolled	642
Extensions Currently Active in Study	55
Device Events	4
Median Follow-up Time (Months)	23.0
Cumulative Follow-up Time (Months)	21,794



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.8% (98.5%, 100%)	99.6% (98.2%, 99.9%)	99.6% (98.2%, 99.9%)	99.6% (98.2%, 99.9%)	99.6% (98.2%, 99.9%)
Sample Size	428	304	212	159	128

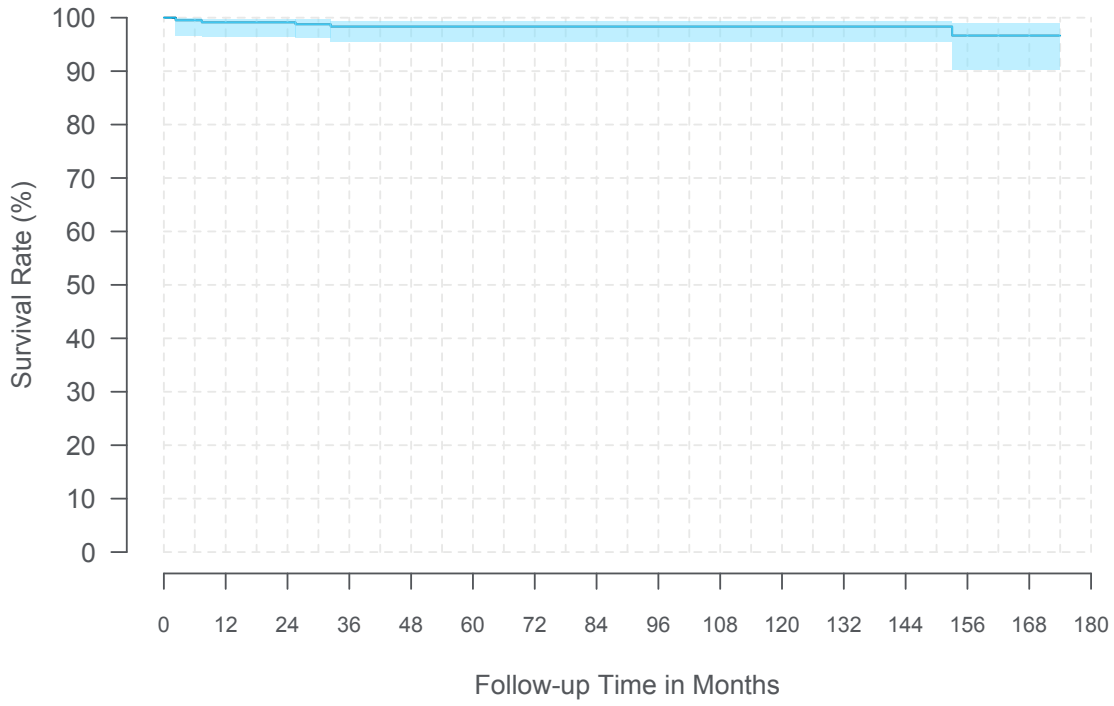
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	99.6% (98.2%, 99.9%)	97.4% (92.0%, 99.2%)	97.4% (92.0%, 99.2%)	97.4% (92.0%, 99.2%)	97.4% (92.0%, 99.2%)
Sample Size	103	82	59	46	28

Specification: Bifurcated Stretch-Coil Extension	
Length (cm)	20, 40, 60
Distal End Compatibility	2 Quad Leads
Distal End Set Screws	8 (4 per Lead)
Proximal End INS Compatibility	Restore Family

Extension Event Summary: Bifurcated Stretch-Coil Extension	N
Device connection issue	2
Extension fracture	2
Total	**4**

4.5.2.3 Model Low Profile Quad Extension

Model Name	Low Profile Quad Extension (model 7489)
FDA Approval Date	October 2002
Extensions Enrolled	758
Extensions Currently Active in Study	71
Device Events	5
Median Follow-up Time (Months)	17.2
Cumulative Follow-up Time (Months)	20,675

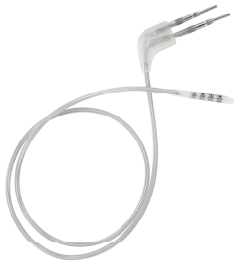


Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.1% (96.5%, 99.8%)	99.1% (96.5%, 99.8%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)
Sample Size	294	290	205	138	104

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)
Sample Size	84	68	67	67	70

Time Interval	11 Years	12 Years	13 Years	14 Years	At 174 Months
Survival (95% CI)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	96.7% (90.2%, 98.9%)	96.7% (90.2%, 98.9%)	96.7% (90.2%, 98.9%)
Sample Size	70	71	55	40	31

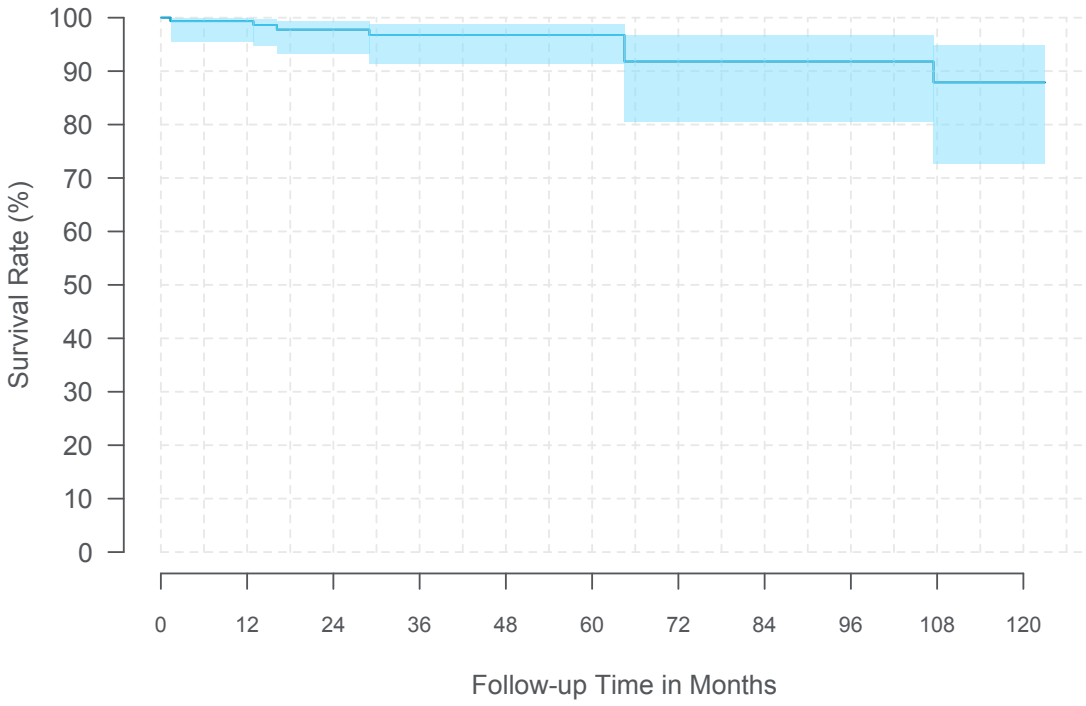
Specification: Low Profile Quad Extension	
Length (cm)	10, 25, 40, 51, 66
Distal End Compatibility	1 Quad Lead
Distal End Set Screws	4
Proximal End INS Compatibility	Itrel 3, Synergy, Versitrel



Extension Event Summary: Low Profile Quad Extension	N
Extension fracture	2
Extension migration	2
Medical device complication	1
Total	**5**

4.5.2.4 Model Single Stretch-Coil Extension

Model Name	Single Stretch-Coil Extension (model 37083)
FDA Approval Date	September 2005
Extensions Enrolled	277
Extensions Currently Active in Study	79
Device Events	8
Median Follow-up Time (Months)	14.8
Cumulative Follow-up Time (Months)	7,622



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.4% (95.5%, 99.9%)	97.8% (93.2%, 99.3%)	96.8% (91.5%, 98.8%)	96.8% (91.5%, 98.8%)	96.8% (91.5%, 98.8%)
Sample Size	138	112	71	58	38

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	91.8% (80.4%, 96.7%)	91.8% (80.4%, 96.7%)	91.8% (80.4%, 96.7%)	87.9% (72.7%, 94.9%)	87.9% (72.7%, 94.9%)
Sample Size	30	30	27	22	22

Time Interval	At 123 Months
Survival (95% CI)	87.9% (72.7%, 94.9%)
Sample Size	21

Specification: Single Stretch-Coil Extension	
Length (cm)	20, 40, 60
Distal End Compatibility	1 Quad Lead
Distal End Set Screws	4
Proximal End INS Compatibility	Restore Family

Extension Event Summary: Single Stretch-Coil Extension	N
Extension fracture	5
Extension migration	2
Device failure	1
Total	**8**

4.5.3 Extension Summary

Table 4.20: Spinal Cord Stimulation Extension Characteristics

Model/Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Extension Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
1x8 Extension (model 37081)	April 2005	1,500	393	17	19.3	42,337
Bifurcated Stretch-Coil Extension (model 37082)	March 2006	642	55	4	23	21,794
Low Profile Quad Extension (model 7489)	October 2002	758	71	5	17.2	20,675
Single Stretch-Coil Extension (model 37083)	September 2005	277	79	8	14.8	7,622

Table 4.21: Spinal Cord Stimulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
1x8 Extension (model 37081)	99.7% (99.0%, 99.9%)	98.8% (97.8%, 99.4%)	98.4% (97.2%, 99.1%)	98.1% (96.6%, 99.0%)	98.1% (96.6%, 99.0%)
Bifurcated Stretch-Coil Extension (model 37082)	99.8% (98.5%, 100%)	99.6% (98.2%, 99.9%)	99.6% (98.2%, 99.9%)	99.6% (98.2%, 99.9%)	99.6% (98.2%, 99.9%)
Low Profile Quad Extension (model 7489)	99.1% (96.5%, 99.8%)	99.1% (96.5%, 99.8%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)
Single Stretch-Coil Extension (model 37083)	99.4% (95.5%, 99.9%)	97.8% (93.2%, 99.3%)	96.8% (91.5%, 98.8%)	96.8% (91.5%, 98.8%)	96.8% (91.5%, 98.8%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
1x8 Extension (model 37081)	98.1% (96.6%, 99.0%)	98.1% (96.6%, 99.0%)	98.1% (96.6%, 99.0%)	96.4% (92.5%, 98.3%)	96.4% (92.5%, 98.3%)
Bifurcated Stretch-Coil Extension (model 37082)	99.6% (98.2%, 99.9%)	97.4% (92.0%, 99.2%)	97.4% (92.0%, 99.2%)	97.4% (92.0%, 99.2%)	97.4% (92.0%, 99.2%)
Low Profile Quad Extension (model 7489)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)
Single Stretch-Coil Extension (model 37083)	91.8% (80.4%, 96.7%)	91.8% (80.4%, 96.7%)	91.8% (80.4%, 96.7%)	87.9% (72.7%, 94.9%)	87.9% (72.7%, 94.9%)

Model Name	11 Years	12 Years	13 Years	14 Years	
1x8 Extension (model 37081)	96.4% (92.5%, 98.3%)				
Bifurcated Stretch-Coil Extension (model 37082)					
Low Profile Quad Extension (model 7489)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	96.7% (90.2%, 98.9%)	96.7% (90.2%, 98.9%)	
Single Stretch-Coil Extension (model 37083)					

5 Deep Brain Stimulation Systems

5.1 Study Participants

5.1.1 Centers

In this section, the deep brain stimulation tables and graphs were generated based on data collected between July 2009 and the report cut-off date of October 31, 2019. Forty-three centers in North America, Europe, South America, and Asia have enrolled and contributed patients to the deep brain stimulation systems section of this report. Figure 5.1 shows a World Map, in which the countries that enrolled DBS patients are highlighted.

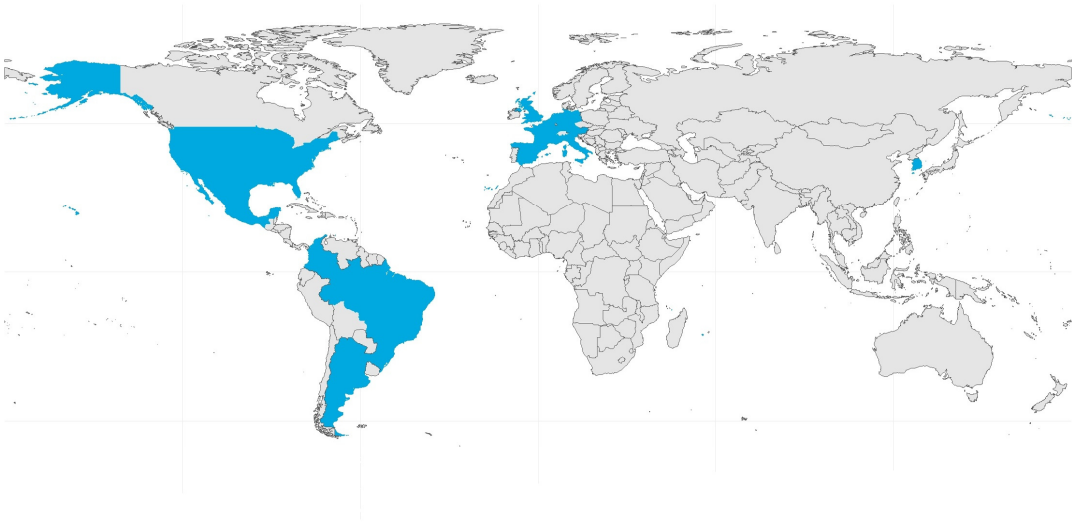


Figure 5.1: Countries with Deep Brain Stimulation Therapy Patients in Registry (Highlighted)

5.1.2 Patients

Of the 2,637 deep brain stimulation patients enrolled, the primary indications for implant were as follows: 62.1% were implanted for the treatment of Parkinson's Disease, 24.2% were implanted for the treatment of essential tremor, 8.8% were implanted for the treatment of dystonia, 1.2% were implanted for the treatment of obsessive compulsive disorder, 1.0% were implanted for the

treatment of epilepsy, 2.4% were implanted for the treatment of other indications, and 0.3% were implanted for indications that were not specified in the database at the time of data cut-off (see Figure 5.2 and Table 5.1).

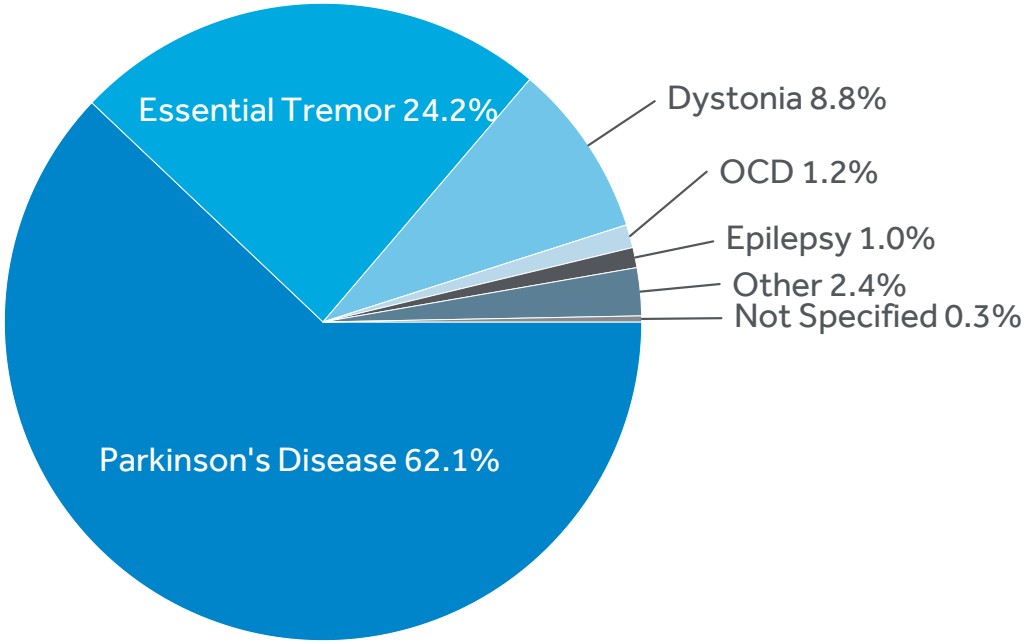


Figure 5.2: Deep Brain Stimulation Primary Treatment Indications

Table 5.1: Deep Brain Stimulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Parkinson's Disease	1,637 (62.1%)
Essential Tremor	637 (24.2%)
Dystonia	233 (8.8%)
OCD	31 (1.2%)
Epilepsy	27 (1.0%)
Other	64 (2.4%)
Not Specified	8 (0.3%)
Total Patients	**2,637(100%)**

[a] For approved indications refer to product labeling for your geography.

It is recognized that healthcare providers prescribe therapies to meet specific patient needs; however, Medtronic only directs the use of its products based on approved regulatory labeling,

which varies by geography. Please contact your local Medtronic representative for region-specific product labeling (http://www.medtronic.com/us-en/about/locations.html).

5.2 Event Summary

There were 366 product performance events reported between July 2009 and October 31, 2019, in patients with deep brain stimulation systems. These events represent 23.0% of the total reported events (366/1,590), occured in 219 of the 2,637 (8.3%) total patients enrolled, and are presented graphically within this report (e.g. events per patient years as well as survival curves). Of the remaining 1,224 reported events 175 were serious (not product performance related) and 1,049 were non-serious (not product performance related). Serious non product performance related events (175) are described in Table 5.6. Non serious non product performance related (1,049) events are not listed in this report.

Any registry devices that are returned to Medtronic are analyzed via a Returned Product Analysis (RPA) process. If available, RPA findings overwrite in the classification of the events. Within this report, Table 5.2 differentiates the events by those determined by the RPA process versus those determined by the physician. Please refer to the Methodology section for more information.

There were 218 deaths reported for patients followed in the PSR with deep brain stimulation systems (see Table 5.7), none of which were reported as a direct result of a product performance event. Early versions of the protocol required events to be reported only when the event required a surgical intervention, resulted in therapy abandonment, or resulted in death. The required event reporting definition was expanded in April 2010 to include all adverse events related to the device, implant procedure, and/or therapy.

5.2.1 Product Performance Events

Table 5.2: Deep Brain Stimulation System Product Performance Events

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=2,637[b]
RPA Determination	**2**	**0.03**	**2 (0.08%)**
Premature Battery Depletion	2	0.03	2 (0.08%)
Physician's Determination	**364**	**4.70**	**218 (8.27%)**
High Impedance	187	2.42	108 (4.10%)
Lead Migration/Dislodgement	44	0.57	32 (1.21%)
Device Malfunction	22	0.28	17 (0.64%)
Lead Fracture	21	0.27	17 (0.64%)
Low Impedance	20	0.26	14 (0.53%)
Extension Migration	19	0.25	10 (0.38%)
Neurostimulator Unable To Recharge[c]	11	0.14	11 (0.42%)
Medical Device Complication	8	0.1	6 (0.23%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=2,637[b]
Extension Fracture	7	0.09	6 (0.23%)
Device Breakage	5	0.06	5 (0.19%)
Lead Insulation Failure	4	0.05	1 (0.04%)
Premature Battery Depletion	4	0.05	4 (0.15%)
Device Connection Issue	2	0.03	2 (0.08%)
Device Lead Issue	2	0.03	2 (0.08%)
Device Material Issue	2	0.03	1 (0.04%)
Electromagnetic Interference	2	0.03	2 (0.08%)
Other[d]	4	0.05	4 (0.15%)
Total	**366**	**4.73**	**219 (8.30%)**

[a] Medical Dictionary for Regulatory Activities (MedDRA) Lower-Level Term or Medtronic's coding system term for events that do not exist in the MedDRA dictionary.

[b] The total number of patients with events may not represent the sum of all rows, as a patient may have experienced more than one type of event.

[c] There were 11 patients that used rechargeable neurostimulators for DBS in the registry. A total of 2.4% (11/461) of patients with a rechargeable neurostimulator experienced a neurostimulator unable to recharge event.

[d] Composed of event codes with 1 event each.

A total of 176 (48.1%) of the 366 product performance events were related to the lead, 73 (19.9%) were related to the extension, 53 (14.5%) were related to the neurostimulator, 17 (4.6%) were related to multiple etiologies, which includes events where at least one device and one non-device etiology was indicated, 25 (6.8%) were related to other component, 12 (3.3%) were related to surgery/anesthesia, 6 (1.6%) were related to recharging process, 2 (0.5%) were related to programming/stimulation, 1 (0.3%) was related to incisional site/device tract, and 1 (0.3%) was related to other etiology (see Figure 5.3). Events could have more than one etiology.

Relatedness is reported by the physician. In cases where the Clinical Events Committee (CEC) has adjudicated relatedness differently from the site, the CEC adjudication is used in this report for analysis purposes. However, both the site's reporting and the CEC's adjudication remain in the database.

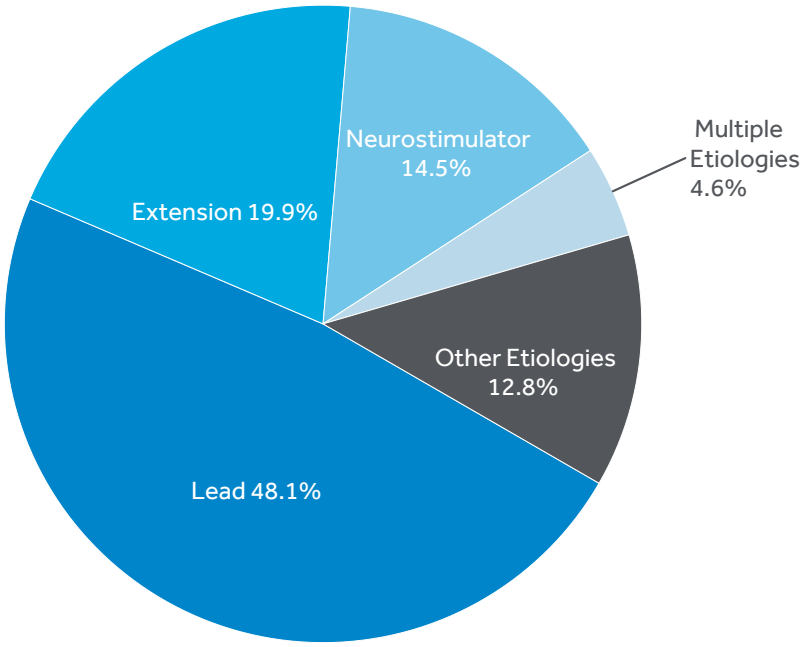


Figure 5.3: Deep Brain Stimulation System Product Performance Events by Relatedness

Table 5.3 and Table 5.4 describe the interventions taken for reported impedance events. In 35.8% and 20.0% of the high and low impedance events, the action taken was a surgical intervention. However, impedance could be used as a diagnostic measurement and may not result in any intervention or clinical impact. The majority of events required no intervention, or device reprogramming only (58.3% for high impedance and 65.0% for low impedance).

Table 5.3: Deep Brain Stimulation System High Impedance Events by Intervention

Intervention	N (%) of High Impedance Events
Device Surgical Intervention	57 (30.5%)
Reprogrammed	45 (24.1%)
Other Surgical Intervention	10 (5.3%)
Medical or Non-surgical Therapy	5 (2.7%)
Other Intervention	5 (2.7%)
Therapy Suspended	1 (0.5%)
No Action Taken	64 (34.2%)
Total	**187 (100%)**

Table 5.4: Deep Brain Stimulation System Low Impedance Events by Intervention

Intervention	N (%) of Low Impedance Events
Device Surgical Intervention	4 (20.0%)
Reprogrammed	4 (20.0%)
Therapy Suspended	3 (15.0%)
No Action Taken	9 (45.0%)
Total	**20 (100%)**

Table 5.5 describes the interventions taken for reported lead migration/dislodgement events; 81.8% of them led to a surgical intervention, and 13.6% were reprogramming.

Table 5.5: Deep Brain Stimulation System Lead Migration/Dislodgement Events by Intervention

Intervention	N (%) of Lead Migration/Dislodgement Events
Device Surgical Intervention	34 (77.3%)
Reprogrammed	6 (13.6%)
Other Surgical Intervention	2 (4.5%)
No Action Taken	2 (4.5%)
Total	**44 (100%)**

5.2.2 Clinical Events Not Related To Product Performance

The clinical events not related to product performance are summarized if:

- The patient was enrolled in the PSR at the time in which the clinical event collection was initiated (N=1,454)
- Categorized as serious adverse events
- Occurred with a System Organ Class (SOC) threshold $\geq$1% of patients
- Other Considerations
  - Some events are described in high level group terms (HLGT) to provide more specificity, if needed
  - Some therapies will provide therapy relevant events

Table 5.6: Deep Brain Stimulation System Clinical Events Not Related To Product Performance

Event Type	Number of SAE	Patients with SAE n (%)[a] N=1,454	SAE Per 100 Patient Months	Patient with SAE Requiring Surgical Intervention n (%) N=1,454
Infections and infestations	**61**	**53 (3.65%)**	**0.14**	**50 (3.44%)**
Infections - pathogen unspecified	53	46 (3.16%)	0.12	43 (2.96%)
Bacterial infectious disorders	8	8 (0.55%)	0.02	7 (0.48%)
Nervous system disorders	**37**	**35 (2.41%)**	**0.08**	**3 (0.21%)**
Central nervous system vascular disorders	16	16 (1.10%)	0.04	1 (0.07%)
Movement disorders (incl parkinsonism)	13	13 (0.89%)	0.03	1 (0.07%)
Other[b]	8	8 (0.55%)	0.02	1 (0.07%)
General disorders and administration site conditions	**29**	**27 (1.86%)**	**0.07**	**19 (1.31%)**
Complications associated with device	22	22 (1.51%)	0.05	19 (1.31%)
Other[b]	7	6 (0.41%)	0.02	1 (0.07%)
Injury, poisoning and procedural complications	**16**	**16 (1.10%)**	**0.04**	**6 (0.41%)**
Injuries NEC	9	9 (0.62%)	0.02	2 (0.14%)
Procedural related injuries and complications NEC	6	6 (0.41%)	0.01	4 (0.28%)
Other[b]	1	1 (0.07%)	0.00	0 (0.00%)
Psychiatric disorders	**17**	**16 (1.10%)**	**0.04**	**1 (0.07%)**
Depressed mood disorders and disturbances	5	5 (0.34%)	0.01	0 (0.00%)
Other[b]	12	11 (0.76%)	0.03	1 (0.07%)
Other SOC Terms (<1.0% Threshold)	**15**	**15 (1.03%)**	**0.03**	**9 (0.62%)**
Total	**175**	**151 (10.39%)**	**0.39**	**83 (5.71%)**

[a] The total number of patients with events may not represent the sum of all rows, as a patient may have experienced more than one type of event.

[b] Composed of high level group term event codes with fewer than 5 events each.

5.2.3 Patient Deaths

There were 218 deaths reported for patients with deep brain stimulation systems, none of which were reported as a direct result of a product performance event. Since July 2009, a total of 176 (80.7%) deaths have been reported in this patient registry study based upon patients receiving therapy for Parkinson's Disease, 30 (13.8%) for essential tremor, 9 (4.1%) for dystonia, 1 (0.5%) for OCD, and 2 (0.9%) for other indications (see Table 5.7). The percentage is based upon the total patient death events and not based upon the rate of occurrence. **All tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 5.7: Deep Brain Stimulation System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Parkinson's Disease	176 (80.7%)
Essential Tremor	30 (13.8%)
Dystonia	9 (4.1%)
OCD	1 (0.5%)
Other	2 (0.9%)
Total	**218 (100%)**

[a] For approved indications refer to product labeling for your geography.

5.3 Neurostimulators

From July 2009 to the report cut-off date of October 31, 2019, there were 3,928 neurostimulators followed in the registry. The difference between the total number of patients (n=2,637) versus the number of neurostimulators (n=3,928) is due to the fact that some patients were implanted with more than one neurostimulator or were subsequently re-implanted. The aggregate prospective follow-up time for all neurostimulators was 99,801 months (8,317 years). Table 5.8 provides the number and percentage of neurostimulators by model.

Table 5.8: Deep Brain Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	
Activa PC	2,392 (60.9%)
Activa SC	957 (24.4%)
Activa RC	469 (11.9%)
Other/Unspecified[a]	31 (0.8%)
No longer manufactured	
Soletra	67 (1.7%)
Kinetra	12 (0.3%)
Total	**3,928 (100%)**

[a] Other includes Activa PC+S and non-Activa systems used for DBS.

5.3.1 Neurostimulator Events

Of the total of 366 product performance-related events, there were 55 product performance-related events with an underlying reported etiology related to neurostimulator

function. This includes 53 events with a neurostimulator etiology and 2 events with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 52 were the initial product performance events that affected neurostimulator survival estimates. For neurostimulators in the registry, the current return rate to Medtronic Returned Product Analysis (RPA) was 4.9% (71/1,438). The proportion was based upon the number of registry neurostimulators received by RPA, divided by the sum of the total number of explanted devices and the total number of neurostimulators in patients who have expired. In the 55 neurostimulator events, 96.4 % (53/55) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 5.9).

Table 5.9: Deep Brain Stimulation Neurostimulator Product Performance Events by Determination

Product Performance Events	N (%)
RPA Determination	**2 (3.6%)**
Premature Battery Depletion	2 (3.6%)
Physician's Determination	**53 (96.4%)**
High Impedance	29 (52.7%)
Device Malfunction	9 (16.4%)
Low Impedance	5 (9.1%)
Premature Battery Depletion	4 (7.3%)
Electromagnetic Interference	2 (3.6%)
Device Issue	1 (1.8%)
Device Lead Issue	1 (1.8%)
Extension Migration	1 (1.8%)
Lead Insulation Failure	1 (1.8%)
Total	**55 (100%)**

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For neurostimulators:

- 52 had follow-up time cut-off due to product performance-related events.
- 2,250 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 1,626 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

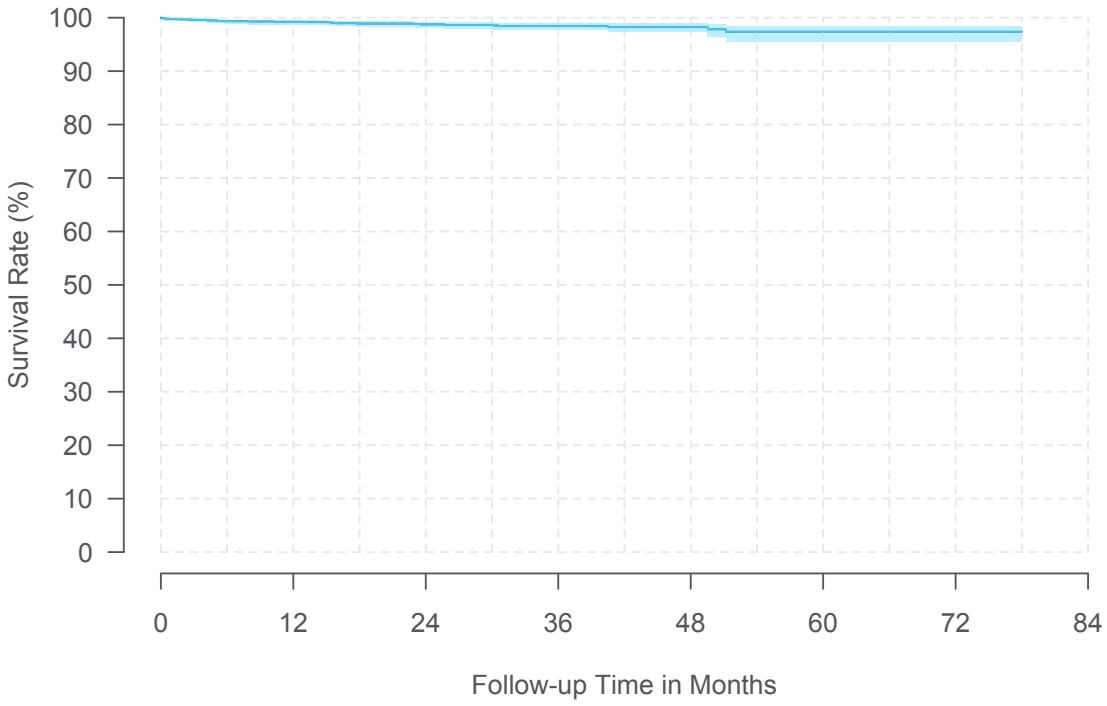
5.3.2 Neurostimulator Models

The following figures and tables represent neurostimulator survival and 95% confidence intervals where at least 20 neurostimulators contributed to each 3-month interval.

The Soletra and Kinetra models were removed from the table due to the limited number of active devices in PSR. For information on survival for those models, please refer to past reports.

5.3.2.1 Model Activa PC

Model Name	Activa PC
FDA Approval Date	April 2009
Neurostimulators Enrolled	2,392
Neurostimulators Currently Active in Study	1,031
Device Events	37
Median Follow-up Time (Months)	23.7
Cumulative Follow-up Time (Months)	60,161



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.2% (98.7%, 99.5%)	98.7% (98.1%, 99.2%)	98.4% (97.6%, 98.9%)	98.2% (97.3%, 98.8%)	97.4% (95.5%, 98.5%)
Sample Size	1,686	1,160	648	275	100

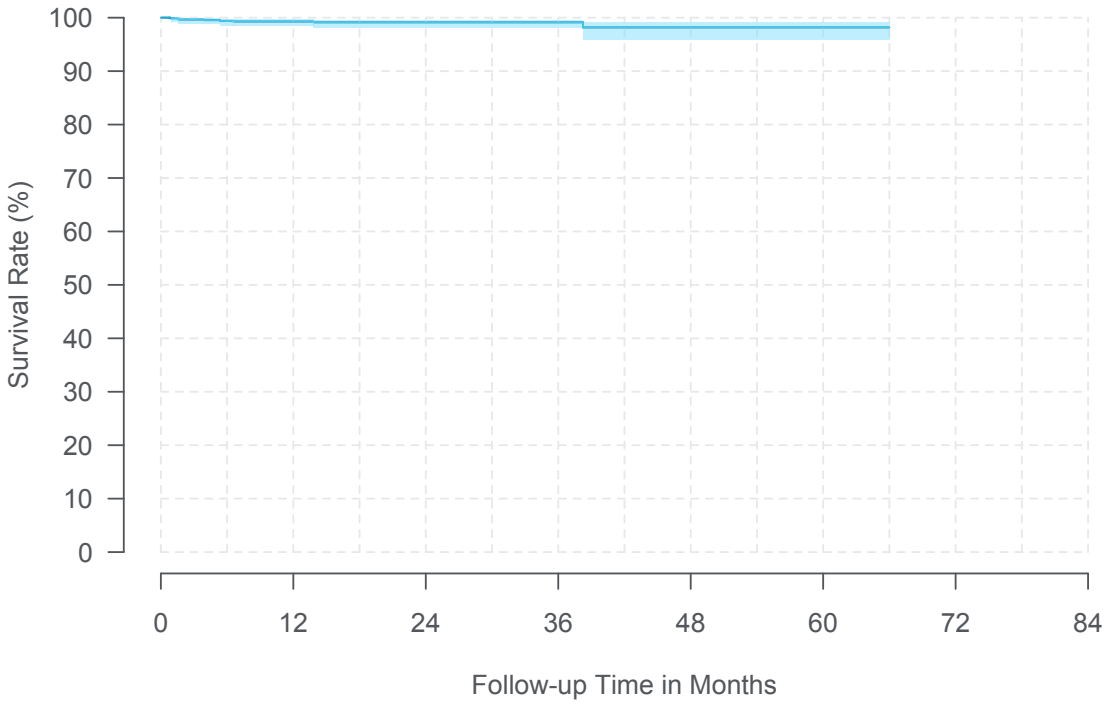
Time Interval	6 Years	At 78 Months			
Survival (95% CI)	97.4% (95.5%, 98.5%)	97.4% (95.5%, 98.5%)			
Sample Size	33	20			

Specification: Activa PC	
Height	2.6 in (65 mm)
Width	1.9 in (49 mm)
Thickness	0.6 in (15 mm)
Volume	39 cc
Battery type	Non-Rechargeable
Expected Battery life	Depends on settings and use
Maximum Electrodes	8
Amplitude	0 - 10.5 V (voltage mode) 0 - 25.5 mA (current mode)
Rate	2 - 250 Hz (voltage mode) 30 - 250 Hz (current mode)
Pulse Width	60 - 450 µsec
Groups	4
Programs	16 (up to 4 per group)
Implant Depth	≤ 4 cm

Neurostimulator Event: Activa PC	N
High impedance	20
Device malfunction	6
Premature battery depletion	5
Low impedance	3
Electromagnetic interference	2
Device issue	1
Total	**37**

5.3.2.2 Model Activa SC

Model Name	Activa SC
FDA Approval Date	January 2011
Neurostimulators Enrolled	957
Neurostimulators Currently Active in Study	296
Device Events	9
Median Follow-up Time (Months)	24.1
Cumulative Follow-up Time (Months)	23,951



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.3% (98.4%, 99.7%)	99.1% (98.2%, 99.6%)	99.1% (98.2%, 99.6%)	98.2% (96.0%, 99.2%)	98.2% (96.0%, 99.2%)
Sample Size	690	480	241	96	35

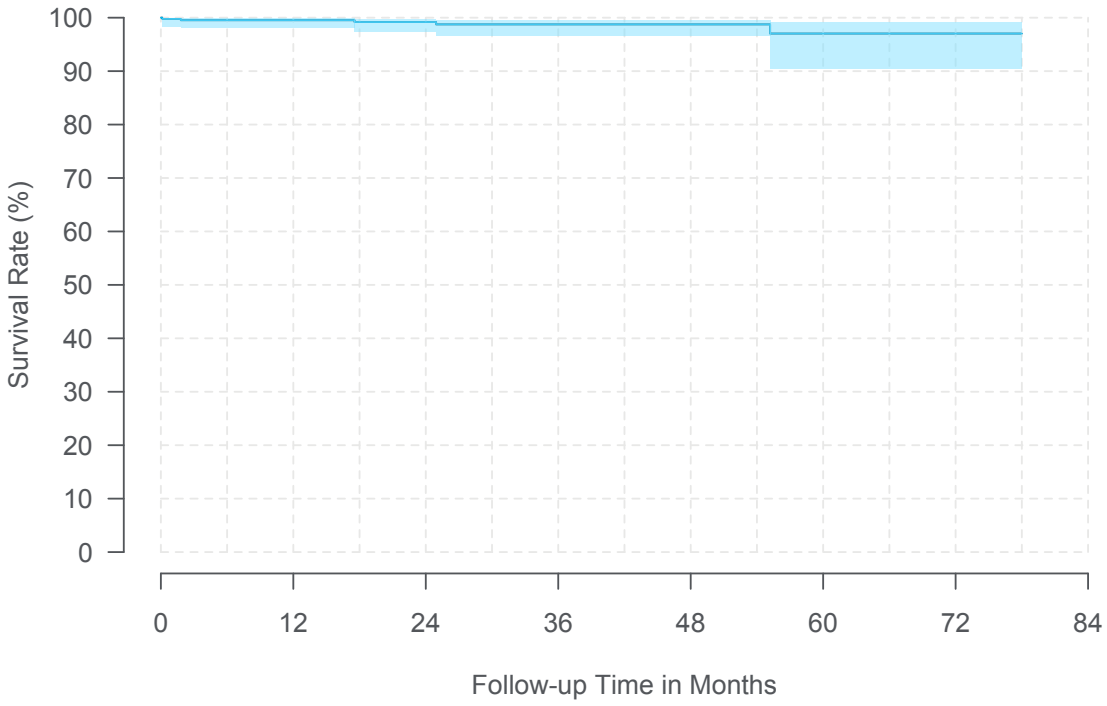
Time Interval	At 66 Months
Survival (95% CI)	98.2% (96.0%, 99.2%)
Sample Size	23

Specification: Activa SC	
Height	2.2 in (55 mm)
Width	2.4 in (60 mm)
Thickness	0.4 in (11 mm)
Volume	28 cc (Model 37602) 27 cc (Model 37603)
Battery type	Non-Rechargeable
Expected Battery life	Depends on settings and use
Maximum Electrodes	4
Amplitude	0 - 10.5 V (voltage mode) 0 - 25.5 mA (current mode)
Rate	2 - 250 Hz (voltage mode) 30 - 250 Hz (current mode)
Pulse Width	60 - 450 µsec
Groups	4
Programs	8 (up to 2 per group)
Implant Depth	≤ 4 cm

Neurostimulator Event: Activa SC	N
High impedance	4
Low impedance	2
Device lead issue	1
Device malfunction	1
Premature battery depletion	1
Total	**9**

5.3.2.3 Model Activa RC

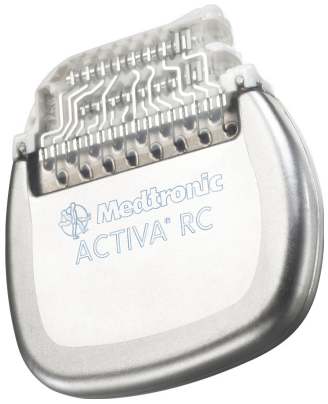
Model Name	Activa RC
FDA Approval Date	March 2009
Neurostimulators Enrolled	469
Neurostimulators Currently Active in Study	298
Device Events	5
Median Follow-up Time (Months)	24.2
Cumulative Follow-up Time (Months)	13,094



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (98.1%, 99.9%)	99.2% (97.4%, 99.7%)	98.7% (96.6%, 99.5%)	98.7% (96.6%, 99.5%)	97.0% (90.3%, 99.1%)
Sample Size	339	236	134	78	49

Time Interval	6 Years	At 78 Months			
Survival (95% CI)	97.0% (90.3%, 99.1%)	97.0% (90.3%, 99.1%)			
Sample Size	35	30			

Specification: Activa RC	
Height	2.1 in (54 mm)
Width	2.1 in (54 mm)
Thickness	0.4 in (9 mm)
Volume	22 cc
Battery type	Rechargeable
Expected Battery life	9 years
Maximum Electrodes	8
Amplitude	0 - 10.5 V (voltage mode) 0 - 25.5 mA (current mode)
Rate	2 - 250 Hz (voltage mode) 30 - 250 Hz (current mode)
Pulse Width	60 - 450 µsec
Groups	4
Programs	16 (up to 4 per group)
Implant Depth	$\leq$ 1 cm



Neurostimulator Event: Activa RC	N
Device malfunction	2
High impedance	2
Extension migration	1
Total	**5**

5.3.3 Neurostimulator Summary

Table 5.10: Deep Brain Stimulation Neurostimulator Characteristics

Model/Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Activa PC	April 2009	2,392	1,031	37	23.7	60,161
Activa SC	January 2011	957	296	9	24.1	23,951
Activa RC	March 2009	469	298	5	24.2	13,094

Table 5.11: Deep Brain Stimulation Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years	6 Years
Activa PC	99.2%	98.7%	98.4%	98.2%	97.4%	97.4%
	(98.7%, 99.5%)	(98.1%, 99.2%)	(97.6%, 98.9%)	(97.3%, 98.8%)	(95.5%, 98.5%)	(95.5%, 98.5%)
Activa SC	99.3%	99.1%	99.1%	98.2%	98.2%	
	(98.4%, 99.7%)	(98.2%, 99.6%)	(98.2%, 99.6%)	(96.0%, 99.2%)	(96.0%, 99.2%)	
Activa RC	99.5%	99.2%	98.7%	98.7%	97.0%	97.0%
	(98.1%, 99.9%)	(97.4%, 99.7%)	(96.6%, 99.5%)	(96.6%, 99.5%)	(90.3%, 99.1%)	(90.3%, 99.1%)

5.4 Leads

From July 2009 to the report cut-off date of October 31, 2019, there were 4,464 leads followed in the registry. The difference between the total number of leads (n=4,464) versus neurostimulators (n=3,928) is due to the fact that some patients were subsequently re-implanted with a lead or were implanted with more than one lead. The aggregate prospective follow-up time for all leads was 159,040 months (13,253 years). Table 5.12 provides the number and percentage of leads by model.

Table 5.12: Deep Brain Stimulation Lead Counts by Model

Model Name	N (%)
3389 (compact electrode spacing)	2,528 (56.6%)
3387 (standard electrode spacing)	1,879 (42.1%)
3391 (large electrodes and wide spacing)	42 (0.9%)
Other/Unspecified[a]	15 (0.3%)
Total	**4,464 (100%)**

[a] Includes leads used in non-Activa systems.

5.4.1 Lead Events

Of the total of 366 product performance-related events, there were 186 product performance-related events with an underlying reported etiology related to lead function. This includes 176 events with a lead etiology and 10 events with both a lead and other etiology (including device and non-device etiologies). Of these, 155 were the initial product performance event that affected lead survival estimates.

Events of other/unspecified models are not shown. Model 3391 did not have any product performance-related events.

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For leads:

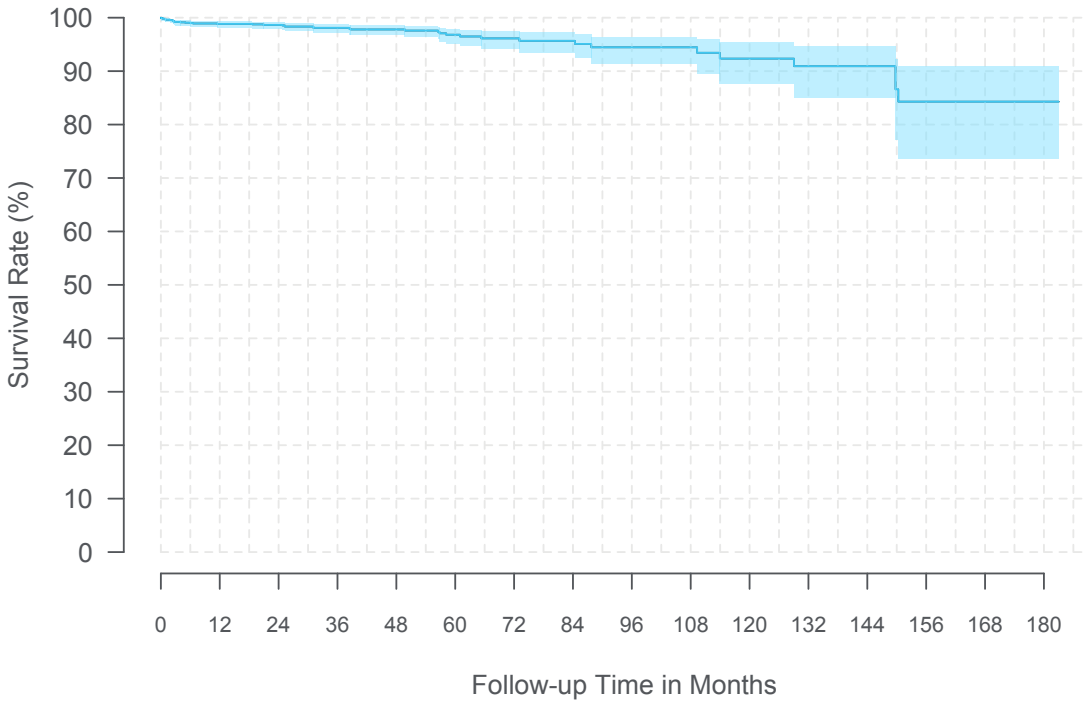
- 155 had follow-up time cut-off due to product performance-related events.
- 1,735 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,574 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

5.4.2 Lead Models

The following figures and tables represent lead survival and 95% confidence intervals where at least 20 leads contributed to each 3-month interval. Due to enrollment of replacement patients with previously implanted leads, sample size may increase at later timepoints.

5.4.2.1 Model 3387

Model Name	3387
FDA Approval Date	July 1997
Leads Enrolled	1,879
Leads Currently Active in Study	1,069
Device Events	43
Median Follow-up Time (Months)	32.4
Cumulative Follow-up Time (Months)	65,233



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.8% (98.1%, 99.3%)	98.7% (97.9%, 99.1%)	98.1% (97.1%, 98.7%)	97.8% (96.7%, 98.5%)	96.8% (95.2%, 97.9%)
Sample Size	1,267	953	694	489	323

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	96.1% (94.2%, 97.4%)	95.7% (93.4%, 97.2%)	94.5% (91.4%, 96.5%)	94.5% (91.4%, 96.5%)	92.3% (87.5%, 95.3%)
Sample Size	210	169	110	87	72

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	90.9% (85.0%, 94.6%)	90.9% (85.0%, 94.6%)	84.3% (73.6%, 90.9%)	84.3% (73.6%, 90.9%)	84.3% (73.6%, 90.9%)
Sample Size	60	42	33	30	24

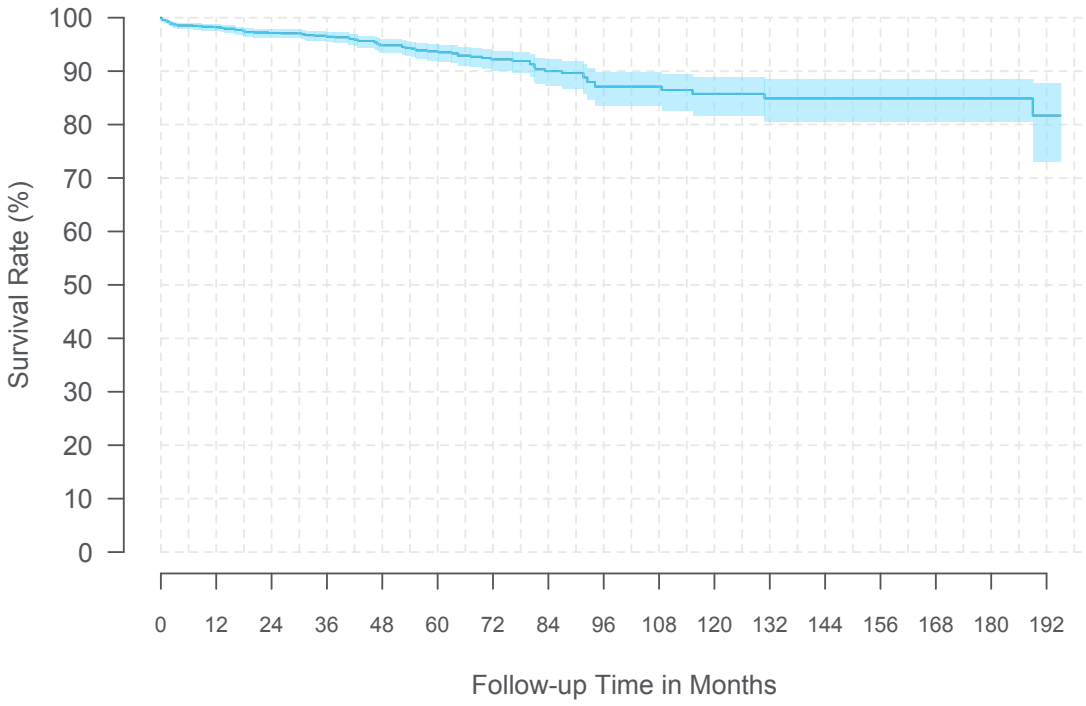
Time Interval	At 183 Months
Survival (95% CI)	84.3% (73.6%, 90.9%)
Sample Size	20

Specification: 3387	
Lead	
Length (cm)	40
Diameter (mm)	1.27
Electrode	
Number	4
Shape	Cylindrical
Length (mm)	1.5
Individual Surface Area (mm^2)	6.0
Inter-Electrode Spacing: Edge to Edge (mm)	1.5
Array Length (mm)	10.5

Lead Event: 3387	N
High impedance	25
Lead migration/dislodgement	9
Low impedance	4
Lead fracture	3
Device lead issue	1
Medical device complication	1
Total	**43**

5.4.2.2 Model 3389

Model Name	3389
FDA Approval Date	September 1999
Leads Enrolled	2,528
Leads Currently Active in Study	1,548
Device Events	107
Median Follow-up Time (Months)	34.4
Cumulative Follow-up Time (Months)	92,058



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.2% (97.5%, 98.7%)	97.2% (96.3%, 97.8%)	96.4% (95.4%, 97.2%)	94.8% (93.4%, 95.9%)	93.7% (92.0%, 95.0%)
Sample Size	1,638	1,317	974	683	493

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	92.2% (90.1%, 93.8%)	90.0% (87.3%, 92.2%)	87.1% (83.6%, 89.9%)	87.1% (83.6%, 89.9%)	85.8% (81.7%, 89.0%)
Sample Size	357	260	188	140	111

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)
Sample Size	100	82	68	61	40

Time Interval	16 Years	At 195 Months
Survival (95% CI)	81.7% (73.1%, 87.8%)	81.7% (73.1%, 87.8%)
Sample Size	23	23

Specification: 3389	
Lead	
Length (cm)	40
Diameter (mm)	1.27
Electrode	
Number	4
Shape	Cylindrical
Length (mm)	1.5
Individual Surface Area (mm^2)	6.0
Inter-Electrode Spacing: Edge to Edge (mm)	0.5
Array Length (mm)	7.5

Lead Event: 3389	N
High impedance	65
Lead migration/dislodgement	21
Lead fracture	10
Low impedance	7
Device material issue	2
Device malfunction	1
Lead insulation failure	1
Total	**107**

5.4.3 Lead Summary

Table 5.13: Deep Brain Stimulation Lead Characteristics

Model/Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
3387	July 1997	1,879	1,069	43	32.4	65,233
3389	September 1999	2,528	1,548	107	34.4	92,058

Table 5.14: Deep Brain Stimulation Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
3387	98.8% (98.1%, 99.3%)	98.7% (97.9%, 99.1%)	98.1% (97.1%, 98.7%)	97.8% (96.7%, 98.5%)	96.8% (95.2%, 97.9%)
3389	98.2% (97.5%, 98.7%)	97.2% (96.3%, 97.8%)	96.4% (95.4%, 97.2%)	94.8% (93.4%, 95.9%)	93.7% (92.0%, 95.0%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
3387	96.1% (94.2%, 97.4%)	95.7% (93.4%, 97.2%)	94.5% (91.4%, 96.5%)	94.5% (91.4%, 96.5%)	92.3% (87.5%, 95.3%)
3389	92.2% (90.1%, 93.8%)	90.0% (87.3%, 92.2%)	87.1% (83.6%, 89.9%)	87.1% (83.6%, 89.9%)	85.8% (81.7%, 89.0%)

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
3387	90.9% (85.0%, 94.6%)	90.9% (85.0%, 94.6%)	84.3% (73.6%, 90.9%)	84.3% (73.6%, 90.9%)	84.3% (73.6%, 90.9%)
3389	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)	84.9% (80.4%, 88.4%)

Model Name	16 Years				
3387					
3389	81.7% (73.1%, 87.8%)				

5.5 Extensions

From July 2009 to the report cut-off date of October 31, 2019, there were 4,532 extensions followed in the registry. The difference between the total number of extensions (n=4,532) versus neurostimulators (n=3,928) is due to some patients implanted with more than 1 extension or subsequently re-implanted with an extension. The aggregate prospective

follow-up time for all extensions was 156,673 months (13,056 years). The table below provides the number and percentage of extensions by model. Table 5.15 provides the number and percentage of extensions by model.

Table 5.15: Deep Brain Stimulation Extension Counts by Model

Model Name	N (%)
Currently manufactured	
37085/37086 (quadripolar stretch)	3,926 (86.6%)
Other/Unspecified[a]	115 (2.5%)
No longer manufactured	
7482[b] (quadripolar)	491 (10.8%)
Total	**4,532 (100%)**

[a] Includes extensions for other legacy stimulation systems.
[b] Includes Models 7482 and 7482a.

5.5.1 Extension Events

Of the total of 366 product performance-related events, there were 77 product performance-related events with an underlying reported etiology related to extension function. This includes 73 events with an extension etiology and 4 events with both an extension and other etiology (including device and non-device etiologies). Of these, 72 were the initial product performance event that affected extension survival estimates.

Events of other/unspecified models and discontinued models are not shown.

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For leads:

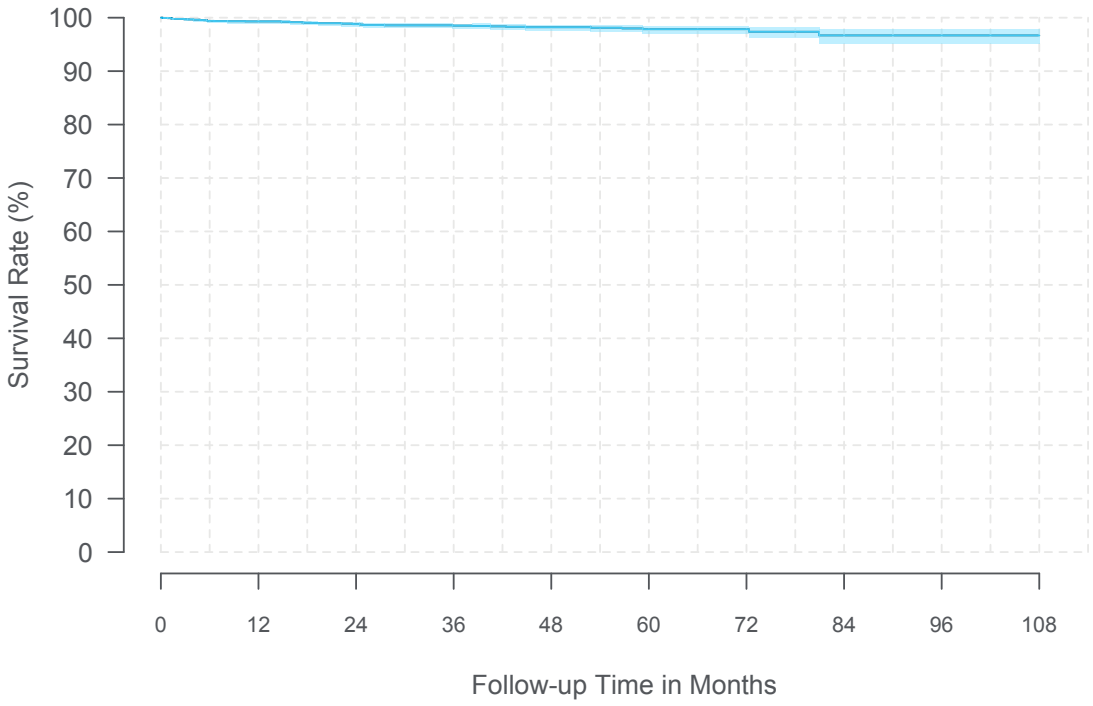
- 72 had follow-up time cut-off due to product performance-related events.
- 1,812 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,648 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

5.5.2 Extension Models

The following figures and tables represent extension survival and 95% confidence intervals where at least 20 extensions contributed to each 3-month interval.

5.5.2.1 Model 37085/37086

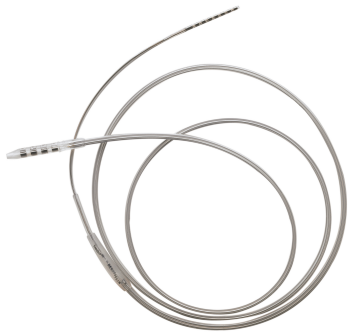
Model Name	37085/37086
FDA Approval Date	March 2009
Extensions Enrolled	3,926
Extensions Currently Active in Study	2,358
Device Events	58
Median Follow-up Time (Months)	31.2
Cumulative Follow-up Time (Months)	132,446



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.3% (99.0%, 99.5%)	98.8% (98.3%, 99.1%)	98.5% (98.0%, 98.9%)	98.2% (97.6%, 98.7%)	97.8% (97.0%, 98.4%)
Sample Size	2,897	2,245	1,622	1,073	642

Time Interval	6 Years	7 Years	8 Years	9 Years	
Survival (95% CI)	97.8% (97.0%, 98.4%)	96.7% (95.1%, 97.8%)	96.7% (95.1%, 97.8%)	96.7% (95.1%, 97.8%)	
Sample Size	410	231	88	28	

Specification: 37085/37086	
Device Name	Stretch-Coil DBS Extension
Length (cm)	40, 40, 95
Distal End Compatibility	3387, 3389, or 3391 DBS lead
Distal End Set Screws	4
Proximal End INS Compatibility	Activa RC, Activa PC, or Activa SC 37603



Extension Event: 37085/37086	Total
High impedance	30
Extension migration	13
Extension fracture	5
Low impedance	4
Medical device complication	4
Device malfunction	1
Lead migration/dislodgement	1
Total Extension Events	**58**

5.5.3 Extension Summary

Table 5.16: Deep Brain Stimulation Extension Characteristics

Model/Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
37085/37086	March 2009	3,926	2,358	58	31.2	132,446

Table 5.17: Deep Brain Stimulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
37085/37086	99.3% (99.0%, 99.5%)	98.8% (98.3%, 99.1%)	98.5% (98.0%, 98.9%)	98.2% (97.6%, 98.7%)	97.8% (97.0%, 98.4%)

Model Name	6 Years	7 Years	8 Years	9 Years	
37085/37086	97.8% (97.0%, 98.4%)	96.7% (95.1%, 97.8%)	96.7% (95.1%, 97.8%)	96.7% (95.1%, 97.8%)	

6 Sacral Neuromodulation Systems

6.1 Study Participants

6.1.1 Centers

In this section, the sacral neuromodulation tables and graphs were generated based on data collected between April 2010 and the report cut-off date of October 31, 2019. Twenty-three centers in North America and South America, have enrolled and contributed patients to the sacral neuromodulation systems section of this report.

6.1.2 Patients

Of the 1,226 sacral neuromodulation patients enrolled, the primary indications for implant were as follows: 43.1% were implanted for the treatment of urinary urge incontinence, 30.2% were implanted for the treatment of urgency-frequency, 13.0% were implanted for the treatment of urinary retention, 6.7% were implanted for the treatment of fecal incontinence, 2.8% were implanted for the treatment of bladder pain syndrome, 3.7% were implanted for the treatment of some other indication, and 0.7% were implanted for indications that were not specified in the database at the time of data cut-off (see Figure 6.1 and Table 6.1).

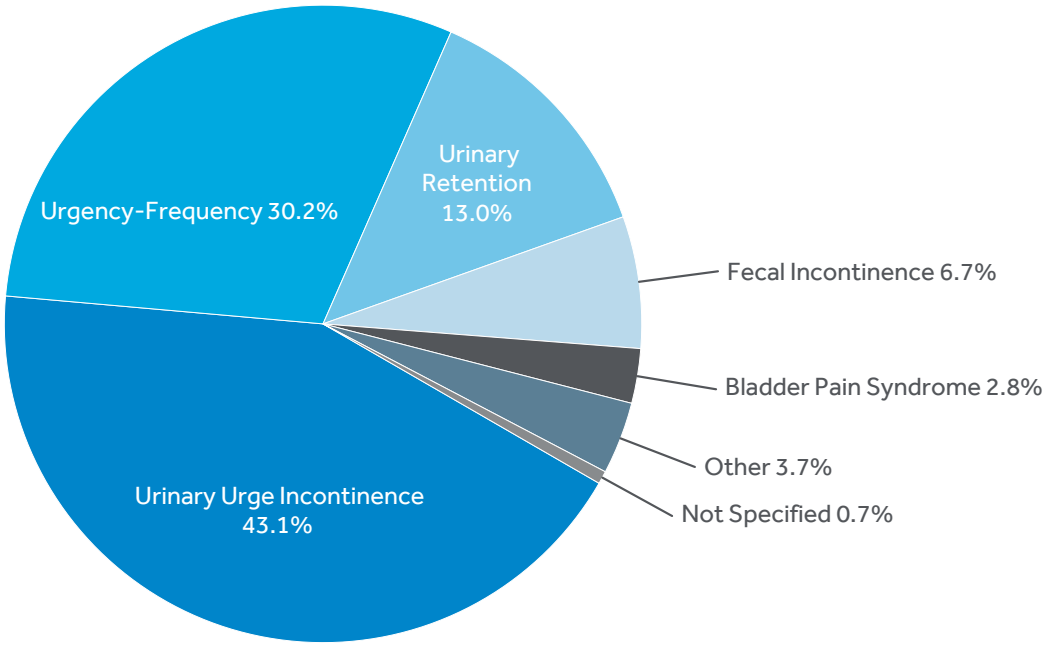


Figure 6.1: Sacral Neuromodulation Primary Treatment Indications

Table 6.1: Sacral Neuromodulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Urinary Urge Incontinence	528 (43.1%)
Urgency-Frequency	370 (30.2%)
Urinary Retention	159 (13.0%)
Fecal Incontinence	82 (6.7%)
Bladder Pain Syndrome	34 (2.8%)
Other	45 (3.7%)
Not Specified	8 (0.7%)
Total Patients	**1,226 (100%)**

[a] For approved indications refer to product labeling for your geography.

It is recognized that healthcare providers prescribe therapies to meet specific patient needs; however, Medtronic only directs the use of its products based on approved regulatory labeling, which varies by geography. Please contact your local Medtronic representative for region-specific product labeling (http://www.medtronic.com/us-en/about/locations.html).

6.2 Event Summary

There were 155 product performance events reported between April 2010 and October 31, 2019, in patients with sacral neuromodulation systems. These events represent 21.1% of the total reported events (155/734), occured in 124 (10.1%) of the 1,226 total patients enrolled, and are presented graphically within this report (e.g. events per patient years as well as survival curves). In addition, there were 577 non-product performance events that were collected to understand patient experience (clinical signs and symptoms) with the sacral neuromodulation systems. As an ongoing registry, events not coded at the time of the data snapshot (waiting on further information) will be included in future reports (n=2).

All registry devices that are returned to Medtronic are analyzed via a Returned Product Analysis (RPA) process. If available, RPA findings assist in the classification of the events. Within this report, Table 6.2 differentiates the events by those determined by the RPA process versus those determined by the physician. Please refer to the Methodology section for more information.

There were 32 deaths reported for patients followed in the PSR with sacral neuromodulation systems, none of which were reported as a direct result of a product performance event.

6.2.1 Product Performance Events

Table 6.2: Sacral Neuromodulation System Product Performance Events

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=1,226[b]
RPA Determination	**0**	**0.00**	**0 (0.00%)**
Physician's Determination	**155**	**6.43**	**124 (10.11%)**
High Impedance	52	2.16	42 (3.43%)
Lead Migration/Dislodgement	35	1.45	30 (2.45%)
Lead Fracture	19	0.79	18 (1.47%)
Device Lead Issue	12	0.50	10 (0.82%)
Device Malfunction	12	0.50	11 (0.90%)
Low Impedance	9	0.37	9 (0.73%)
Device Battery Issue	5	0.21	4 (0.33%)
Device Electrical Impedance Issue	3	0.12	2 (0.16%)
Device Failure	2	0.08	1 (0.08%)
Device Lead Damage	1	0.04	1 (0.08%)
Device Placement At Incorrect Location	1	0.04	1 (0.08%)
Device Stimulation Issue	1	0.04	1 (0.08%)
Device Telemetry Issue	1	0.04	1 (0.08%)
Neurostimulator Migration	1	0.04	1 (0.08%)
Therapeutic Product Ineffective	1	0.04	1 (0.08%)
Total	**155**	**6.43**	**124 (10.11%)**

[a] Medical Dictionary for Regulatory Activities (MedDRA) Lower-Level Term or Medtronic's coding system term for events that do not exist in the MedDRA dictionary.

[b] The total number of patients with events may not represent the sum of all rows, as a patient may have experienced more than one type of event.

A total of 115 (74.2%) of 155 product performace events were related to the the lead only, 25 (16.1%) related to the neurostimulator only, 2 (1.3%) related to the extension only, 3 (1.9%) related to multiple etiologies (which includes events where at least one device and one non-device etiology was indicated), and 10 (6.5%) related to other etiologies. Relatedness is determined by the physician.

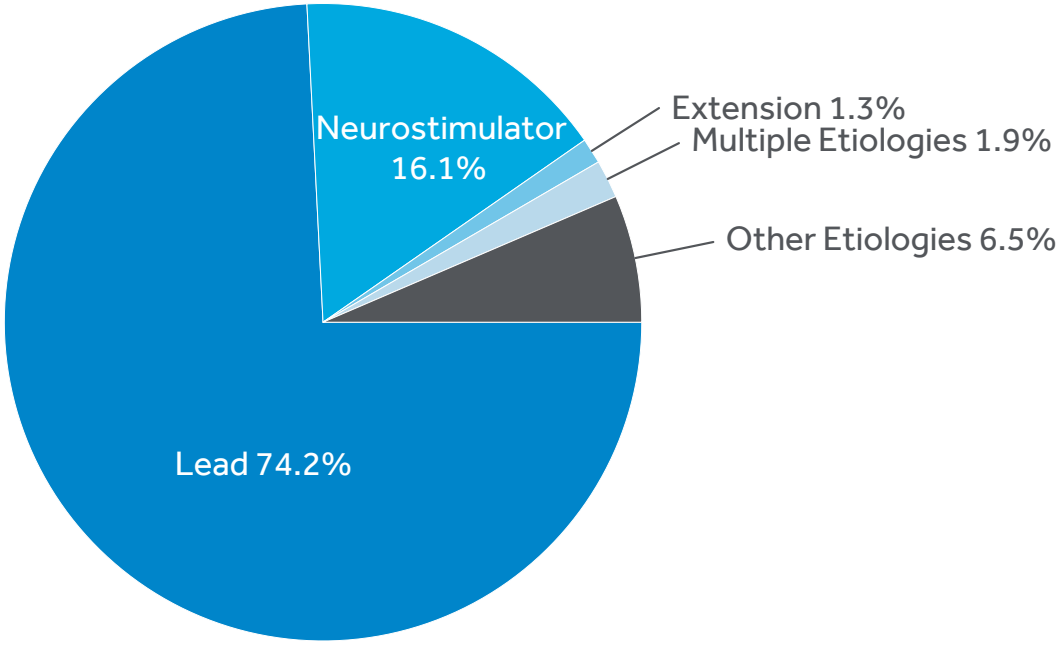


Figure 6.2: Sacral Neuromodulation System Product Performance Events by Relatedness

Table 6.3 and Table 6.4 describe the interventions taken for reported impedance events. In 51.9% and 33.3% of the high and low impedance events, the action taken was a surgical intervention. However, impedance could be used as a diagnostic measurement and may not result in any intervention or clinical impact. In addition, 48.1% of the high impedance events and 55.6% of the low impedance events required no intervention or device reprogramming only.

Table 6.3: Sacral Neuromodulation System High Impedance Events by Intervention

Intervention	N (%) of High Impedance Events
Device Surgical Intervention	26 (50.0%)
Reprogrammed	20 (38.5%)
Other Surgical Intervention	1 (1.9%)
No Action Taken	5 (9.6%)
Total	**52 (100%)**

Table 6.4: Sacral Neuromodulation System Low Impedance Events by Intervention

Intervention	N (%) of Low Impedance Events
Device Surgical Intervention	3 (33.3%)
Reprogrammed	3 (33.3%)
Other intervention	1 (11.1%)
No Action Taken	2 (22.2%)
Total	**9 (100%)**

Table 6.5 describes the interventions taken for reported lead migration/dislodgement events; 71.4% of them led to a surgical intervention, and 8.6% were reprogramming.

Table 6.5: Sacral Neuromodulation System Lead Migration/Dislodgement Events by Intervention

Intervention	N (%) of Lead Migration/Dislodgement Events
Device Surgical Intervention	25 (71.4%)
Reprogrammed	3 (8.6%)
Medical or non-sugical Therapy	1 (2.9%)
No Action Taken	6 (17.1%)
Total	**35 (100%)**

6.2.2 Clinical Events Not Related To Product Performance

The clinical events not related to product performance are summarized if:

- The patient was enrolled in the PSR at the time in which the clinical event collection was initiated (N=916)
- Categorized as serious adverse events
- Occurred with a System Organ Class (SOC) threshold $\geq$0.5% of patients

- Other Considerations
  - Some events are described in high level group terms (HLGT) to provide more specificity, if needed

Table 6.6: Sacral Neuromodulation System Clinical Events Not Related To Product Performance

Event Type	Number of SAE	Patients with SAE n (%) N=916	SAE Per 100 Patient Months	Patient with SAE Requiring Surgical Intervention n (%) N=916
Infections and infestations	**7**	**7 (0.76%)**	**0.04**	**6 (0.66%)**
Infections - pathogen unspecified	6	6 (0.66%)	0.03	5 (0.55%)
Other[a]	1	1 (0.11%)	0.01	1 (0.11%)
Other SOC Terms (<0.5% Threshold)	**1**	**1 (0.11%)**	**0.01**	**1 (0.11%)**
Total	**8**	**8 (0.87%)**	**0.46**	**7 (0.76%)**

[a] Composed of high level group term event codes with fewer than 5 events each.

6.2.3 Patient Deaths

In earlier versions of the protocol, deaths were only assessed for the relatedness to the device product performance. After 2010, death assessments were expanded to also include the relationship to the implant procedure and/or therapy. As of the report cut-off, a total of 32 patients in the registry had expired. As with previous reports, no deaths were reported as a direct result of a product performance event.

The percentage is based upon the total patient death events and not based upon the rate of occurrence. **All tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 6.7: Sacral Neuromodulation System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Urgency-Frequency	14 (43.8%)
Urinary Urge Incontinence	7 (21.9%)
Urinary Retention	5 (15.6%)
Fecal Incontinence	1 (3.1%)
Other	5 (15.6%)
Total	**32 (100%)**

[a] For approved indications refer to product labeling for your geography.

6.3 Neurostimulators

From April 2010 to the report cut-off date of October 31, 2019, there were 1,207 neurostimulators followed in the registry. The difference between the total number of patients (n=1,226) versus the total number of neurostimulators (n=1,207) is due to the fact that patients could enroll prior to implant but may not have received an implanted device, or patients were enrolled but not implanted before the data cut-off.

In total, 91.6% (1,106/1,207) of neurostimulators were InterStim II, and 8.4% (101/1,207) were InterStim. The aggregate prospective follow-up time for all neurostimulators was 27,920 months (2,327 years).

6.3.1 Neurostimulator Events

There were 26 product performance-related events with an underlying reported etiology related to neurostimulator function. This includes 25 events with a neurostimulator etiology and 1 event with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 24 were the initial product performance events that affected neurostimulator survival estimates. For neurostimulators in the registry, the current return rate to Medtronic Returned Product Analysis (RPA) was 14.8% (37/250). The proportion was based upon the number of registry neurostimulators received by RPA, divided by the sum of the total number of explanted devices and the total number of neurostimulators in patients who have expired. In the 26 neurostimulator events, 100.0 % (26/26) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 6.8).

Table 6.8: Sacral Neuromodulation Neurostimulator PPE by Determination

Product Performance Events	N (%)
Physician's Determination	**26 (100%)**
Device Malfunction[a]	8 (30.8%)
High Impedance	5 (19.2%)
Device Battery Issue	4 (15.4%)
Device Lead Issue	2 (7.7%)
Lead Migration/Dislodgement	2 (7.7%)
Device Electrical Impedance Issue	1 (3.8%)
Device Failure	1 (3.8%)
Device Stimulation Issue	1 (3.8%)
Neurostimulator Migration	1 (3.8%)
Therapeutic Product Ineffective	1 (3.8%)

[a] See Neurostimulator Event Summary Tables for device malfunction by model.

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a

censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For neurostimulators:

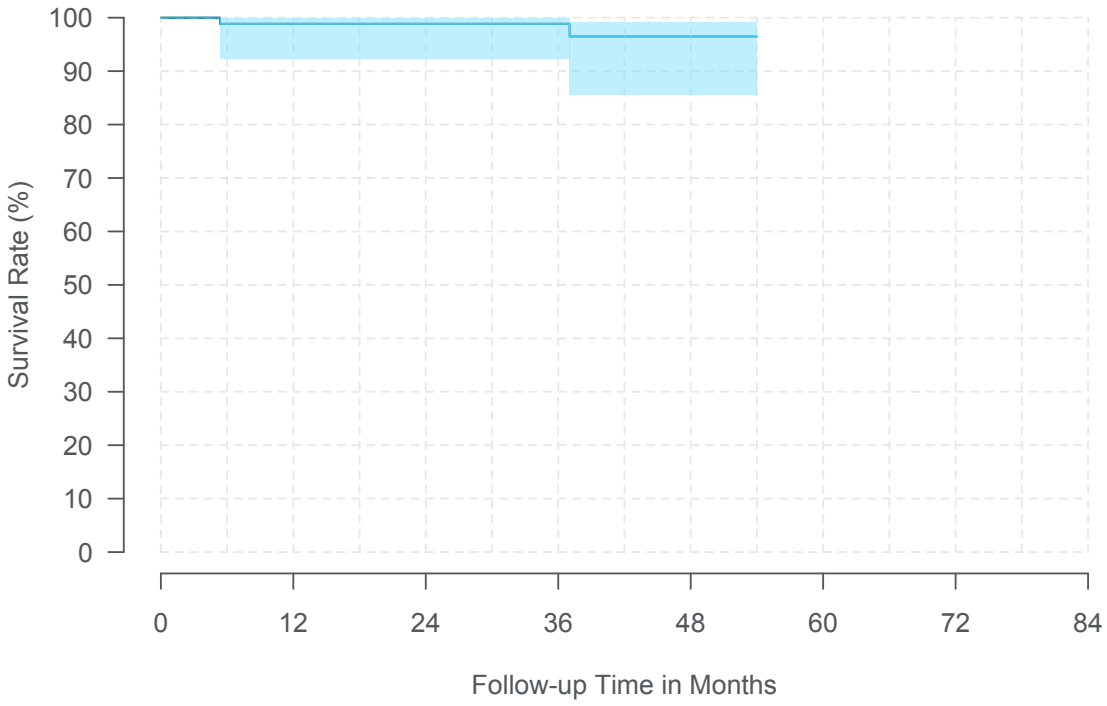
- 24 had follow-up time cut-off due to product performance-related events.
- 592 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 591 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

6.3.2 Neurostimulator Models

The following figures and tables represent neurostimulator survival and 95% confidence intervals where at least 20 neurostimulators contributed to each 3-month interval.

6.3.2.1 Model 3023

Model Name	InterStim
FDA Approval Date	July 1998
Neurostimulators Enrolled	101
Neurostimulators Currently Active in Study	20
Device Events	2
Median Follow-up Time (Months)	27.3
Cumulative Follow-up Time (Months)	3,327



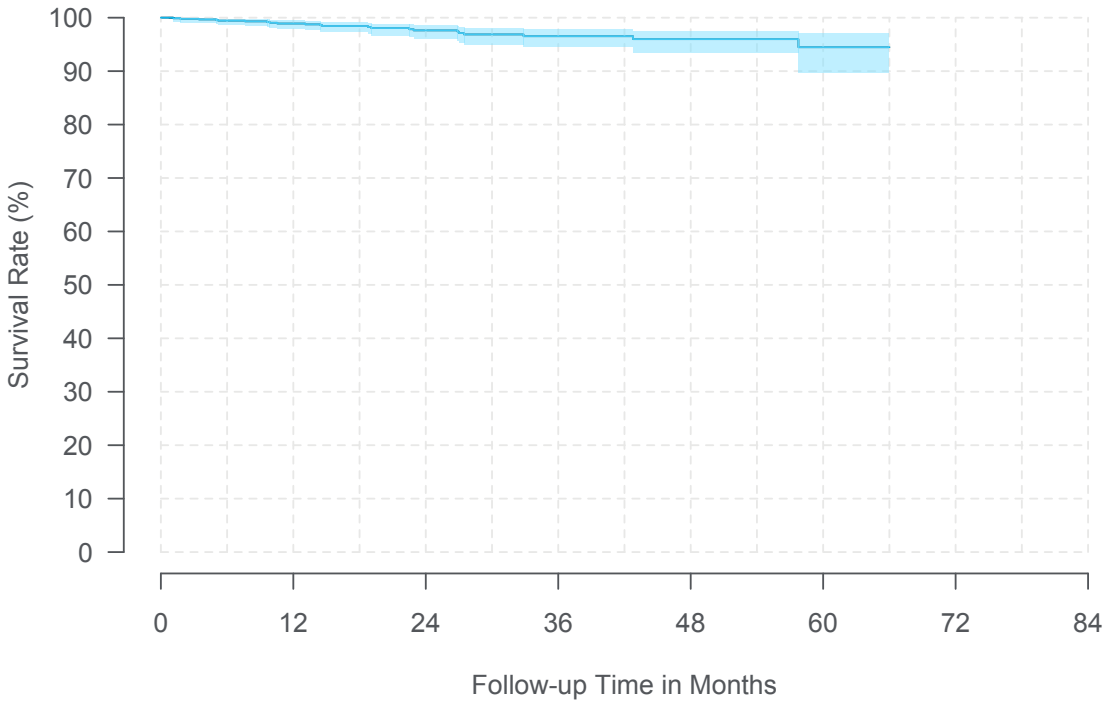
Time Interval	1 Year	2 Years	3 Years	4 Years	At 54 Months
Survival (95% CI)	98.9% (92.2%, 99.8%)	98.9% (92.2%, 99.8%)	98.9% (92.2%, 99.8%)	96.5% (85.5%, 99.2%)	96.5% (85.5%, 99.2%)
Sample Size	69	58	41	25	21

Specification: 3023	
Height	2.2 in (55 mm)
Width	2.4 in (60 mm)
Thickness	0.4 in (10 mm)
Volume	25 cc
Battery type	Non-Rechargeable
Expected Battery life	Depends on settings and use
Maximum Electrodes	4
Amplitude	0 - 10.5 V
Rate	2.1 - 130 Hz
Pulse Width	60 - 450 µsec
Programs	4
Implant Depth	≤ 4 cm

Neurostimulator Event Summary: 3023	N
Device Battery Issue	1
Device Malfunction	1
Total	**2**

6.3.2.2 Model 3058

Model Name	InterStim II
FDA Approval Date	June 2006
Neurostimulators Enrolled	1,106
Neurostimulators Currently Active in Study	576
Device Events	22
Median Follow-up Time (Months)	17.8
Cumulative Follow-up Time (Months)	24,593



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.9% (97.9%, 99.4%)	97.6% (96.1%, 98.6%)	96.5% (94.5%, 97.8%)	96.0% (93.6%, 97.5%)	94.5% (89.7%, 97.1%)
Sample Size	683	424	264	133	54

Time Interval	At 66 Months
Survival (95% CI)	94.5% (89.7%, 97.1%)
Sample Size	26

Specification: 3058	
Height	1.7 in (44 mm)
Width	2.0 in (51 mm)
Thickness	0.3 in (7.7 mm)
Volume	14 cc
Battery type	Non-Rechargeable
Expected Battery life	Depends on settings and use
Maximum Electrodes	4
Amplitude	0 - 8.5 V
Rate	2.1 - 130 Hz
Pulse Width	60 - 450 µsec
Programs	4
Implant Depth	≤ 2.5 cm

Neurostimulator Event Summary: 3058	N
Device Malfunction	7
High Impedance	5
Device Battery Issue	2
Lead Migration/Dislodgement	2
Device Electrical Impedance Issue	1
Device Failure	1
Device Lead Issue	1
Device Stimulation Issue	1
Neurostimulator Migration	1
Therapeutic Product Ineffective	1
Total	**22**

6.3.3 Neurostimulator Summary

Table 6.9: Sacral Neuromodulation Neurostimulator Characteristics

Model Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Neurostimulator Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
InterStim	July 1998	101	20	2	27.3	3,327
InterStim II	June 2006	1,106	576	22	17.8	24,593

Table 6.10: Sacral Neuromodulation Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
InterStim	98.9%	98.9%	98.9%	96.5%	
	(92.2%, 99.8%)	(92.2%, 99.8%)	(92.2%, 99.8%)	(85.5%, 99.2%)	
InterStim II	98.9%	97.6%	96.5%	96.0%	94.5%
	(97.9%, 99.4%)	(96.1%, 98.6%)	(94.5%, 97.8%)	(93.6%, 97.5%)	(89.7%, 97.1%)

6.4 Leads

From April 2010 to the report cut-off date of October 31, 2019, there were 1,172 leads followed in the registry. The difference between the total number of leads (n=1,172) versus the total number of neurostimulators (n=1,207) is due to the fact that some patients were subsequently re-implanted with a new neurostimulator. The aggregate prospective follow-up time for all leads was 28,109 months (2,342 years). Table 6.11 provides the number and percentage of leads by model.

Table 6.11: Sacral Neuromodulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**1,068 (91.1%)**
InterStim Quad Lead Tined (3889)	1,068 (91.1%)
No longer manufactured	**103 (8.8%)**
InterStim Extended Electrode Quad Lead Tined (3093)	98 (8.4%)
InterStim Quad Lead (3080)	3 (0.3%)
InterStim Extended Electrode Quad Lead (3092)	2 (0.2%)
Other/Unspecified	**1 (0.1%)**
Total	**1,172 (100%)**

6.4.1 Lead Events

There were 117 product performance-related events with an underlying reported etiology related to lead function. This includes 115 events with a lead etiology and 2 events with both a lead and other etiology (including device and non-device etiologies). Of these, 103 were the initial product performance event that affected lead survival estimates.

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For leads:

- 103 had follow-up time cut-off due to product performance-related events.

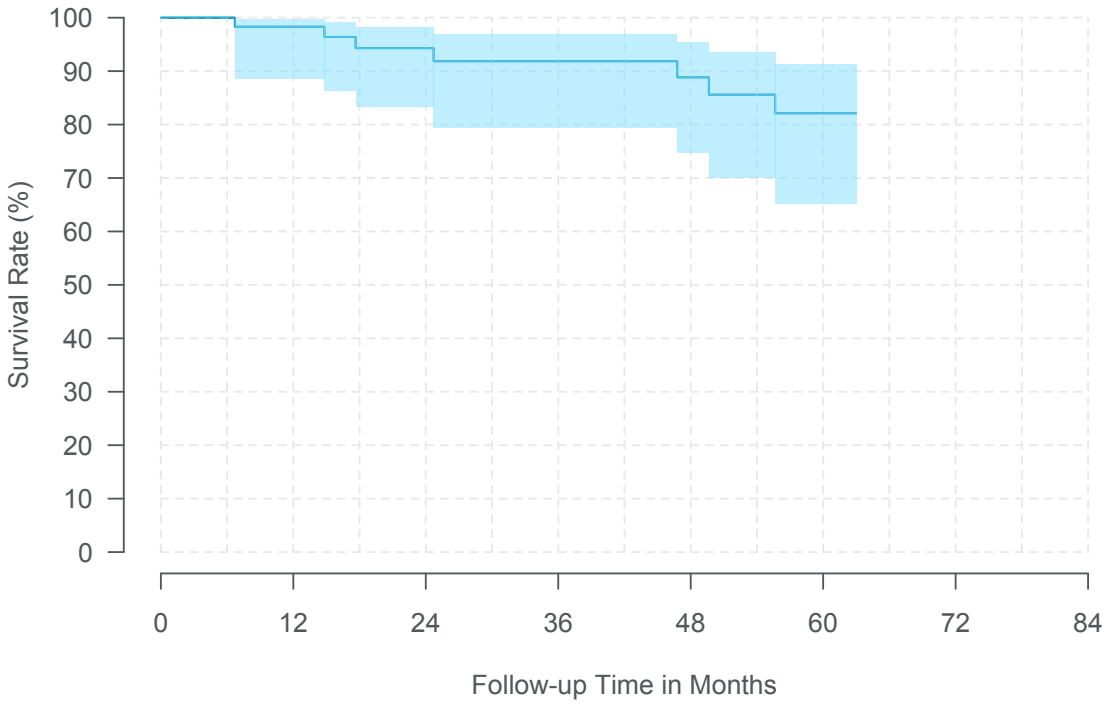
- 492 were censored in the survival analysis for the following reasons: patient expired, lead explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 577 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

6.4.2 Lead Models

The following figures and tables represent lead survival and 95% confidence intervals where at least 20 leads contributed to each 3-month interval.

6.4.2.1 Model 3093

Model Name	InterStim Extended Electrode Quad Lead Tined
FDA Approval Date	September 2002
Leads Enrolled	98
Leads Currently Active in Study	36
Device Events	8
Median Follow-up Time (Months)	23.3
Cumulative Follow-up Time (Months)	3,106



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.3% (88.7%, 99.8%)	94.3% (83.2%, 98.1%)	91.8% (79.5%, 96.9%)	88.8% (74.7%, 95.3%)	82.1% (65.2%, 91.3%)
Sample Size	51	38	30	28	24

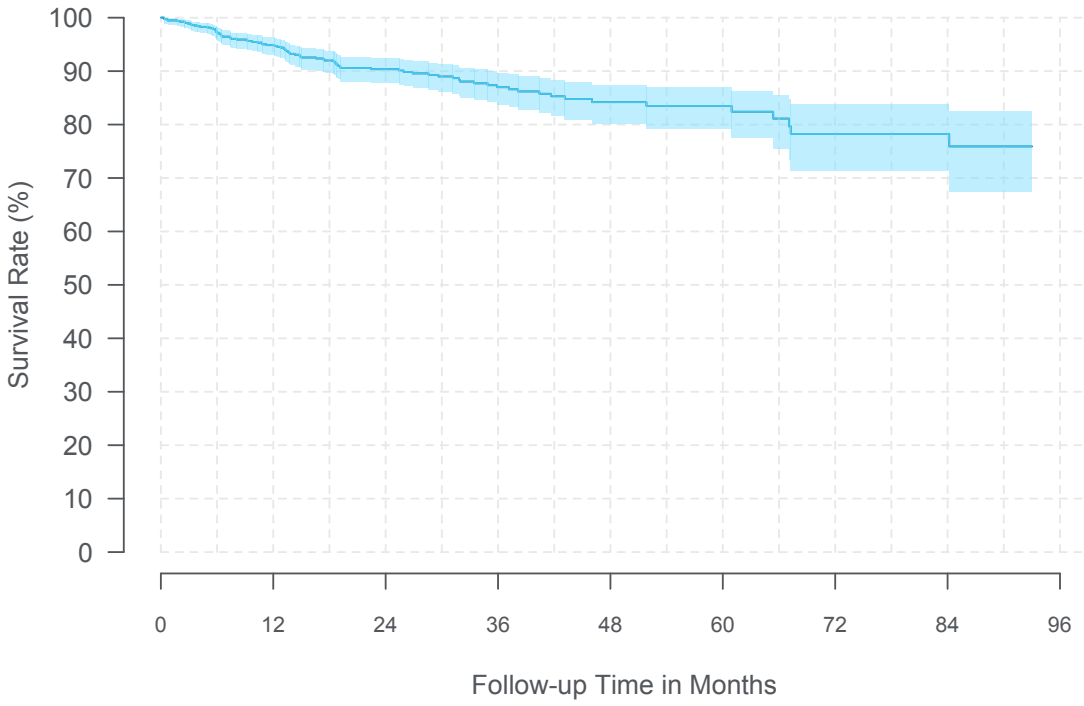
Time Interval	At 63 Months
Survival (95% CI)	82.1% (65.2%, 91.3%)
Sample Size	21

Specification: 3093	
Lead	
Length (cm)	28, 33, 41
Diameter (mm)	1.27
Electrode	
Number	4
Shape	Cylindrical/coiled
Length (mm)	3.0 (3x) and 10.2 (1x)
Individual Surface Area (mm^2)	12.0 and 40.7
Inter-Electrode Spacing: Edge to Edge (mm)	1.5
Array Length (mm)	23.7

Lead Event Summary: 3093	N
High Impedance	3
Device Electrical Impedance Issue	1
Device Lead Damage	1
Device Placement At Incorrect Location	1
Lead Fracture	1
Lead Migration/Dislodgement	1
Total	**8**

6.4.2.2 Model 3889

Model Name	InterStim Quad Lead Tined
FDA Approval Date	September 2002
Leads Enrolled	1,068
Leads Currently Active in Study	560
Device Events	93
Median Follow-up Time (Months)	18.1
Cumulative Follow-up Time (Months)	24,853



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	94.9% (93.0%, 96.2%)	90.4% (87.8%, 92.4%)	87.0% (83.7%, 89.7%)	84.2% (80.2%, 87.5%)	83.5% (79.2%, 87.0%)
Sample Size	603	372	235	137	78

Time Interval	6 Years	7 Years	At 93 Months		
Survival (95% CI)	78.2% (71.3%, 83.7%)	78.2% (71.3%, 83.7%)	75.9% (67.4%, 82.5%)		
Sample Size	48	32	21		

Specification: 3889	
Lead	
Length (cm)	28, 33, 41
Diameter (mm)	1.27
Electrode	
Number	4
Shape	Cylindrical/coiled
Length (mm)	3.0
Individual Surface Area (mm^2)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	3.0
Array Length (mm)	21.0

Lead Event Summary: 3889	N
High Impedance	33
Lead Migration/Dislodgement	26
Lead Fracture	14
Device Lead Issue	9
Low Impedance	7
Device Battery Issue	1
Device Electrical Impedance Issue	1
Device Failure	1
Device Malfunction	1
Total	**93**

6.4.3 Lead Summary

Table 6.12: Sacral Neuromodulation Lead Characteristics

Model Name	FDA Approval Date	Leads Enrolled	Leads Active	Lead Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
InterStim Extended Electrode Quad Lead Tined (model 3093)	September 2002	98	36	8	23.3	3,106
InterStim Quad Lead Tined (model 3889)	September 2002	1,068	560	93	18.1	24,853

Table 6.13: Sacral Neuromodulation Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
InterStim Extended Electrode Quad Lead Tined (model 3093)	98.3% (88.7%, 99.8%)	94.3% (83.2%, 98.1%)	91.8% (79.5%, 96.9%)	88.8% (74.7%, 95.3%)	82.1% (65.2%, 91.3%)
InterStim Quad Lead Tined (model 3889)	94.9% (93.0%, 96.2%)	90.4% (87.8%, 92.4%)	87.0% (83.7%, 89.7%)	84.2% (80.2%, 87.5%)	83.5% (79.2%, 87.0%)

Model Name	6 Years	7 Years			
InterStim Extended Electrode Quad Lead Tined (model 3093)					
InterStim Quad Lead Tined (model 3889)	78.2% (71.3%, 83.7%)	78.2% (71.3%, 83.7%)			

6.5 Extensions

From April 2010 to the report cut-off date of October 31, 2019, there were 102 extensions followed in the registry. The difference between the total number of extensions (n=102) versus the total number of neurostimulators (n=1,207) is due to the fact that not all systems require an extension, or some patients were subsequently re-implanted with a new neurostimulator.

All extensions were Model 3095. The aggregate prospective follow-up time for all extensions was 3,442 months (287 years).

6.5.1 Extension Events

There were 2 product performance-related events with an underlying reported etiology related to extension function. Of these, 1 was the initial product performance event that affected extension survival estimates.

For the purposes of survival analysis, a device's follow-up time is cut-off for one of three reasons: 1) the occurrence of a product performance-related event; 2) the occurrence of a censoring event; or 3) the device is event-free and censored at the patient's last follow-up prior to the data cut-off. For extensions:

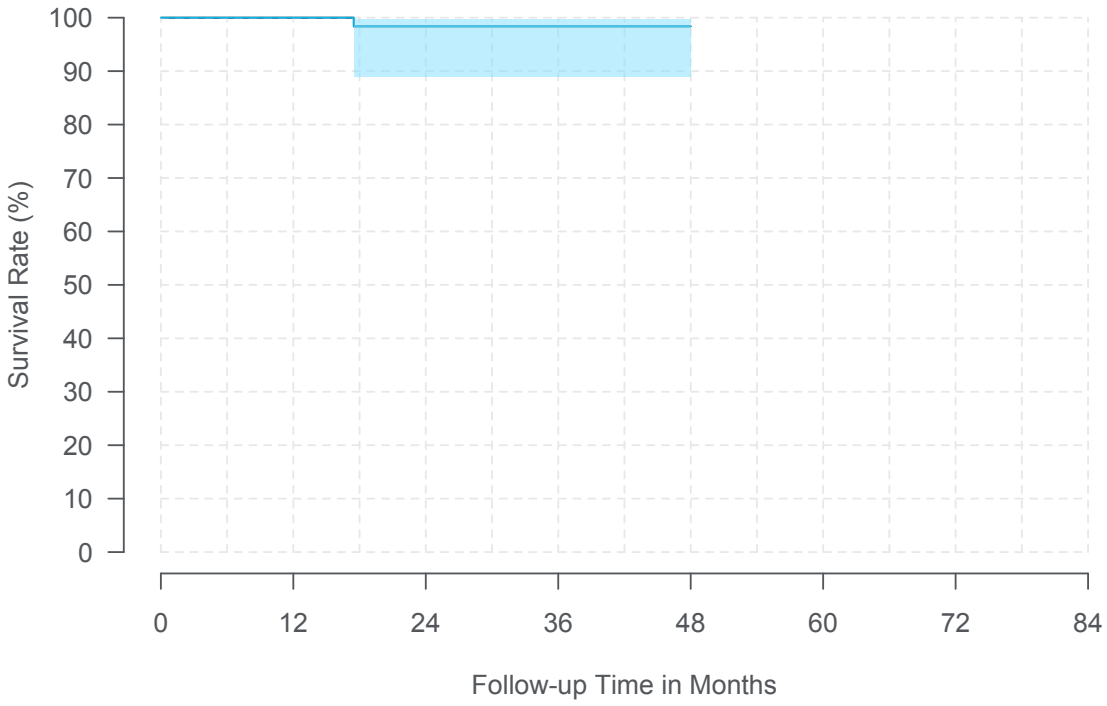
- 1 had follow-up time cut-off due to product performance-related events.
- 77 were censored in the survival analysis for the following reasons: patient expired, extension explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 24 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

6.5.2 Extension Models

The following figures and tables represent extension survival and 95% confidence intervals where at least 20 extensions contributed to each 3-month interval.

6.5.2.1 Model 3095

Model Name	Quadripolar extension
FDA Approval Date	July 1998
Extensions Enrolled	102
Extensions Currently Active in Study	24
Device Events	1
Median Follow-up Time (Months)	27.2
Cumulative Follow-up Time (Months)	3,442



Time Interval	1 Year	2 Years	3 Years	4 Years
Survival (95% CI)	100.0% (NA)	98.4% (89.0%, 99.8%)	98.4% (89.0%, 99.8%)	98.4% (89.0%, 99.8%)
Sample Size	64	51	32	20

Specification: 3095	
Length (cm)	10, 25, 51
Distal End Compatibility	Tined lead models 3889 and 3093
Distal End Set Screws	4
Proximal End INS Compatibility	InterStim Model 3023

Extension Event Summary: 3095	N
Lead Fracture	1
Total	**1**

6.5.3 Extension Summary

Table 6.14: Sacral Neuromodulation Extension Characteristics

Model Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Extension Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Quadripolar extension (model 3095)	July 1998	102	24	1	27.2	3,442

Table 6.15: Sacral Neuromodulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years
Quadripolar extension (model 3095)	100.0%	98.4%	98.4%	98.4%
	(NA)	(89.0%, 99.8%)	(89.0%, 99.8%)	(89.0%, 99.8%)