PRODUCT PERFORMANCE REPORT

SUMMARY OF DATA FROM THE MEDTRONIC POST-MARKET REGISTRY

2020

v.1.0 30March2021

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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 targeted 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 2020 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, 49 centers for DBS systems, and 24 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 13th 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 19,375 patients in our ongoing post-market registry. The registry has enrolled 59,214 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
Senior Clinical Research Manager, Post-Approval Clinical Surveillance
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
	Percept™ neurostimulator
	Soletra™ neurostimulator
Sacral Neuromodulation	InterStim™ neurostimulator
	InterStim™ Micro neurostimulator
	InterStim™ SureScan™ MRI Lead

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 determine 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.

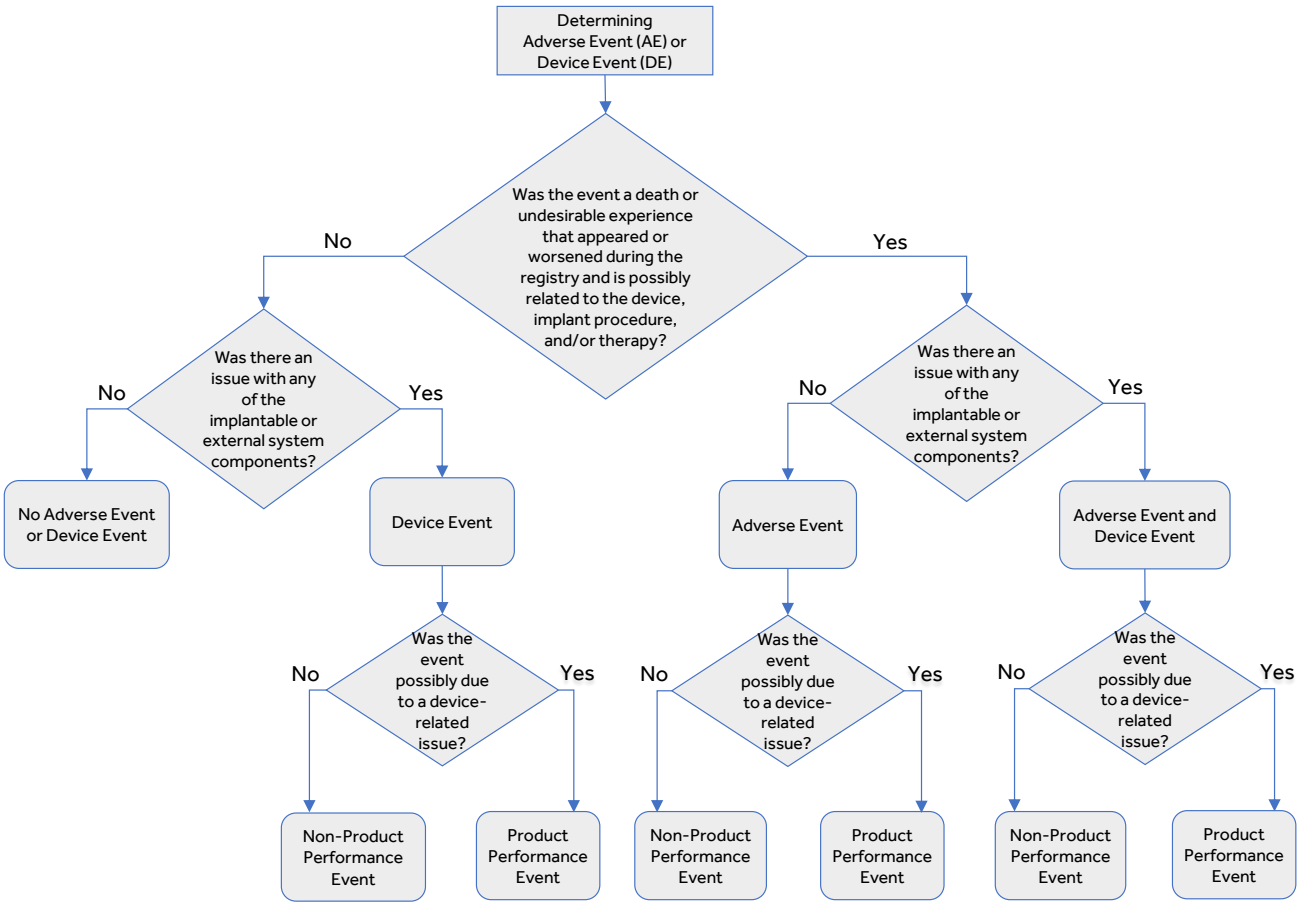


Figure 2.1: Adverse Event/Device Event Flowchart

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, 2020. Seventy-six centers spanning 13 countries/territories 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.

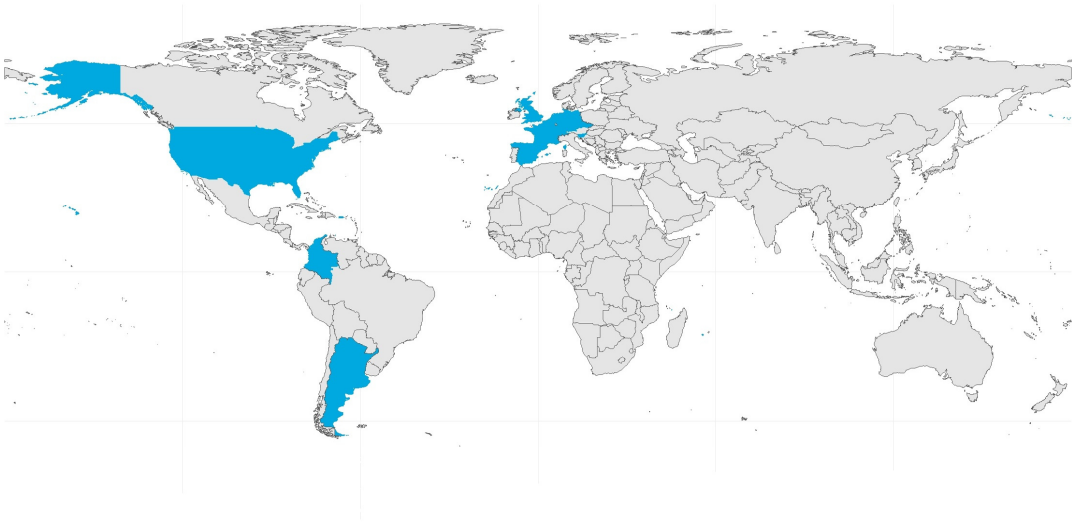


Figure 3.1: Countries with Targeted Drug Delivery Therapy Patients in Registry (Highlighted)

3.1.2 Patients

There were 9,370 total targeted drug delivery system patients enrolled through October 31, 2020. In Table 3.1 and Figure 3.2, 58.1% 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 22.1% for treatment of spasticity, and 17.7% 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.

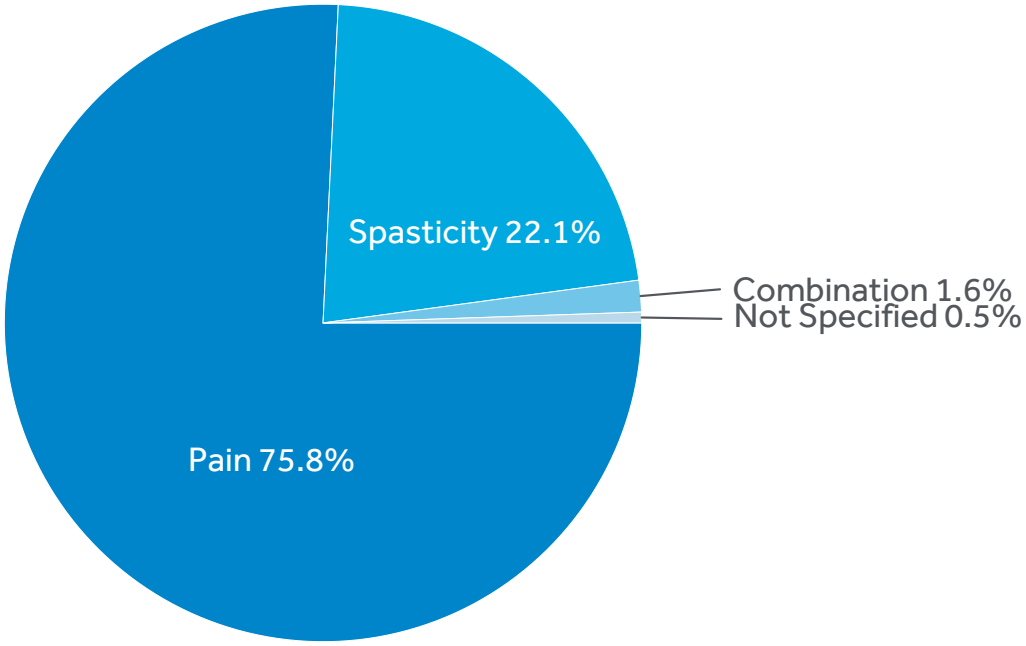


Figure 3.2: Targeted Drug Delivery Primary Treatment Indications

Table 3.1: Targeted Drug Delivery Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Pain	**7,099 (75.8%)**
Non-malignant pain	5,444 (58.1%)
Malignant pain	1,654 (17.7%)
Pain, Not specified	1 (0.0%)
Spasticity	**2,070 (22.1%)**
Combination	**150 (1.6%)**
Non-malignant pain & Spasticity	148 (1.6%)
Malignant pain & Spasticity	1 (0.0%)
Non-malignant pain & Chemotherapy	1 (0.0%)
Not Specified[b]	**51 (0.5%)**
Total Patients	**9,370 (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	629
Abdominal/Visceral	382
Extremity	284
Pelvic	227
Thoracic	184
Head/Neck	107
Other	162
Not Specified	439
Total Sites of Pain[a]	**2,414**

[a] In 1,655 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	1,866 (33.4%)
Back Pain without Leg Pain	1,568 (28.0%)
General Neuropathic Condition	240 (4.3%)
CRPS I[a]	181 (3.2%)
Peripheral Neuropathy	82 (1.5%)
Joint Pain/Arthritis	70 (1.3%)
General Nociceptive Condition	52 (0.9%)
CRPS II[a]	37 (0.7%)
Osteoporosis	20 (0.4%)
Other	522 (9.3%)
Not Specified	955 (17.1%)
Total Patients[b]	**5,593**

[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	356 (77.6%)	243 (13.8%)	599 (27.0%)
Multiple Sclerosis	0 (0.0%)	543 (30.9%)	543 (24.5%)
Spinal Cord Injury	7 (1.5%)	342 (19.4%)	349 (15.7%)
Brain Injury	35 (7.6%)	120 (6.8%)	155 (7.0%)
Stroke	1 (0.2%)	91 (5.2%)	92 (4.1%)
Other	16 (3.5%)	191 (10.9%)	207 (9.3%)
Not Specified	44 (9.6%)	230 (13.1%)	274 (12.3%)
Total Patients[a]	**459**	**1,760**	**2,219**

[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 2,271 product performance events reported between August 7, 2003 and October 31, 2020, in patients with targeted drug delivery systems. These events represent 20.6% of the total reported events (2,271/11,042), which occurred in 1,467 (15.7%) of the 9,370 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=4).

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 2,374 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

A total of 1,554 (68.4%) of the 2,271 product performance events were only related to the catheter, while 511 (22.5%) events were only related to the pump. Since the SynchroMed II pump temporarily stops the rotor of the pump motor and suspends drug infusion for the duration of the MRI exposure for patient safety, the motor stall event counts do not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. For the remaining events, 148 (6.5%) were related to other component and 58 (2.6%) were related to other etiologies. Relatedness is reported by the physician.

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=9,370[b]
RPA Determination	**316**	**1.02**	**288 (3.07%)**
Pump Motor Stall	178	0.57	172 (1.84%)
Laboratory Overinfusion Finding[c]	34	0.11	33 (0.35%)
Corrosion And/Or Gear Wear	28	0.09	28 (0.30%)
Battery High Resistance	11	0.04	11 (0.12%)
Confirmed Overinfusion[d]	11	0.04	5 (0.05%)
Reduced Battery Performance	10	0.03	10 (0.11%)
Deformed Pump Tube	8	0.03	7 (0.07%)
Motor Feedthrough Anomaly	7	0.02	7 (0.07%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=9,370[b]
Reservoir Access Issues Due To Residue	7	0.02	6 (0.06%)
Concave Pump Shield	3	0.01	3 (0.03%)
Alarm And/Or Resonator Anomaly	2	0.01	2 (0.02%)
Hole In Pump Tube	2	0.01	1 (0.01%)
Other[e]	15	0.05	15 (0.16%)
Physician's Determination	**1,955**	**6.28**	**1,309 (13.97%)**
Catheter Occlusion	427	1.37	381 (4.07%)
Catheter Dislodgement	394	1.27	330 (3.52%)
Catheter Break/Cut	233	0.75	207 (2.21%)
Catheter Kink	227	0.73	198 (2.11%)
Pump Motor Stall[f]	108	0.35	90 (0.96%)
Device Malfunction[g]	101	0.32	91 (0.97%)
Catheter Related Complication	99	0.32	92 (0.98%)
Catheter Leakage	68	0.22	64 (0.68%)
Pump Reservoir Volume Discrepancy	50	0.16	37 (0.39%)
Catheter Disconnection At Pump	49	0.16	48 (0.51%)
Pump Unable To Enter/Withdraw From Catheter Access Port	37	0.12	31 (0.33%)
Device Difficult To Use	24	0.08	24 (0.26%)
Pump Underinfusion	22	0.07	18 (0.19%)
Device Connection Issue	21	0.07	19 (0.20%)
Pump Connector Break/Cut	17	0.05	16 (0.17%)
Medical Device Complication[h]	11	0.04	10 (0.11%)
Catheter Disconnection Between Catheter Segments	8	0.03	8 (0.09%)
Catheter Access Port Issue	6	0.02	6 (0.06%)
Catheter Damage	6	0.02	6 (0.06%)
Device Breakage	6	0.02	6 (0.06%)
Device Issue	5	0.02	5 (0.05%)
Device Alarm Issue	4	0.01	4 (0.04%)
Catheter Dysfunction	3	0.01	2 (0.02%)
Pump Not Infusing	3	0.01	3 (0.03%)
Device Damage	2	0.01	2 (0.02%)
Physician Reported Overinfusion[i]	2	0.01	2 (0.02%)
Other[e]	22	0.07	22 (0.23%)
Total	**2,271**	**7.30**	**1,467 (15.66%)**

[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] Includes pumps that had a laboratory finding consistent with pump overinfusion.
[d] Patient had clinical signs and symptoms consistent with pump overinfusion, pump returned and positive laboratory test.
[e] Composed of event codes with 1 event each.
[f] Of the 108 physician determined motor stalls, 93 had a pump etiology; 1 had another etiology and 14 had a MRI (>24 hr) etiology. Of the 14 MRI (>24 hr) etiology, 2 pumps were replaced and 12 remain active in the patients.
[g] The majority of these events were attributed to the PTM.
[h] This category includes a combination of mechanical and electrical observations.
[i] Patient had clinical signs and symptoms, but pump was not returned and analyzed.

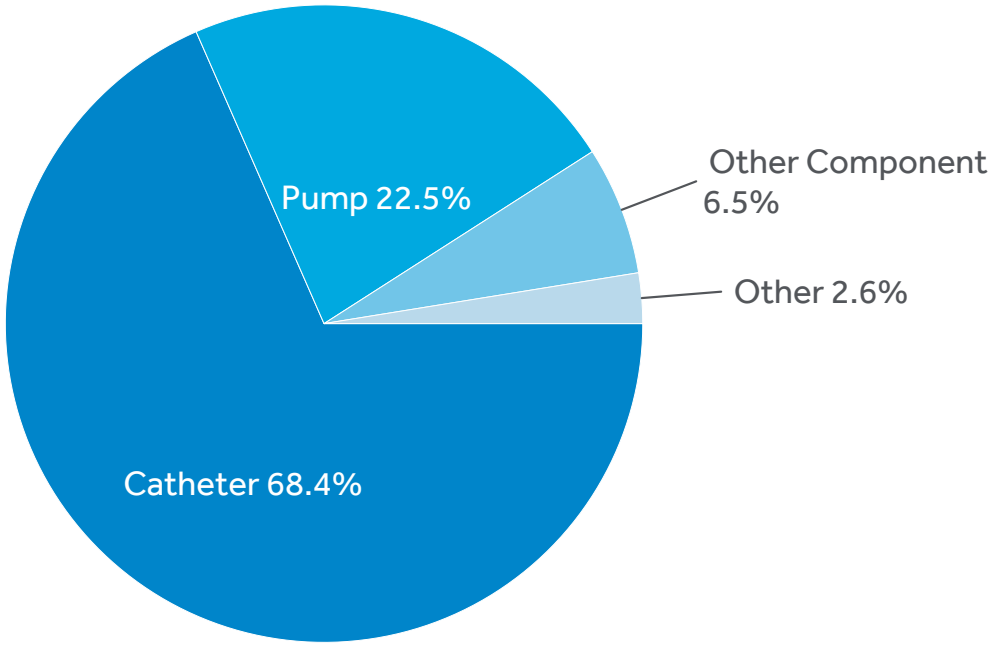


Figure 3.3: Targeted Drug Delivery System Product Performance Events by Relatedness

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=2,794)
- 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=2,794	SAE Per 100 Patient Months	Patients with SAE Requiring Surgical Intervention n (%) N=2,794
General disorders and administration site conditions	**91**	**85 (3.04%)**	**0.16**	**21 (0.75%)**
Therapeutic and nontherapeutic effects (excl toxicity)	57	53 (1.90%)	0.10	3 (0.11%)
Complications associated with device	24	24 (0.86%)	0.04	16 (0.57%)
General system disorders NEC [a]	7	7 (0.25%)	0.01	1 (0.04%)
Other[b]	3	3 (0.11%)	0.01	2 (0.07%)
Infections and infestations	**65**	**60 (2.15%)**	**0.12**	**52 (1.86%)**
Infections - pathogen unspecified	46	43 (1.54%)	0.08	40 (1.43%)
Bacterial infectious disorders	19	19 (0.68%)	0.03	13 (0.47%)
Nervous system disorders	**39**	**36 (1.29%)**	**0.07**	**12 (0.43%)**
Neurological disorders NEC [a]	16	16 (0.57%)	0.03	7 (0.25%)
Neuromuscular disorders	9	9 (0.32%)	0.02	3 (0.11%)
Headaches	5	5 (0.18%)	0.01	0 (0.00%)
Other[b]	9	9 (0.32%)	0.02	3 (0.11%)
Injury, poisoning and procedural complications	**34**	**33 (1.18%)**	**0.06**	**10 (0.36%)**
Procedural related injuries and complications NEC [a]	15	15 (0.54%)	0.03	8 (0.29%)
Overdoses and underdoses NEC [a]	13	13 (0.47%)	0.02	0 (0.00%)
Other[b]	6	6 (0.21%)	0.01	2 (0.07%)
Other SOC Terms (<1.0% Threshold)	**26**	**24 (0.86%)**	**0.05**	**6 (0.21%)**
Total	**255**	**216 (7.73%)**	**0.45**	**95 (3.40%)**

[a] Not Elsewhere Classified.
[b] 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 ▪ Contrast study demonstrates extravasation of contrast 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 contrast study performed or contrast study result inconclusive.
Possible CSF Leak	**Intermittent** post-operative **positional** headache for >14 days without report of subcutaneous fluid collection. No contrast study performed or contrast study result inconclusive.
Not CSF Leak	Acute post-operative non-positional headache lasting less than 14 days.

The potential CSF leak status (N=339) at the time of this analysis is presented in Table 3.8 with a definitive and probable CSF leak rate of 1.4% (130/9,370). 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]
339	114	16	21	171	17

[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 (IM), 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 132 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 2020 indicates an incidence of 0.23% (16/7,099) for pain patients and 0.00% (0/2,070) for 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	9			1	8
2018	4	1			3
2019	5	1			4
2020	1				1
Total	**132**	**9**	**7**	**23**	**93**

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 2,374 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 1,315 (55.4%) deaths have been reported in this patient registry study based upon patients receiving therapy for malignant pain, 806 (34.0%) for non-malignant pain, 236 (9.9%) for spasticity, 12 (0.5%) for non-malignant pain & spasticity, and 5 (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. **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	1,315 (55.4%)
Non-malignant pain	806 (34.0%)
Spasticity	236 (9.9%)
Non-malignant pain & Spasticity	12 (0.5%)
Not Specified	5 (0.2%)
Total	**2,374 (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, 2020, there were 11,671 pumps followed in the registry. The difference between the total number of patients (n=9,370) 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 365,003 months (30,417 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	**6,420 (61.22%)**
Pre-Enhancements[a]	4,631 (44.16%)
GW3/FT/DLC Enhancements	1,252 (11.94%)
GW3/FT Enhancements[a]	537 (5.12%)
SynchroMed II 20 mL	**4,066 (38.78%)**
Pre-Enhancements[a]	2,962 (28.25%)
GW3/FT/DLC Enhancements	741 (7.07%)
GW3/FT Enhancements[a]	363 (3.46%)
SynchroMed EL 18 mL[a]	**1,146 (5.16%)**
SynchroMed EL 10 mL[a]	**34 (0.15%)**
SynchroMed Classic[a]	**5 (0.02%)**
Total	**11,671 (100%)**

[a] No longer manufactured.

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

3.3.2 Pump Events

There were 516 product performance-related events with an underlying reported etiology related to pump function. This includes 511 events with a pump etiology and 5 events with both a pump and other etiology (including device and non-device etiologies). Of these, 433 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 29.7% (1,691/5,692). 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 516 pump events, 39.7% (205/516) 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:

- 433 had follow up time cut-off due to product performance-related events.
- 8,642 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.
- 2,596 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.

3.3.3 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.

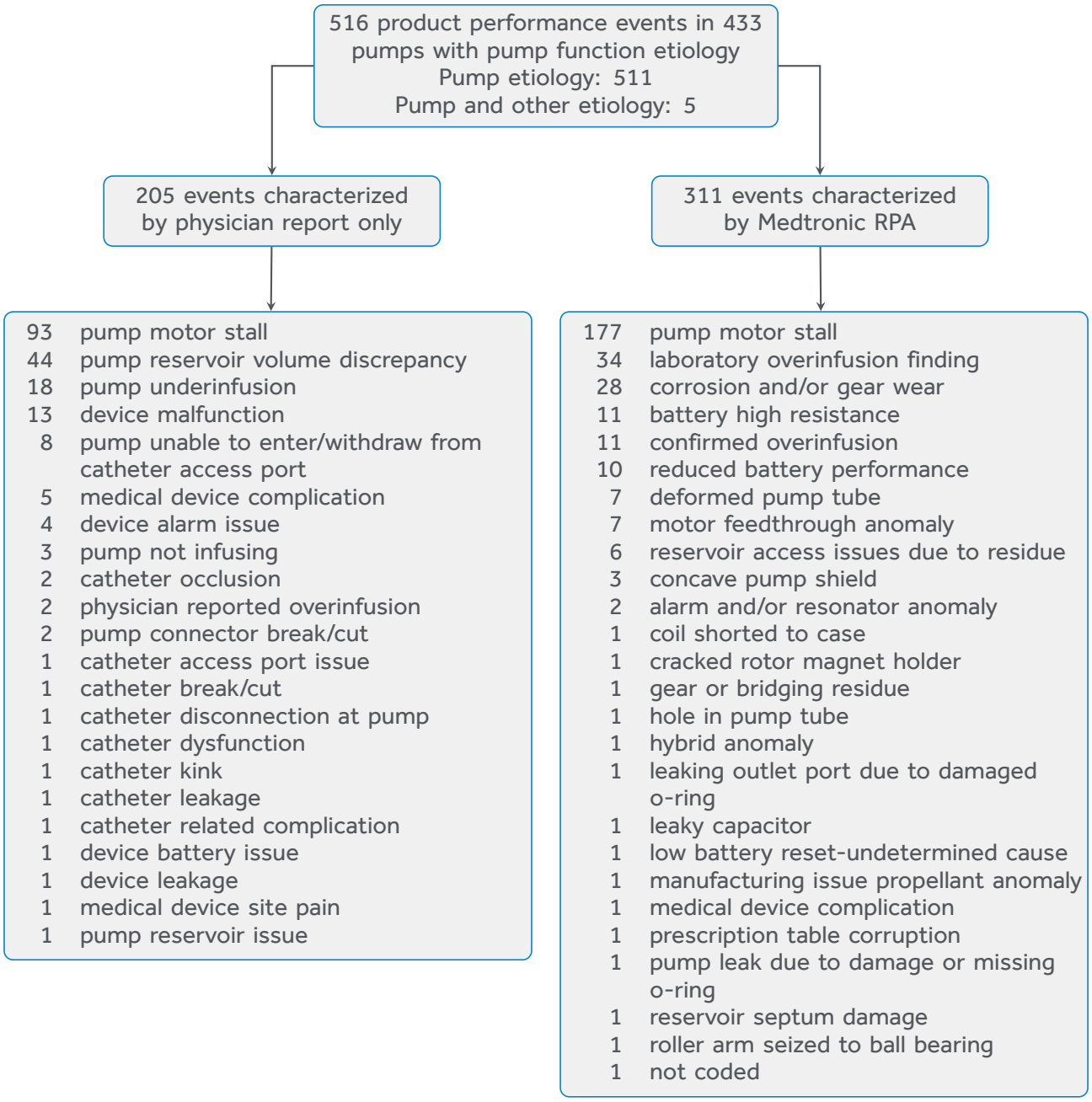
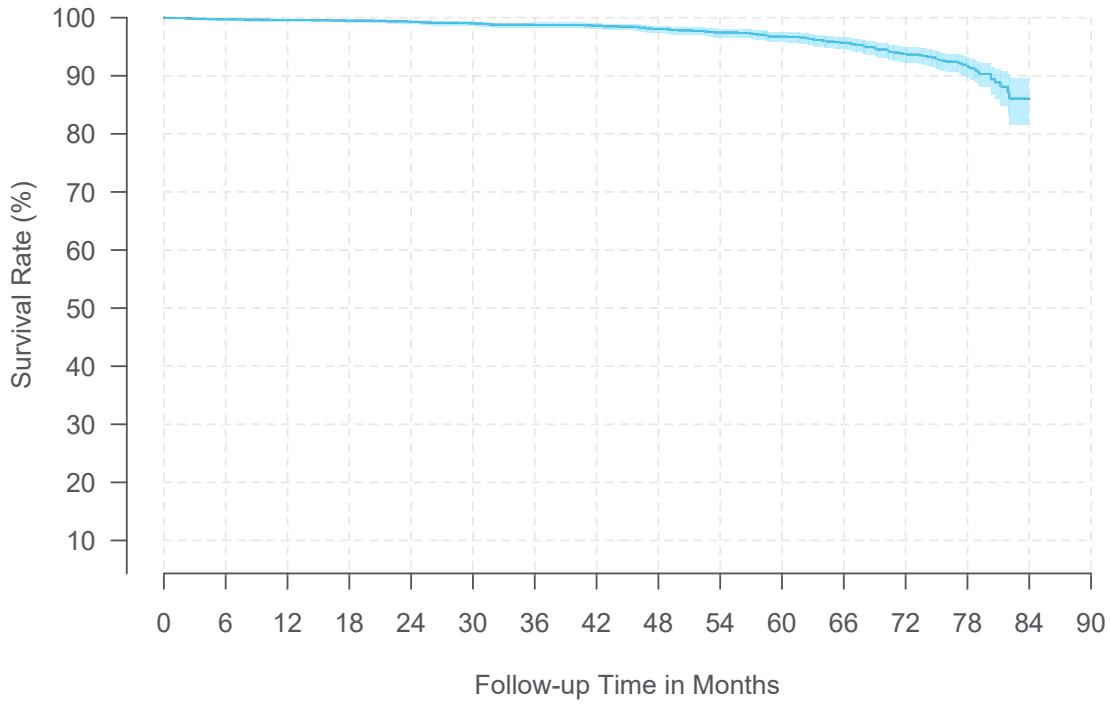


Figure 3.4: Distribution of Pump Function Etiology Product Performance Events

3.3.3.1 Model SynchroMed II 20 mL

Model/Name	SynchroMed II 20 mL
FDA Approval Date	September 2003
Pumps Enrolled	4,066
Pumps Currently Active in Study	1,026
Device Events	119
Median Follow-up Time (Months)	31.4
Cumulative Follow-up Time (Months)	150,696



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (99.3%, 99.8%)	99.3% (98.9%, 99.5%)	98.7% (98.2%, 99.1%)	98.1% (97.4%, 98.6%)	96.7% (95.8%, 97.5%)
Sample Size	2,972	2,418	1,911	1,509	1,178

Time Interval	6 Years	7 Years			
Survival (95% CI)	93.8% (92.3%, 95.0%)	86.1% (81.5%, 89.6%)			
Sample Size	820	20			

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.

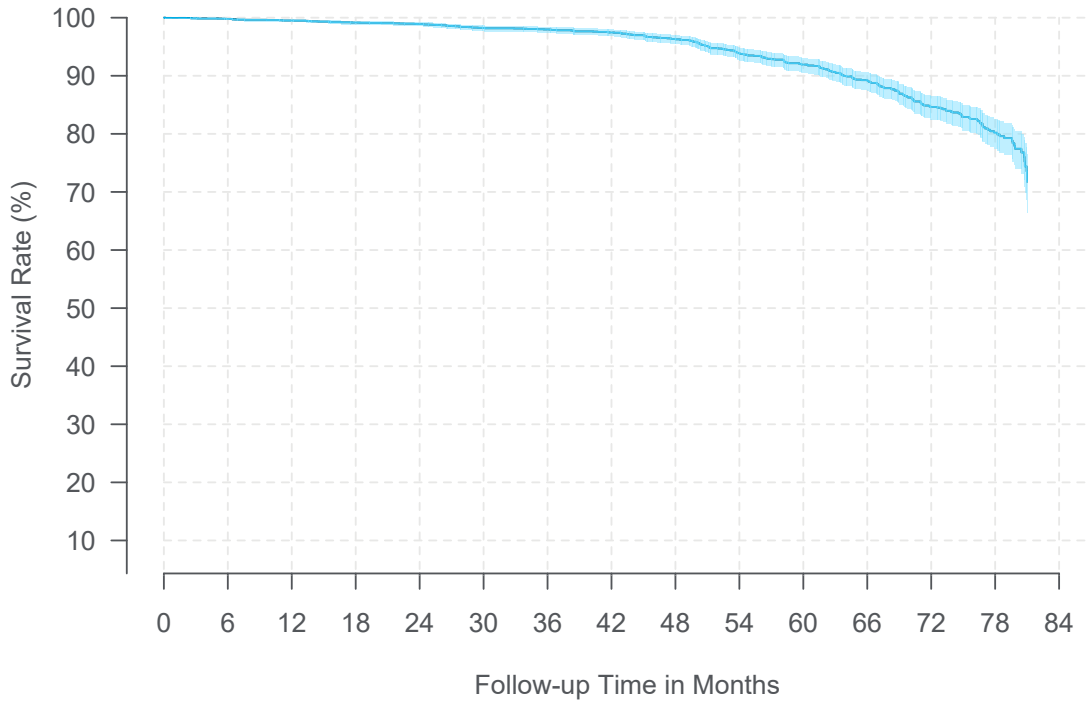
[c] Nontherapeutic (if therapy is to be temporarily discontinued).

Pump Event Summary: SynchroMed II 20 mL	N
RPA Determination	**65**
Pump Motor Stall	33
Laboratory Overinfusion Finding	7
Battery High Resistance	6
Corrosion And/Or Gear Wear	4
Motor Feedthrough Anomaly	3
Reduced Battery Performance	2
Other[a]	10
Physician's Determination	**54**
Pump Motor Stall	22
Pump Reservoir Volume Discrepancy	10
Device Malfunction	5
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Device Alarm Issue	3
Medical Device Complication	3
Other[a]	7
Total	**119**

[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	6,420
Pumps Currently Active in Study	1,584
Device Events	280
Median Follow-up Time (Months)	20.2
Cumulative Follow-up Time (Months)	182,123



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (99.3%, 99.7%)	98.9% (98.5%, 99.2%)	98.0% (97.4%, 98.4%)	96.3% (95.4%, 97.0%)	91.9% (90.6%, 93.1%)
Sample Size	3,861	2,963	2,231	1,666	1,142

Time Interval	6 Years	At 81 Months			
Survival (95% CI)	84.6% (82.5%, 86.5%)	71.8% (66.4%, 76.5%)			
Sample Size	688	79			

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.

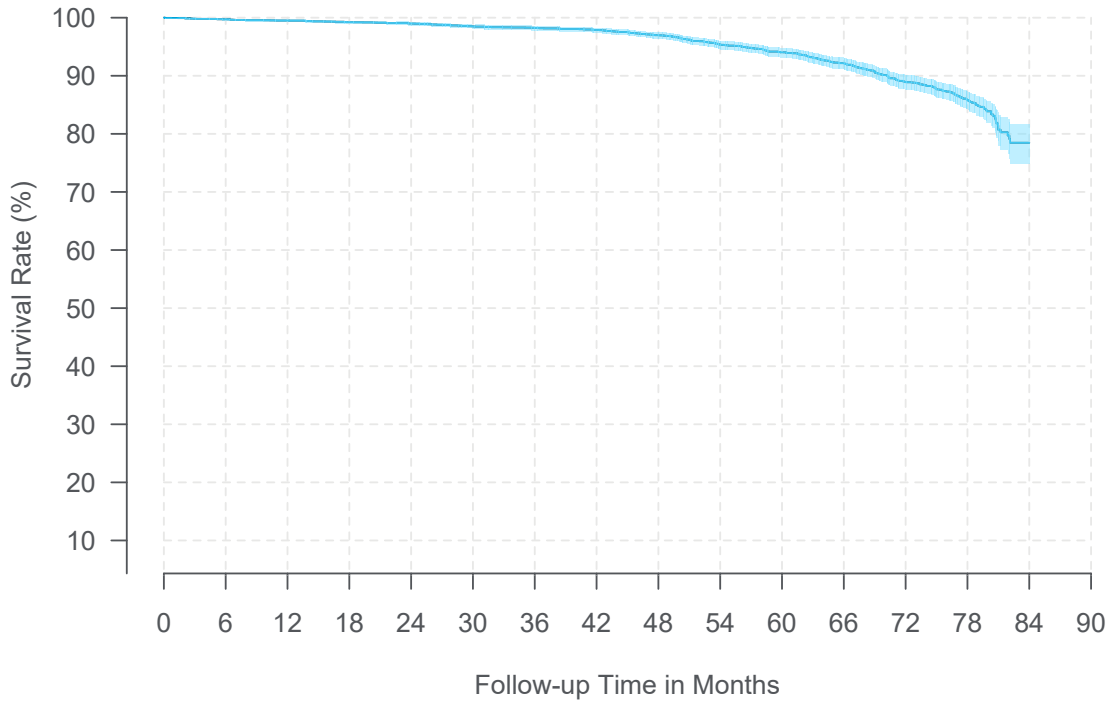
[c] Nontherapeutic (if therapy is to be temporarily discontinued).

Pump Event Summary: SynchroMed II 40 mL	N
RPA Determination	**184**
Pump Motor Stall	121
Laboratory Overinfusion Finding	24
Reduced Battery Performance	7
Corrosion And/Or Gear Wear	6
Deformed Pump Tube	5
Confirmed Overinfusion	4
Battery High Resistance	3
Concave Pump Shield	3
Reservoir Access Issues Due To Residue	3
Motor Feedthrough Anomaly	2
Other[a]	6
Physician's Determination	**96**
Pump Motor Stall	41
Pump Reservoir Volume Discrepancy	22
Pump Underinfusion	10
Device Malfunction	6
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Pump Not Infusing	2
Other[a]	11
Total	**280**

[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	7,593
Pumps Currently Active in Study	568
Device Events	384
Median Follow-up Time (Months)	34.7
Cumulative Follow-up Time (Months)	285,210



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%)	97.0% (96.4%, 97.4%)	94.0% (93.2%, 94.8%)
Sample Size	5,295	4,573	3,813	3,093	2,320

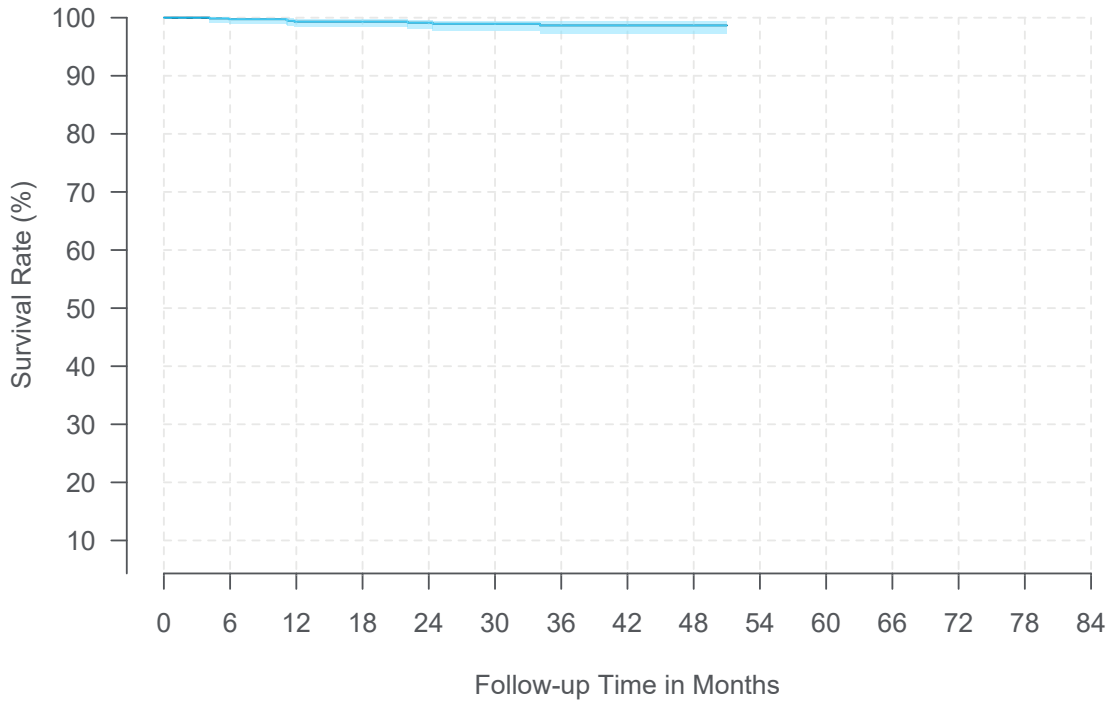
Time Interval	6 Years	7 Years			
Survival (95% CI)	88.9% (87.7%, 90.1%)	78.5% (74.9%, 81.6%)			
Sample Size	1,508	33			

Pump Event Summary: SynchroMed II Pre-Enhancements	Total
RPA Determination	**245**
Pump Motor Stall	154
Laboratory Overinfusion Finding	30
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
Concave Pump Shield	2
Other[a]	9
Physician's Determination	**139**
Pump Motor Stall	62
Pump Reservoir Volume Discrepancy	29
Device Malfunction	9
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]	6
Total	**384**

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

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	900
Pumps Currently Active in Study	487
Device Events	8
Median Follow-up Time (Months)	30.4
Cumulative Follow-up Time (Months)	24,585



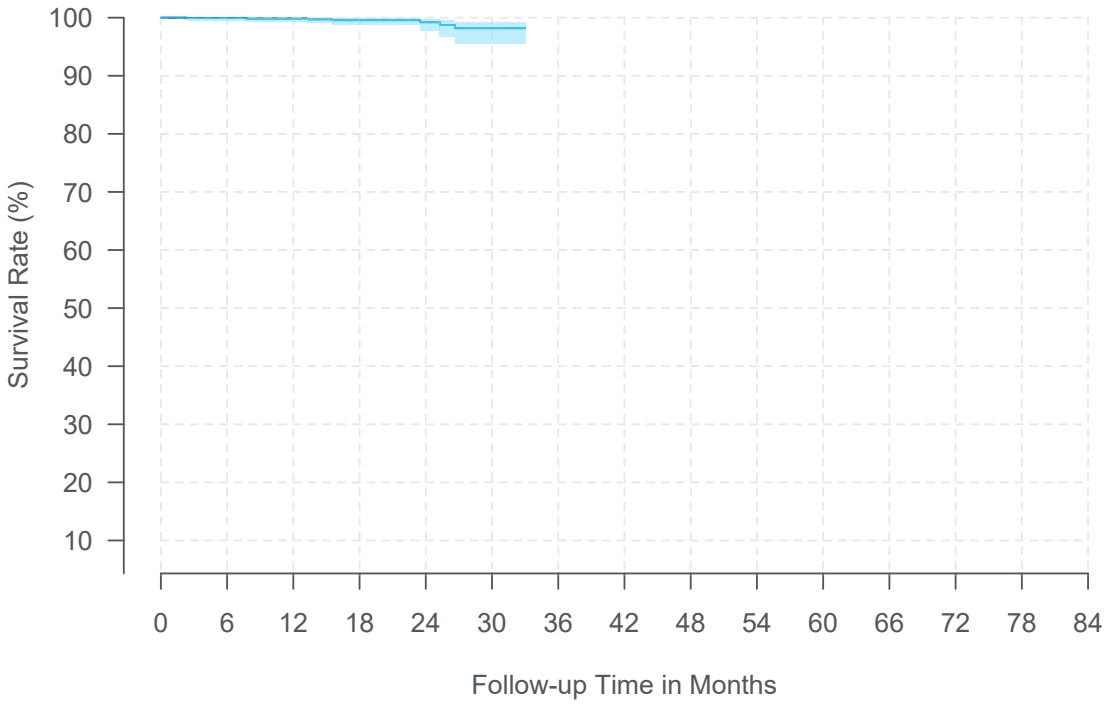
Time Interval	1 Year	2 Years	3 Years	4 Years	At 51 Months
Survival (95% CI)	99.3% (98.4%, 99.7%)	99.1% (98.1%, 99.6%)	98.7% (97.3%, 99.4%)	98.7% (97.3%, 99.4%)	98.7% (97.3%, 99.4%)
Sample Size	686	542	313	82	51

Pump Event Summary: SynchroMed II GW3/FT Enhancements	Total
RPA Determination	**0**
Physician's Determination	**8**
Pump Reservoir Volume Discrepancy	3
Other[a]	5
Total	**8**

[a] 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	1,993
Pumps Currently Active in Study	1,555
Device Events	7
Median Follow-up Time (Months)	9.9
Cumulative Follow-up Time (Months)	23,024



Time Interval	1 Year	2 Years	At 33 Months
Survival (95% CI)	99.8% (99.4%, 100%)	99.2% (97.8%, 99.7%)	98.2% (95.6%, 99.3%)
Sample Size	852	266	40

Pump Event Summary: SynchroMed II GW3/FT/DLC Enhancements	Total
RPA Determination	**4**
Concave Pump Shield	1
Laboratory Overinfusion Finding	1
Pump Leak Due To Damage Or Missing O-Ring	1
Reservoir Septum Damage	1
Physician's Determination	**3**
Pump Underinfusion	2
Device Malfunction	1
Total	**7**

3.3.4 Pump Summary

Table 3.13: 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	4,066	1,026	119	31.4	150,696
SynchroMed II 40 mL	September 2003	6,420	1,584	280	20.2	182,123
SynchroMed II Pre-Enhancements[a]	September 2003	7,593	568	384	34.7	285,210
SynchroMed II GW3/FT Enhancements[a]	September 2015 (GW3) November 2015 (FT)	900	487	8	30.4	24,585
SynchroMed II GW3/FT/DLC Enhancements[a]	April 2017 (DLC)	1,993	1,555	7	9.9	23,024

[a] For explanation of enhancements see Section 3.3.1.

Table 3.14: 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% (99.3%, 99.8%)	99.3% (98.9%, 99.5%)	98.7% (98.2%, 99.1%)	98.1% (97.4%, 98.6%)	96.7% (95.8%, 97.5%)
SynchroMed II 40 mL	99.5% (99.3%, 99.7%)	98.9% (98.5%, 99.2%)	98.0% (97.4%, 98.4%)	96.3% (95.4%, 97.0%)	91.9% (90.6%, 93.1%)
SynchroMed II Pre-Enhancements	99.5% (99.3%, 99.7%)	99.0% (98.7%, 99.2%)	98.2% (97.8%, 98.6%)	97.0% (96.4%, 97.4%)	94.0% (93.2%, 94.8%)
SynchroMed II GW3/FT Enhancements	99.3% (98.4%, 99.7%)	99.1% (98.1%, 99.6%)	98.7% (97.3%, 99.4%)	98.7% (97.3%, 99.4%)	
SynchroMed II GW3/FT/DLC Enhancements	99.8% (99.4%, 100%)	99.2% (97.8%, 99.7%)			

Model Name	6 Years	7 Years			
SynchroMed II 20 mL	93.8% (92.3%, 95.0%)	86.1% (81.5%, 89.6%)			
SynchroMed II 40 mL	84.6% (82.5%, 86.5%)				
SynchroMed II Pre-Enhancements	88.9% (87.7%, 90.1%)	78.5% (74.9%, 81.6%)			
SynchroMed II GW3/FT Enhancements					
SynchroMed II GW3/FT/DLC Enhancements					

Table 3.15: TDD SynchroMed II Pump Events by Enhancements

Pump Event	Pre-Enhancements	GW3/FT Enhancements	GW3/FT/DLC Enhancements
RPA Determination	**245**	**0**	**4**
Pump Motor Stall	154	0	0
Laboratory Overinfusion Finding	30	0	1
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
Concave Pump Shield	2	0	1
Pump Leak Due To Damage Or Missing O-Ring	0	0	1
Reservoir Septum Damage	0	0	1
Other [a]	9	0	0
Physician's Determination	**139**	**8**	**3**
Pump Motor Stall	62	1	0
Pump Reservoir Volume Discrepancy	29	3	0
Device Malfunction	9	1	1
Pump Unable To Enter/Withdraw From Catheter Access Port	8	0	0
Pump Underinfusion	8	0	2
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
Catheter Access Port Issue	0	1	0
Catheter Disconnection At Pump	0	1	0
Pump Reservoir Issue	0	1	0
Other [a]	6	0	0
Total	**384**	**8**	**7**

[a] Composed of event codes with 1 event each for SynchroMed II Pre-Enhancements.

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 drug approved intrathecal formulations. Medtronic has not performed long-term drug stability/compatibility and safety and/or efficacy of drugs not listed in the approved SynchroMed II labeling. 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, 2020, 8,398 patients (56.0% female, mean/SD age 54.1/17.5 years) have enrolled in the registry and have been implanted with 10,486 SynchroMed II pumps. At least one drug record was available on each of 10,113 pumps; if no drug records were available (n=373 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 3,062 (30.3%) SynchroMed II pumps were classified as On-Label where there was no evidence of Off-Label drug/admixture exposure. A total of 7,051 (69.7 %) pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. There were a total of 399 reported SynchroMed II pump product performance events during the study observation period. In addition to the 396 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 399 pump failure events occurred in pumps with no drug records available. Of the remaining 396 SynchroMed II pump failures, 217 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 3.92% (396/10,113) with a median follow-up of 25.9 months.

For the 217 pump failures due to motor stall, 116 of the events were associated with the patient presenting clinical signs or symptoms of possible drug withdrawal or increasing pain or spasticity. The other 101 events had no patient reported signs or symptoms associated with the event, but had a physician report of a motor stall occurrence.

Table 3.16: Targeted Drug Delivery Primary Indications by On/Off-Label Pump Groups

Primary Indication[a]	On-Label N=3,062	Off-Label N=7,051
Non-malignant Pain	912 (15.0%)	5,181 (85.0%)
Malignant Pain	46 (3.0%)	1,469 (97.0%)
Spasticity	2,104 (89.9%)	236 (10.1%)
Multiple/Unknown	0 (0.0%)	165 (100.0%)

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

3.4.3.1 Total Study Population

A total of 3,062 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 7,051 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.

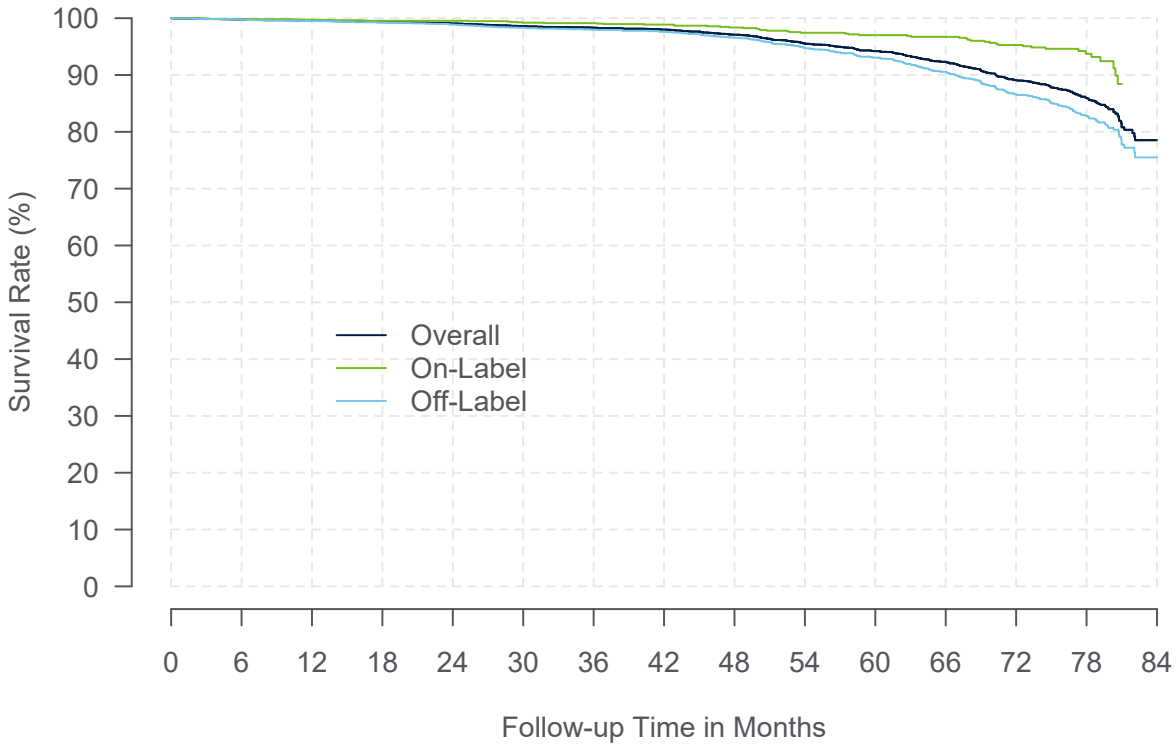


Figure 3.5: SynchroMed II Cumulative Survival (All Therapies)

Table 3.17: 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	99.6%	99.1%	98.3%	97.1%	94.2%	89.1%	80.8%	78.5%
	Sample Size	6,732	5,322	4,107	3,146	2,308	1,502	211	33
On-Label	Survival	99.7%	99.5%	99.1%	98.4%	97.0%	95.3%	88.4%	
	Sample Size	2,120	1,648	1,208	898	669	467	49	
Off-Label	Survival	99.5%	98.9%	98.0%	96.5%	93.1%	86.6%	77.7%	75.5%
	Sample Size	4,612	3,674	2,899	2,248	1,639	1,035	162	22

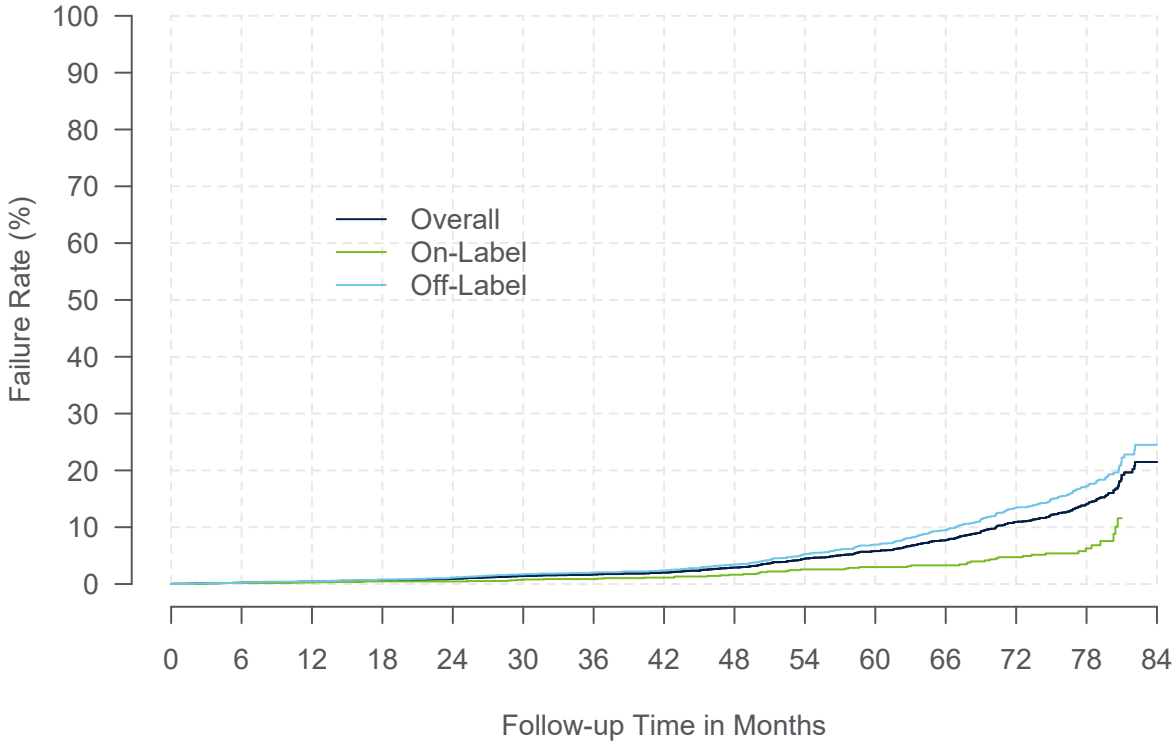


Figure 3.6: SynchroMed II Cumulative Failure (All Therapies)

Table 3.18: 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	0.4%	0.9%	1.7%	2.9%	5.8%	10.9%	19.2%	21.5%
	Sample Size	6,732	5,322	4,107	3,146	2,308	1,502	211	33
On-Label	Failure	0.3%	0.5%	0.9%	1.6%	3.0%	4.7%	11.6%	
	Sample Size	2,120	1,648	1,208	898	669	467	49	
Off-Label	Failure	0.5%	1.1%	2.0%	3.5%	6.9%	13.4%	22.3%	24.5%
	Sample Size	4,612	3,674	2,899	2,248	1,639	1,035	162	22

3.4.3.2 Pain Study Population

A total of 958 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 6,650 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.

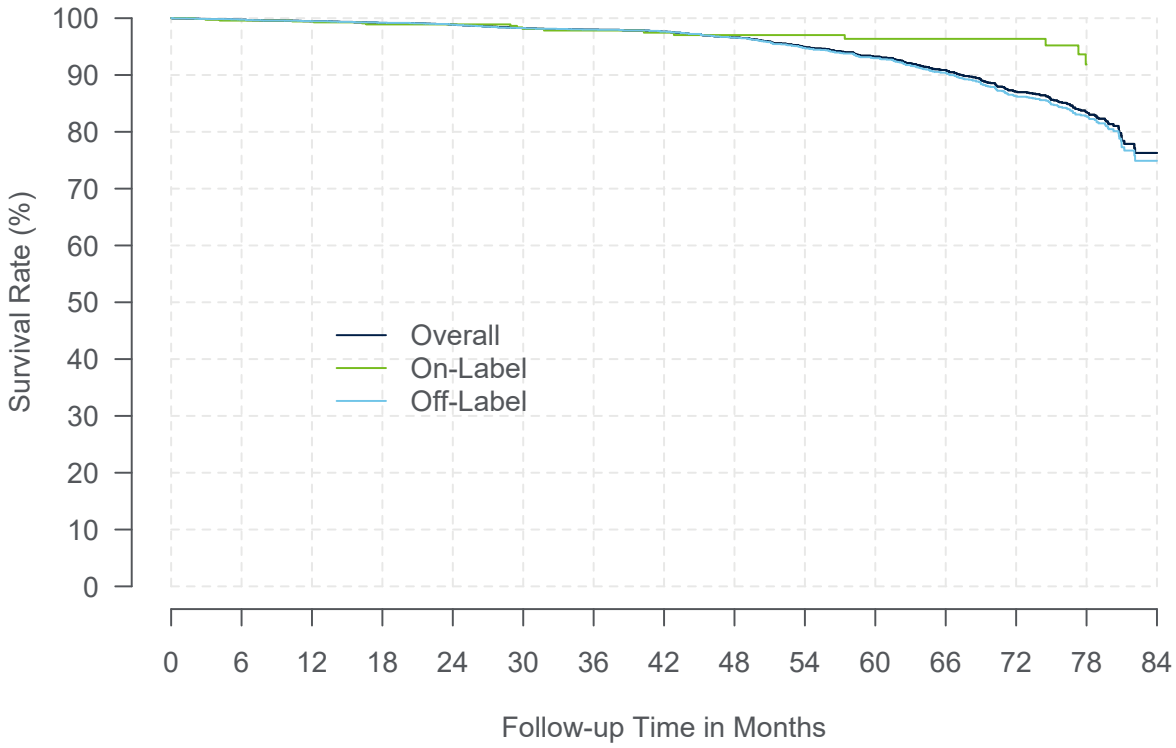


Figure 3.7: SynchroMed II Cumulative Survival (Pain Therapies)

Table 3.19: Survival Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	7 Yrs
Overall	Survival	99.5%	98.9%	98.0%	96.6%	93.2%	87.1%	83.5%	76.3%
	Sample Size	4,934	3,879	3,006	2,283	1,655	1,052	561	24
On-Label	Survival	99.4%	98.9%	97.8%	97.0%	96.4%	96.4%	91.8%	
	Sample Size	626	448	299	192	133	92	49	
Off-Label	Survival	99.5%	98.9%	98.0%	96.6%	93.0%	86.3%	82.7%	74.9%
	Sample Size	4,308	3,431	2,707	2,091	1,522	960	512	21

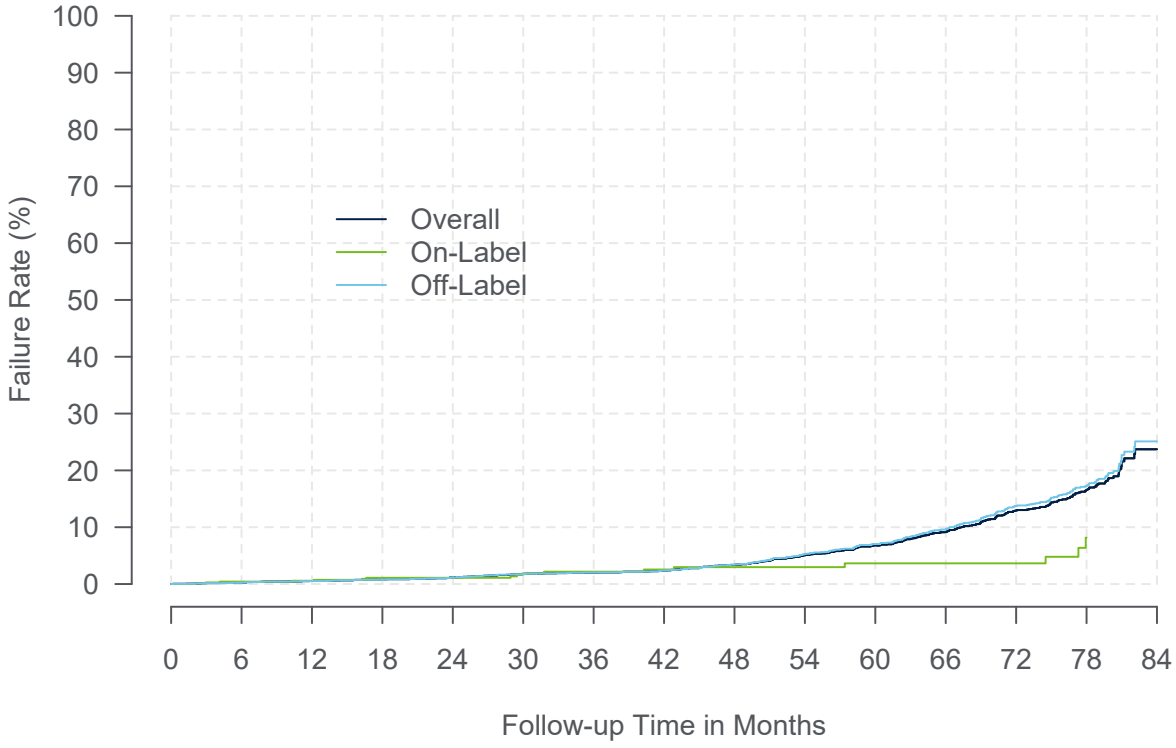


Figure 3.8: SynchroMed II Cumulative Failure (Pain Therapies)

Table 3.20: Failure Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	7 Yrs
Overall	Failure	0.5%	1.1%	2.0%	3.4%	6.8%	12.9%	16.5%	23.7%
	Sample Size	4,934	3,879	3,006	2,283	1,655	1,052	561	24
On-Label	Failure	0.6%	1.1%	2.2%	3.0%	3.6%	3.6%	8.2%	
	Sample Size	626	448	299	192	133	92	49	
Off-Label	Failure	0.5%	1.1%	2.0%	3.4%	7.0%	13.7%	17.3%	25.1%
	Sample Size	4,308	3,431	2,707	2,091	1,522	960	512	21

3.4.3.3 Spasticity Study Population

A total of 2,104 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 236 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.

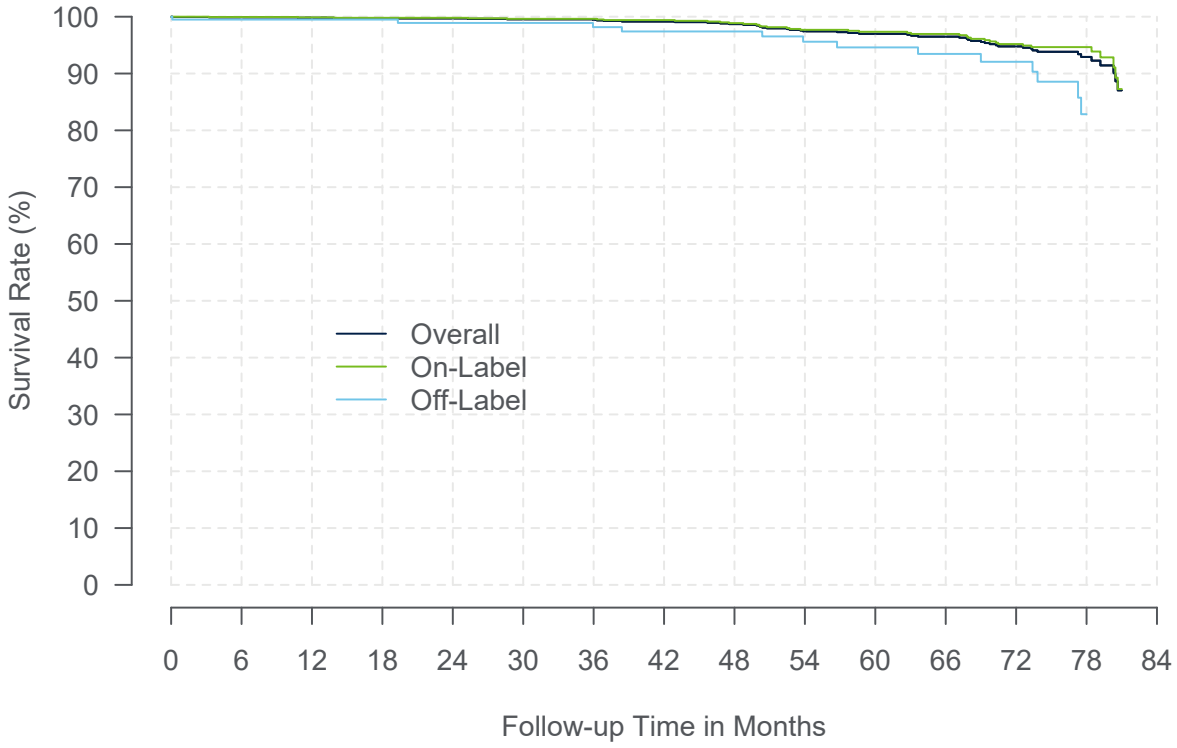


Figure 3.9: SynchroMed II Cumulative Survival (Spasticity Therapies)

Table 3.21: 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%	99.7%	99.4%	98.7%	97.0%	94.8%	92.9%	87.0%
	Sample Size	1,680	1,356	1,040	819	624	435	159	44
On-Label	Survival	99.9%	99.8%	99.6%	98.9%	97.3%	95.2%	94.6%	87.3%
	Sample Size	1,494	1,200	909	706	536	375	137	34
Off-Label	Survival	99.5%	98.9%	98.2%	97.4%	94.6%	92.1%	82.8%	
	Sample Size	186	156	131	113	88	60	22	

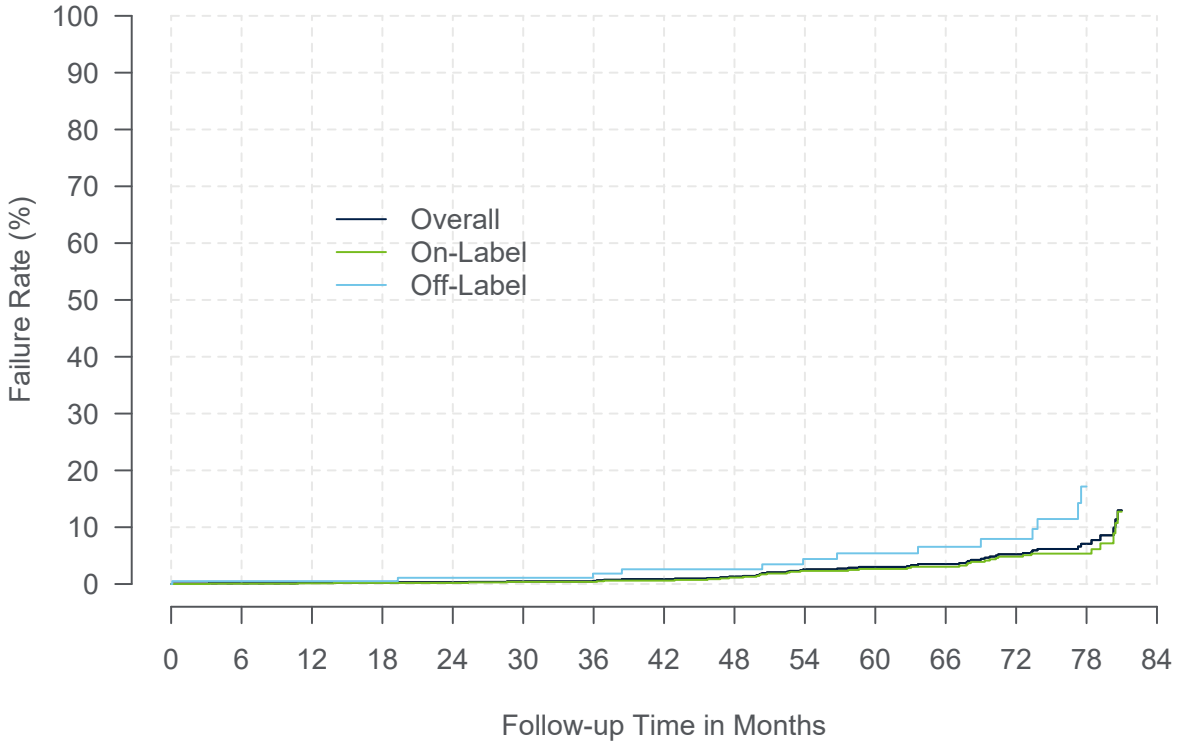


Figure 3.10: SynchroMed II Cumulative Failure (Spasticity Therapies)

Table 3.22: 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%	0.3%	0.6%	1.3%	3.0%	5.2%	7.1%	13.0%
	Sample Size	1,680	1,356	1,040	819	624	435	159	44
On-Label	Failure	0.1%	0.2%	0.4%	1.1%	2.7%	4.8%	5.4%	12.7%
	Sample Size	1,494	1,200	909	706	536	375	137	34
Off-Label	Failure	0.5%	1.1%	1.8%	2.6%	5.4%	7.9%	17.2%	
	Sample Size	186	156	131	113	88	60	22	

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 2.5 times greater risk of pump failure (95% confidence interval [1.909, 3.361]) 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, with 40 ml pumps more likely to be exposed

to off-label use than 20 ml pumps. At 81 months of follow-up the survival from pump failure for On-Label pumps was 88.4% compared to a survival of 77.7% for Off-Label pumps.

- The data represent the reported registry experience with a median follow-up time of 25.9 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 68.7% of pumps with Spasticity as the indication (2,104 vs. 958: Spasticity versus Pain pumps respectively). While the Off-Label group consisted of 94.3% of pumps with pain indications (6,650 vs. 236: 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, 2020, there were 10,529 catheters followed in the registry. The total number of catheters was not equal to the total number of pumps (n=11,671) 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 361,107 months (30,092 years). Table 3.23 provides the number and percentage of catheters by model.

Table 3.23: Targeted Drug Delivery Catheter Counts by Model

Model Name	N (%)
Currently Manufactured[a]	**2,707 (25.7%)**
8780 (US & OUS)	1,337 (12.7%)
8781 (US & OUS)	1,089 (10.3%)
8731SC (OUS)	281 (2.7%)
Revised Catheters	**2,085 (19.8%)**
Revised Not As Designed[b]	713 (6.8%)
Revised As Designed[d]	529 (5.0%)
Grafted Not As Designed[c]	490 (4.7%)
Ascenda Revised As Designed[e]	353 (3.4%)
No Longer Manufactured	**5,379 (51.1%)**
8709	2,912 (27.7%)
8709SC	1,094 (10.4%)
8711	659 (6.3%)
8731	529 (5.0%)
8703W	185 (1.8%)
Other/Unspecified	**358 (3.4%)**
Total	**10,529 (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 1,565 product performance-related events with an underlying reported etiology related to catheter function. This includes 1,554 events with a catheter etiology and 11 events with both a catheter and other etiology (including device and non-device etiologies). The majority of the events were catheter occlusion (n=419), catheter dislodgement (n=387), catheter break/cut (n=231), or catheter kink (n=224). Of the 1,565 events, 1,342 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:

- 1,342 had follow-up time cut-off due to product performance-related events.
- 6,784 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.
- 2,403 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.

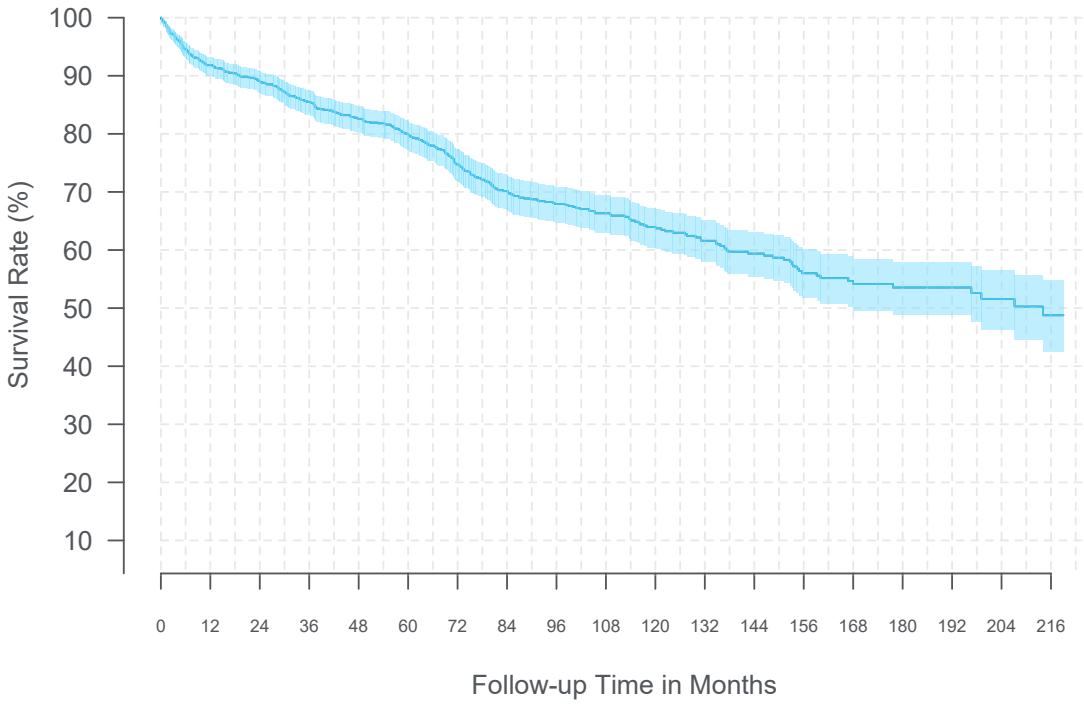
3.5.2 Catheter Models

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	2,912
Catheters Currently Active in Study	178
Device Events	359
Median Follow-up Time (Months)	17.4
Cumulative Follow-up Time (Months)	96,554



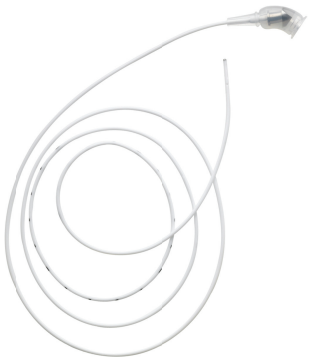
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.8% (90.1%, 93.3%)	89.1% (87.1%, 90.8%)	85.5% (83.3%, 87.5%)	82.6% (80.2%, 84.7%)	79.9% (77.4%, 82.2%)
Sample Size	987	932	867	774	664

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	74.8% (71.9%, 77.4%)	70.1% (67.0%, 73.0%)	67.9% (64.7%, 70.9%)	66.3% (63.0%, 69.4%)	64.0% (60.5%, 67.2%)
Sample Size	571	502	420	330	269

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	61.6% (57.9%, 65.1%)	59.4% (55.5%, 63.1%)	56.0% (51.7%, 60.1%)	54.1% (49.6%, 58.5%)	53.5% (48.9%, 58.0%)
Sample Size	216	171	140	104	84

Time Interval	16 Years	17 Years	18 Years	At 219 Months	
Survival (95% CI)	53.5% (48.9%, 58.0%)	51.6% (46.3%, 56.6%)	48.8% (42.5%, 54.8%)	48.8% (42.5%, 54.8%)	
Sample Size	63	42	27	20	

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

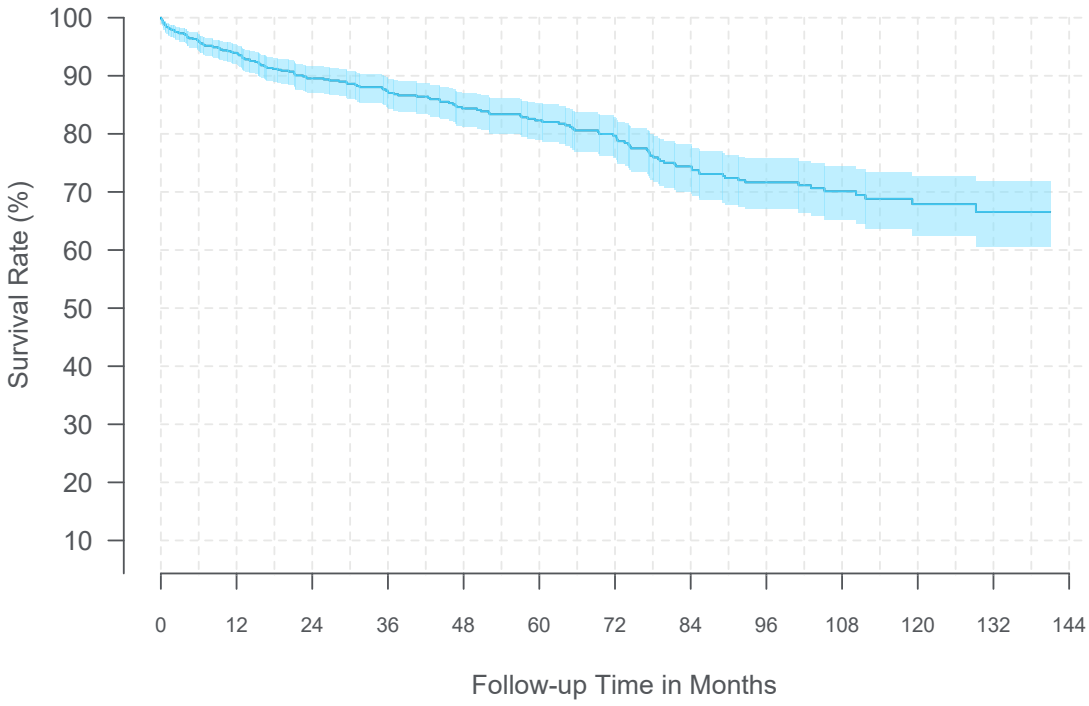


Catheter Event Summary: 8709	N
Catheter Dislodgement	97
Catheter Occlusion	84
Catheter Break/Cut	77
Catheter Kink	32
Catheter Disconnection At Pump	20
Catheter Related Complication	14
Catheter Leakage	13
Pump Connector Break/Cut	10
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Other[a]	9
Total	**359**

[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	1,094
Catheters Currently Active in Study	182
Device Events	151
Median Follow-up Time (Months)	26.5
Cumulative Follow-up Time (Months)	44,143



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	94.0% (92.1%, 95.4%)	89.5% (87.1%, 91.6%)	87.2% (84.5%, 89.5%)	84.4% (81.2%, 87.0%)	82.3% (78.9%, 85.2%)
Sample Size	668	517	433	358	297

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	79.7% (75.9%, 82.9%)	74.4% (70.1%, 78.2%)	71.7% (67.1%, 75.7%)	70.1% (65.3%, 74.4%)	67.9% (62.5%, 72.7%)
Sample Size	257	229	166	118	73

Time Interval	11 Years	At 141 Months			
Survival (95% CI)	66.6% (60.6%, 71.8%)	66.6% (60.6%, 71.8%)			
Sample Size	40	20			

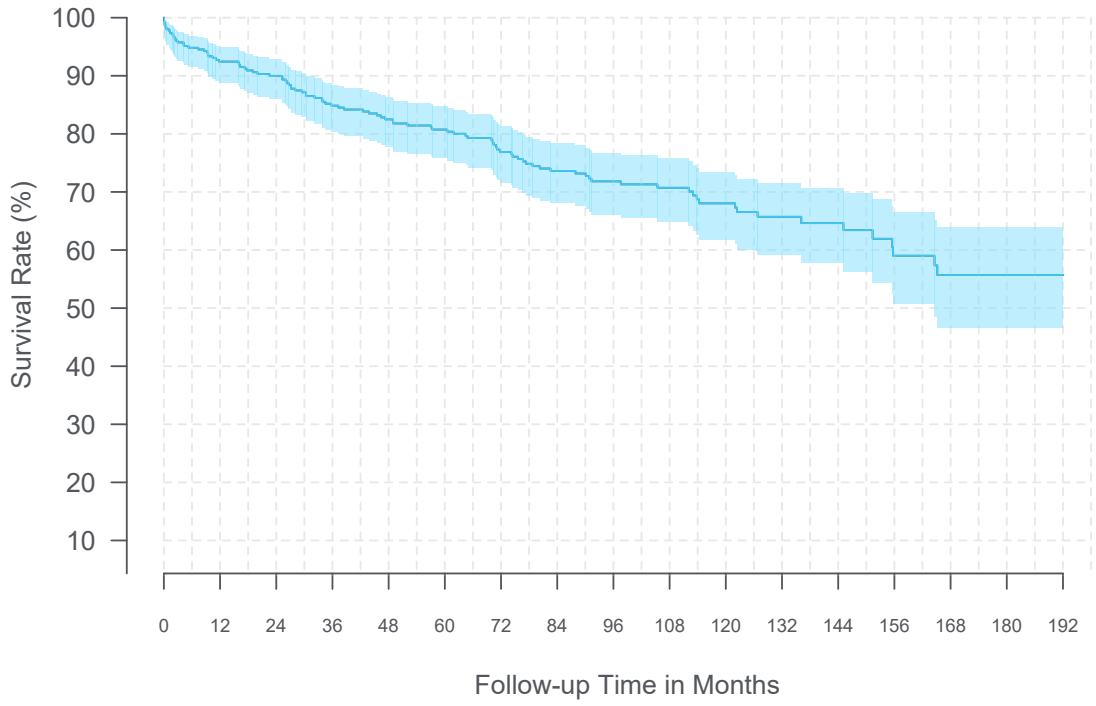
Specification: 8709SC	
Total Length	89 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed tip, radiopaque, titanium with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Pump end

Catheter Event Summary: 8709SC	N
Catheter Occlusion	39
Catheter Dislodgement	35
Catheter Break/Cut	34
Catheter Related Complication	11
Catheter Kink	8
Catheter Leakage	8
Catheter Disconnection At Pump	5
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Catheter Damage	2
Other[a]	6
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	659
Catheters Currently Active in Study	78
Device Events	98
Median Follow-up Time (Months)	31.2
Cumulative Follow-up Time (Months)	30,390



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)	76.9% (71.6%, 81.3%)	73.6% (68.1%, 78.3%)	71.8% (66.1%, 76.7%)	70.7% (64.9%, 75.8%)	68.0% (61.8%, 73.5%)
Sample Size	189	178	145	115	95

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	65.7% (59.1%, 71.5%)	64.6% (57.8%, 70.7%)	59.0% (50.7%, 66.4%)	55.7% (46.6%, 63.9%)	55.7% (46.6%, 63.9%)
Sample Size	69	55	40	31	26

Time Interval	16 Years
Survival (95% CI)	55.7% (46.6%, 63.9%)
Sample Size	21

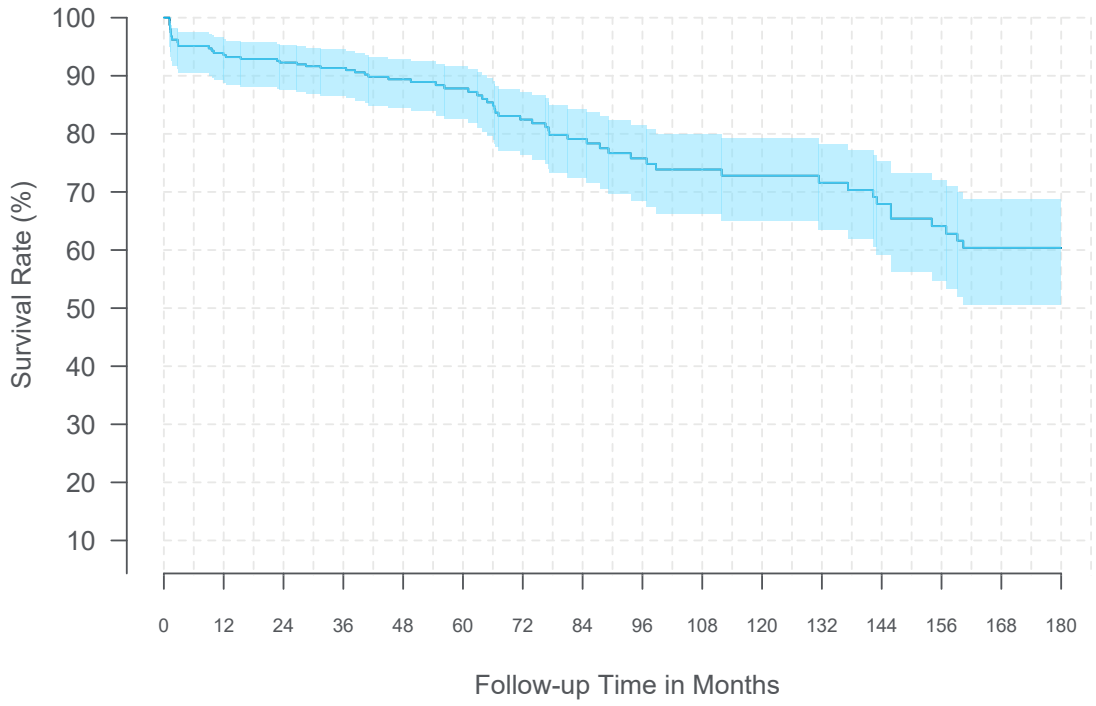
Specification: 8711	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Spinal and pump ends

Catheter Event Summary: 8711	N
Catheter Occlusion	30
Catheter Break/Cut	19
Catheter Related Complication	15
Catheter Dislodgement	14
Catheter Kink	7
Catheter Leakage	4
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Catheter Disconnection At Pump	2
Other[a]	3
Total	**98**

[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	529
Catheters Currently Active in Study	48
Device Events	61
Median Follow-up Time (Months)	31.8
Cumulative Follow-up Time (Months)	23,378



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% (82.6%, 91.6%)
Sample Size	261	305	255	197	149

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	82.5% (76.3%, 87.1%)	79.1% (72.5%, 84.3%)	75.8% (68.5%, 81.6%)	73.9% (66.3%, 80.0%)	72.8% (65.0%, 79.1%)
Sample Size	133	105	81	69	63

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	71.6% (63.5%, 78.2%)	67.9% (59.1%, 75.2%)	64.1% (54.7%, 72.0%)	60.4% (50.6%, 68.8%)	60.4% (50.6%, 68.8%)
Sample Size	59	54	48	40	20

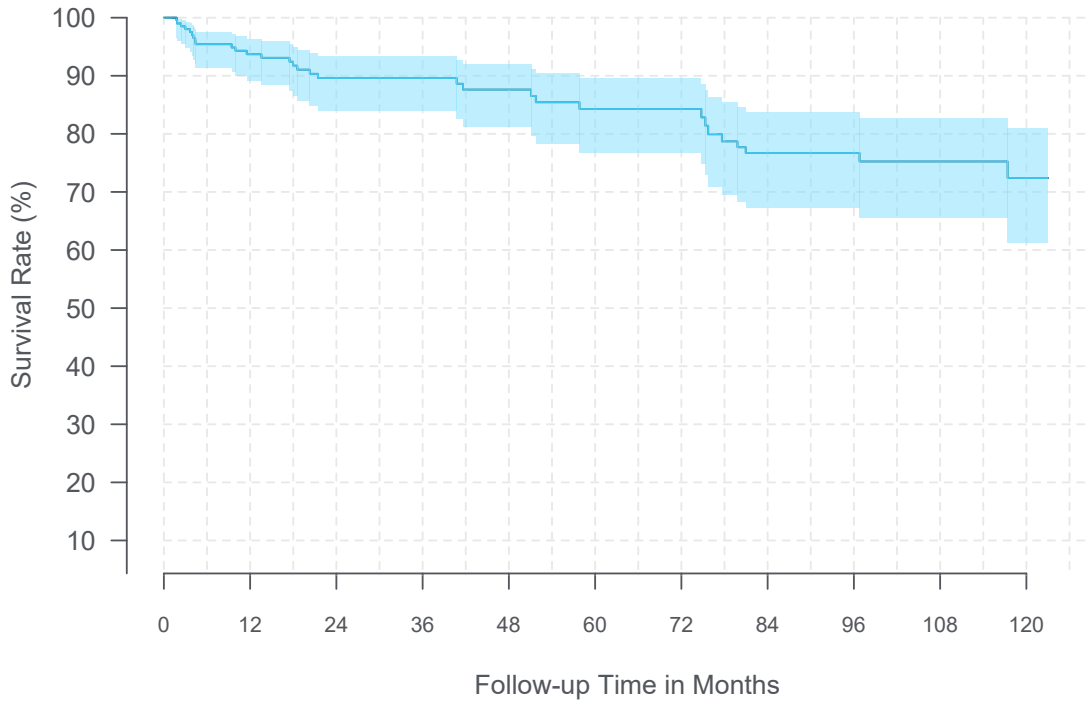
Specification: 8731	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed tip, radiopaque, titanium with 6 side holes
Catheter Volume	2.22 mL/cm
Trimmable Segments	Spinal end

Catheter Event Summary: 8731	N
Catheter Occlusion	23
Catheter Dislodgement	19
Catheter Related Complication	5
Catheter Kink	4
Catheter Break/Cut	3
Catheter Disconnection At Pump	3
Other[a]	4
Total	**61**

[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	281
Catheters Currently Active in Study	80
Device Events	31
Median Follow-up Time (Months)	30.7
Cumulative Follow-up Time (Months)	11,071



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.7% (89.2%, 96.4%)	89.6% (83.9%, 93.4%)	89.6% (83.9%, 93.4%)	87.6% (81.2%, 92.0%)	84.3% (76.8%, 89.5%)
Sample Size	155	117	97	82	72

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	84.3% (76.8%, 89.5%)	76.7% (67.3%, 83.7%)	76.7% (67.3%, 83.7%)	75.2% (65.5%, 82.6%)	72.4% (61.2%, 80.9%)
Sample Size	61	77	57	41	23

Time Interval	At 123 Months
Survival (95% CI)	72.4% (61.2%, 80.9%)
Sample Size	22

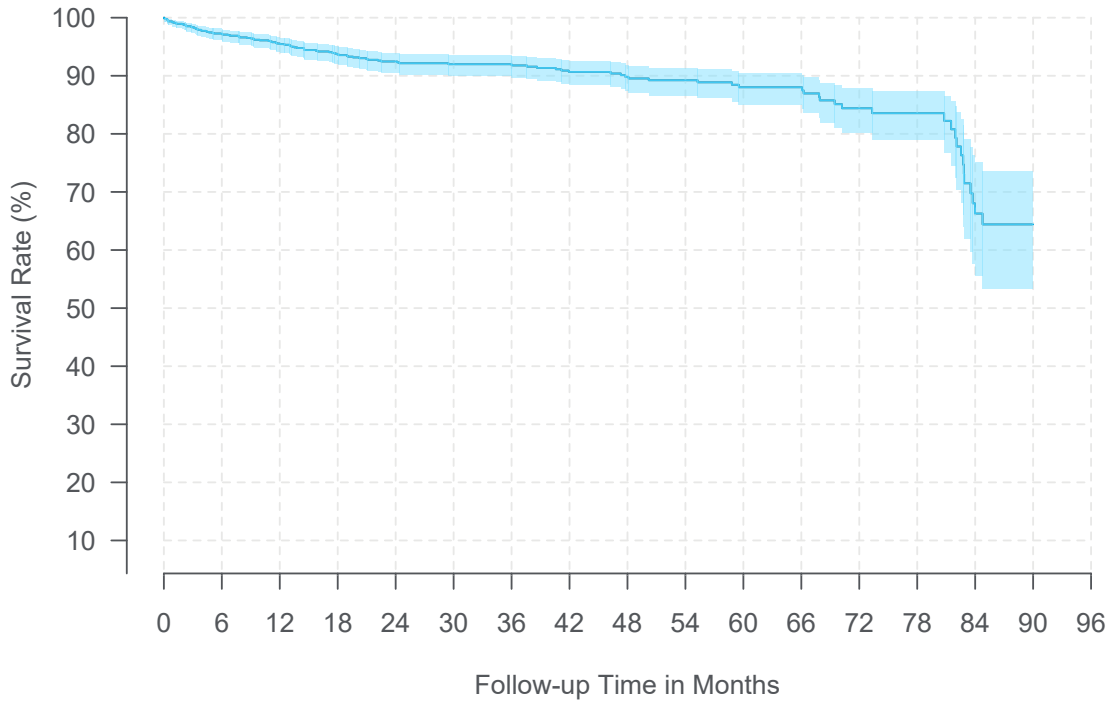
Specification: 8731SC	
Total Length	104.1 cm
Outer Diameter (spinal segment)	1.4 mm (4.2 French)
Inner Diameter (spinal segment)	0.53 mm
Catheter Tip Description	Closed with 6 side holes
Catheter Volume	0.0022 mL/cm
Trimmable Segments	Spinal and pump ends

Catheter Event Summary: 8731SC	N
Catheter Occlusion	12
Catheter Dislodgement	8
Catheter Related Complication	4
Catheter Kink	3
Pump Unable To Enter/Withdraw From Catheter Access Port	2
Other[a]	2
Total	**31**

[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	1,337
Catheters Currently Active in Study	720
Device Events	112
Median Follow-up Time (Months)	22.7
Cumulative Follow-up Time (Months)	39,607



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	95.4% (94.0%, 96.5%)	92.5% (90.6%, 94.0%)	92.0% (90.0%, 93.6%)	89.8% (87.4%, 91.8%)	88.0% (85.0%, 90.4%)
Sample Size	871	616	438	311	202

Time Interval	6 Years	7 Years[a]	At 90 Months		
Survival (95% CI)	84.4% (80.1%, 87.8%)	66.3% (55.5%, 75.0%)	64.4% (53.3%, 73.5%)		
Sample Size	106	37	22		

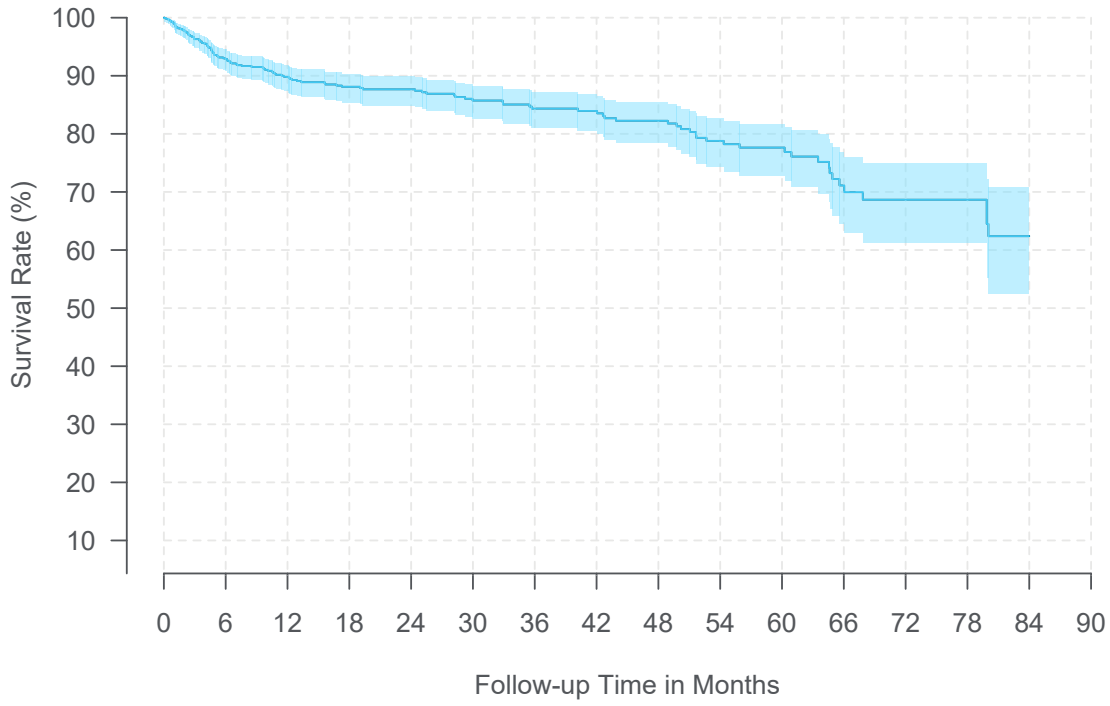
[a] During post-analysis, the majority of the incremental change in survival between 6-7 years was determined to be attributed to catheter observations at a single study site. These events were predominately observed during normal pump replacement in patients without any clinically relevant symptoms.

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	47
Catheter Kink	22
Catheter Dislodgement	20
Catheter Break/Cut	8
Catheter Related Complication	8
Catheter Leakage	3
Catheter Damage	2
Catheter Disconnection At Pump	2
Total	**112**

3.5.2.7 Model 8781

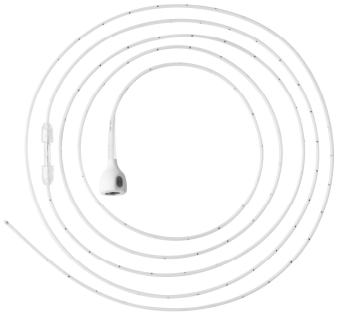
Model/Name	8781/Ascenda
FDA Approval Date	May 2012
Catheters Enrolled	1,089
Catheters Currently Active in Study	411
Device Events	131
Median Follow-up Time (Months)	12.4
Cumulative Follow-up Time (Months)	23,917



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	89.8% (87.4%, 91.8%)	87.7% (84.9%, 89.9%)	84.3% (81.0%, 87.2%)	82.2% (78.4%, 85.5%)	77.6% (72.8%, 81.7%)
Sample Size	496	356	239	178	102

Time Interval	6 Years	7 Years			
Survival (95% CI)	68.7% (61.2%, 74.9%)	62.4% (52.5%, 70.8%)			
Sample Size	36	20			

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

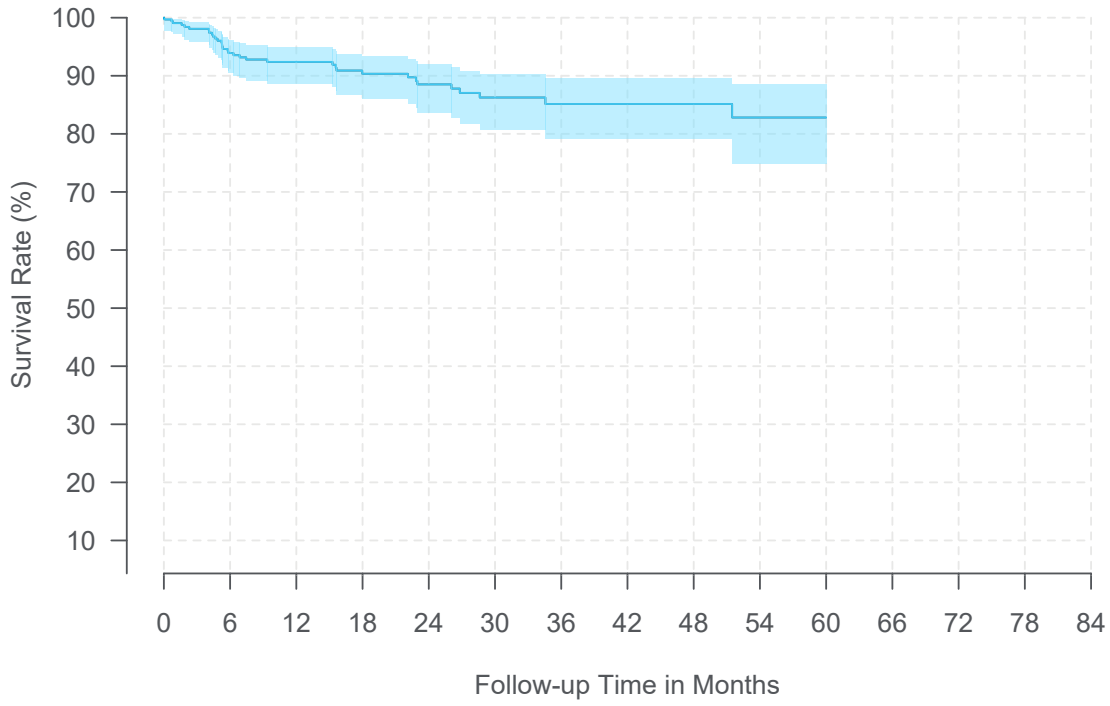


Catheter Event Summary: 8781	N
Catheter Kink	55
Catheter Dislodgement	32
Catheter Occlusion	23
Catheter Break/Cut	5
Catheter Related Complication	5
Catheter Disconnection At Pump	3
Catheter Leakage	3
Catheter Dysfunction	2
Other[a]	3
Total	**131**

[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	353
Catheters Currently Active in Study	167
Device Events	34
Median Follow-up Time (Months)	16.8
Cumulative Follow-up Time (Months)	7,866



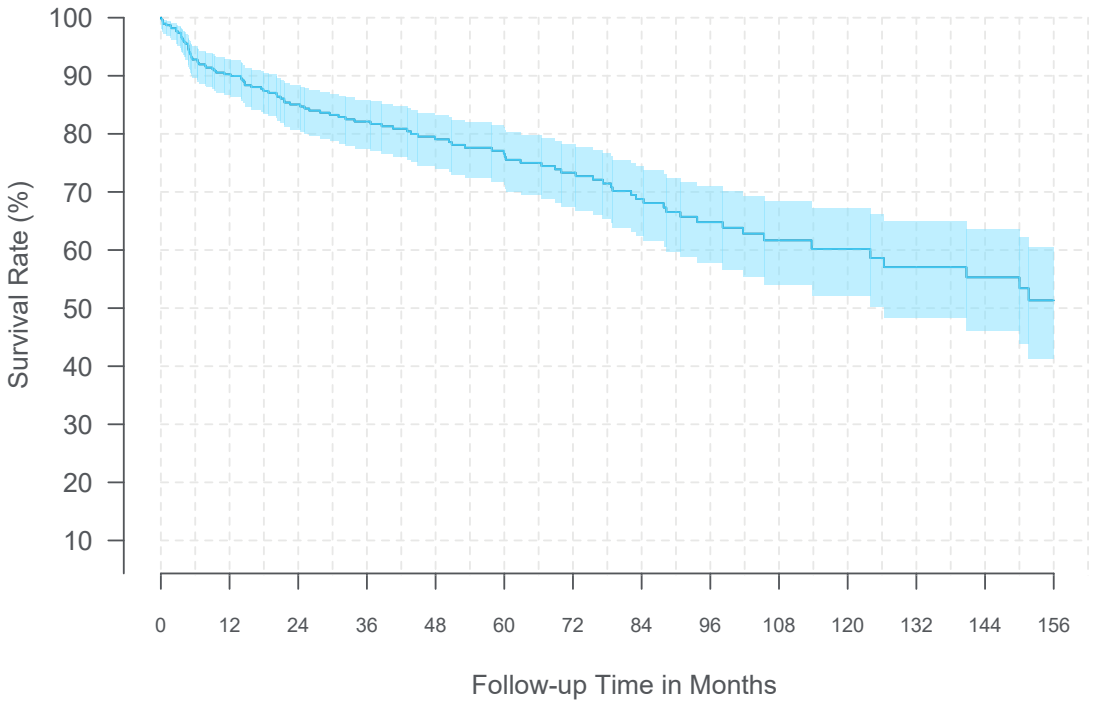
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.4% (88.7%, 94.9%)	88.5% (83.7%, 92.0%)	85.1% (79.1%, 89.5%)	85.1% (79.1%, 89.5%)	82.8% (74.8%, 88.5%)
Sample Size	213	134	73	42	20

Catheter Event Summary: Ascenda RAD	N
Catheter Dislodgement	11
Catheter Kink	9
Catheter Occlusion	8
Other[a]	6
Total	**34**

[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	490
Catheters Currently Active in Study	127
Device Events	102
Median Follow-up Time (Months)	34.1
Cumulative Follow-up Time (Months)	22,143



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	90.3% (86.7%, 92.9%)	85.1% (80.8%, 88.4%)	82.1% (77.5%, 85.9%)	79.1% (74.0%, 83.2%)	76.6% (71.2%, 81.1%)
Sample Size	301	243	204	168	147

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	73.3% (67.5%, 78.3%)	68.8% (62.4%, 74.4%)	64.8% (57.8%, 71.0%)	61.7% (54.1%, 68.4%)	60.2% (52.2%, 67.3%)
Sample Size	123	97	67	47	38

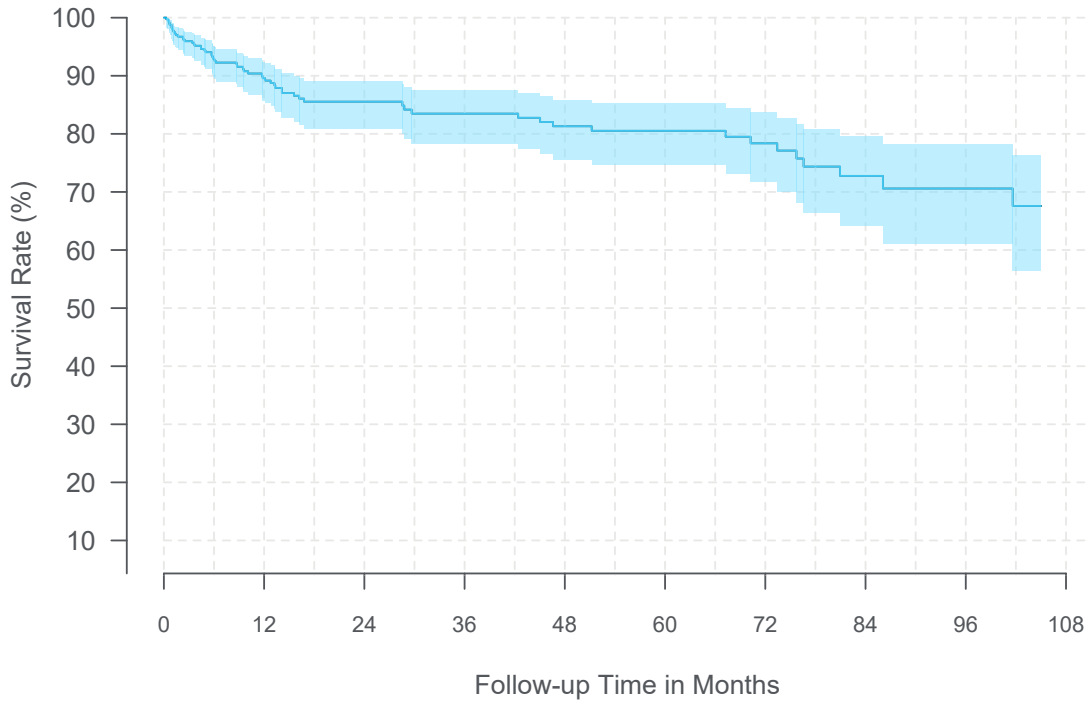
Time Interval	11 Years	12 Years	13 Years		
Survival (95% CI)	57.1% (48.3%, 64.9%)	55.3% (46.1%, 63.5%)	51.3% (41.3%, 60.5%)		
Sample Size	34	29	20		

Catheter Event Summary: Grafted Not As Designed	N
Catheter Occlusion	30
Catheter Dislodgement	27
Catheter Break/Cut	12
Catheter Related Complication	8
Catheter Kink	7
Catheter Leakage	7
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Medical Device Complication	2
Other[a]	5
Total	**102**

[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	529
Catheters Currently Active in Study	284
Device Events	64
Median Follow-up Time (Months)	10.4
Cumulative Follow-up Time (Months)	12,886



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	89.6% (85.8%, 92.4%)	85.5% (80.9%, 89.1%)	83.5% (78.3%, 87.5%)	81.3% (75.6%, 85.8%)	80.5% (74.6%, 85.2%)
Sample Size	220	136	118	106	91

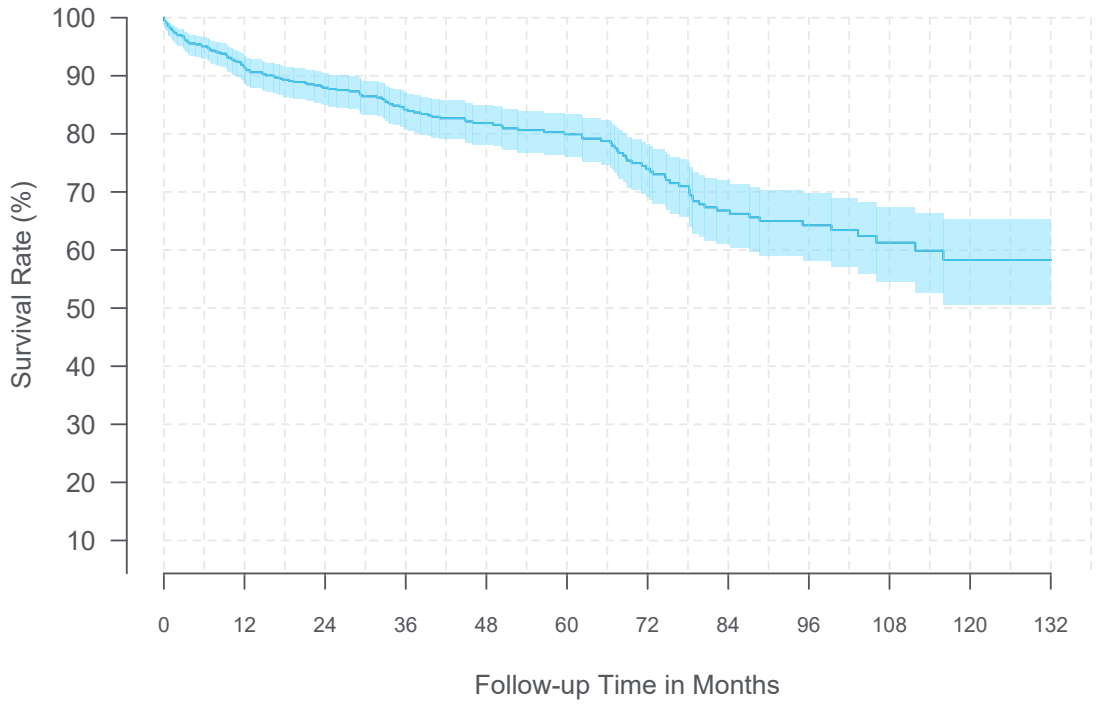
Time Interval	6 Years	7 Years	8 Years	At 105 Months	
Survival (95% CI)	78.4% (71.7%, 83.6%)	72.8% (64.2%, 79.6%)	70.6% (61.1%, 78.2%)	67.6% (56.5%, 76.4%)	
Sample Size	63	35	23	20	

Catheter Event Summary: Revised As Designed	N
Catheter Dislodgement	32
Catheter Occlusion	18
Catheter Kink	6
Catheter Break/Cut	3
Catheter Related Complication	3
Other[a]	2
Total	**64**

[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	713
Catheters Currently Active in Study	160
Device Events	137
Median Follow-up Time (Months)	39.6
Cumulative Follow-up Time (Months)	31,915



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.3% (88.7%, 93.4%)	87.9% (84.9%, 90.4%)	84.1% (80.7%, 87.0%)	81.9% (78.2%, 85.0%)	79.9% (76.0%, 83.3%)
Sample Size	507	438	357	285	221

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	74.0% (69.2%, 78.2%)	66.8% (61.1%, 71.9%)	64.3% (58.2%, 69.7%)	61.3% (54.5%, 67.3%)	58.3% (50.6%, 65.2%)
Sample Size	153	117	84	50	34

Time Interval	11 Years
Survival (95% CI)	58.3% (50.6%, 65.2%)
Sample Size	20

Catheter Event Summary: Revised Not As Designed	N
Catheter Occlusion	50
Catheter Dislodgement	26
Catheter Break/Cut	17
Catheter Kink	14
Catheter Related Complication	8
Catheter Leakage	7
Pump Unable To Enter/Withdraw From Catheter Access Port	5
Catheter Disconnection At Pump	4
Other[a]	6
Total	**137**

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

3.5.3 Catheter Summary

Table 3.24: 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	2,912	178	359	17.4	96,554
8709SC	March 2006	1,094	182	151	26.5	44,143
8711	October 1999	659	78	98	31.2	30,390
8731	October 2002	529	48	61	31.8	23,378
8731SC	March 2006	281	80	31	30.7	11,071
8780	May 2012	1,337	720	112	22.7	39,607
8781	May 2012	1,089	411	131	12.4	23,917
Ascenda Revised As Designed	May 2012	353	167	34	16.8	7,866
Grafted Not As Designed	NA	490	127	102	34.1	22,143
Revised As Designed	October 2002	529	284	64	10.4	12,886
Revised Not As Designed	NA	713	160	137	39.6	31,915

Table 3.25: Targeted Drug Delivery Catheter Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
8709	91.8% (90.1%, 93.3%)	89.1% (87.1%, 90.8%)	85.5% (83.3%, 87.5%)	82.6% (80.2%, 84.7%)	79.9% (77.4%, 82.2%)
8709SC	94.0% (92.1%, 95.4%)	89.5% (87.1%, 91.6%)	87.2% (84.5%, 89.5%)	84.4% (81.2%, 87.0%)	82.3% (78.9%, 85.2%)
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% (82.6%, 91.6%)
8731SC	93.7% (89.2%, 96.4%)	89.6% (83.9%, 93.4%)	89.6% (83.9%, 93.4%)	87.6% (81.2%, 92.0%)	84.3% (76.8%, 89.5%)
8780	95.4% (94.0%, 96.5%)	92.5% (90.6%, 94.0%)	92.0% (90.0%, 93.6%)	89.8% (87.4%, 91.8%)	88.0% (85.0%, 90.4%)
8781	89.8% (87.4%, 91.8%)	87.7% (84.9%, 89.9%)	84.3% (81.0%, 87.2%)	82.2% (78.4%, 85.5%)	77.6% (72.8%, 81.7%)
Ascenda Revised As Designed	92.4% (88.7%, 94.9%)	88.5% (83.7%, 92.0%)	85.1% (79.1%, 89.5%)	85.1% (79.1%, 89.5%)	82.8% (74.8%, 88.5%)
Grafted Not As Designed	90.3% (86.7%, 92.9%)	85.1% (80.8%, 88.4%)	82.1% (77.5%, 85.9%)	79.1% (74.0%, 83.2%)	76.6% (71.2%, 81.1%)
Revised As Designed	89.6% (85.8%, 92.4%)	85.5% (80.9%, 89.1%)	83.5% (78.3%, 87.5%)	81.3% (75.6%, 85.8%)	80.5% (74.6%, 85.2%)
Revised Not As Designed	91.3% (88.7%, 93.4%)	87.9% (84.9%, 90.4%)	84.1% (80.7%, 87.0%)	81.9% (78.2%, 85.0%)	79.9% (76.0%, 83.3%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
8709	74.8% (71.9%, 77.4%)	70.1% (67.0%, 73.0%)	67.9% (64.7%, 70.9%)	66.3% (63.0%, 69.4%)	64.0% (60.5%, 67.2%)
8709SC	79.7% (75.9%, 82.9%)	74.4% (70.1%, 78.2%)	71.7% (67.1%, 75.7%)	70.1% (65.3%, 74.4%)	67.9% (62.5%, 72.7%)
8711	76.9% (71.6%, 81.3%)	73.6% (68.1%, 78.3%)	71.8% (66.1%, 76.7%)	70.7% (64.9%, 75.8%)	68.0% (61.8%, 73.5%)
8731	82.5% (76.3%, 87.1%)	79.1% (72.5%, 84.3%)	75.8% (68.5%, 81.6%)	73.9% (66.3%, 80.0%)	72.8% (65.0%, 79.1%)
8731SC	84.3% (76.8%, 89.5%)	76.7% (67.3%, 83.7%)	76.7% (67.3%, 83.7%)	75.2% (65.5%, 82.6%)	72.4% (61.2%, 80.9%)
8780	84.4% (80.1%, 87.8%)	66.3% (55.5%, 75.0%)			
8781	68.7% (61.2%, 74.9%)	62.4% (52.5%, 70.8%)			
Ascenda Revised As Designed					
Grafted Not As Designed	73.3% (67.5%, 78.3%)	68.8% (62.4%, 74.4%)	64.8% (57.8%, 71.0%)	61.7% (54.1%, 68.4%)	60.2% (52.2%, 67.3%)
Revised As Designed	78.4% (71.7%, 83.6%)	72.8% (64.2%, 79.6%)	70.6% (61.1%, 78.2%)		
Revised Not As Designed	74.0% (69.2%, 78.2%)	66.8% (61.1%, 71.9%)	64.3% (58.2%, 69.7%)	61.3% (54.5%, 67.3%)	58.3% (50.6%, 65.2%)

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
8709	61.6% (57.9%, 65.1%)	59.4% (55.5%, 63.1%)	56.0% (51.7%, 60.1%)	54.1% (49.6%, 58.5%)	53.5% (48.9%, 58.0%)
8709SC	66.6% (60.6%, 71.8%)				
8711	65.7% (59.1%, 71.5%)	64.6% (57.8%, 70.7%)	59.0% (50.7%, 66.4%)	55.7% (46.6%, 63.9%)	55.7% (46.6%, 63.9%)
8731	71.6% (63.5%, 78.2%)	67.9% (59.1%, 75.2%)	64.1% (54.7%, 72.0%)	60.4% (50.6%, 68.8%)	60.4% (50.6%, 68.8%)
8731SC					
8780					
8781					
Ascenda Revised As Designed					
Grafted Not As Designed	57.1% (48.3%, 64.9%)	55.3% (46.1%, 63.5%)	51.3% (41.3%, 60.5%)		
Revised As Designed					
Revised Not As Designed	58.3% (50.6%, 65.2%)				

Model Name	16 Years	17 Years	18 Years		
8709	53.5% (48.9%, 58.0%)	51.6% (46.3%, 56.6%)	48.8% (42.5%, 54.8%)		
8709SC					
8711	55.7% (46.6%, 63.9%)				
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, 2020. Eighty-four centers, 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.

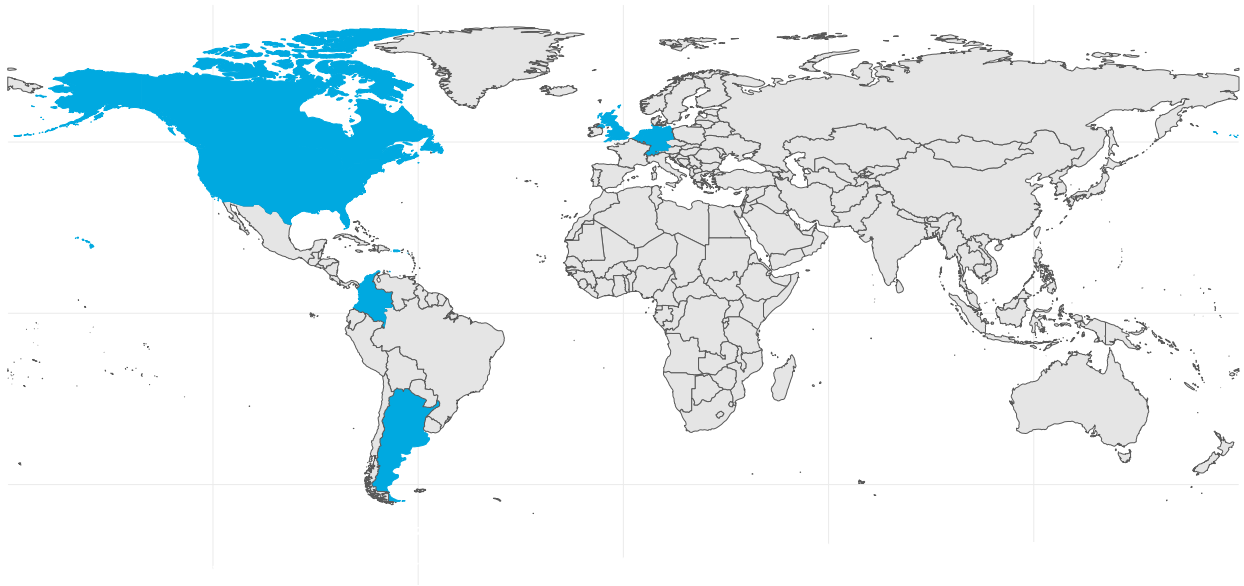


Figure 4.1: Countries with Spinal Cord Stimulation Therapy Patients in Registry (Highlighted)

4.1.2 Patients

Of the 5,931 spinal cord stimulation patients enrolled, 45.6% were implanted for the treatment of failed back pain, 25.5% were implanted for the treatment of other primary indications, 18.0% were implanted for the treatment of trunk and limb pain, 10.2% were implanted for the treatment

of CRPS, and 0.7% were implanted for indications that were not specified in the database (see Figure 4.2 and Table 4.1).

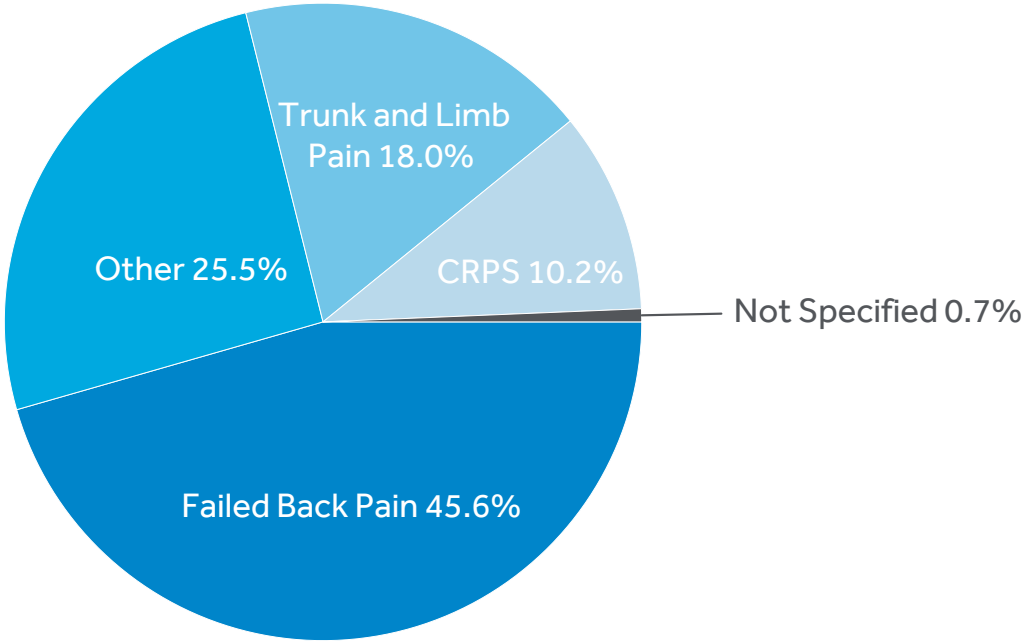


Figure 4.2: Spinal Cord Stimulation Primary Treatment Indications

Table 4.1: Spinal Cord Stimulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Failed Back Pain	**2,702 (45.56%)**
Failed Back Surgery Syndrome (FBSS)	938 (15.82%)
Post Laminectomy Pain	922 (15.55%)
Combination Back and Leg Pain	716 (12.07%)
Multiple Back Operations	92 (1.55%)
Arachnoiditis	22 (0.37%)
Unsuccessful Disc Surgery	12 (0.20%)
Other Primary Indication	**1,515 (25.54%)**
Other Chronic Pain	851 (14.35%)
Cervical Pain	76 (1.28%)
Traumatic Nerve Injury	52 (0.88%)
Chronic Cluster Headache	49 (0.83%)
Diabetic Neuropathy	34 (0.57%)
Post Herpetic Neuralgia	18 (0.30%)
Angina	9 (0.15%)
Facial Pain	8 (0.13%)
Epidural Fibrosis	4 (0.07%)
Post Herniorrhaphy Pain	3 (0.05%)
Other Secondary Indication	411 (6.93%)
Trunk and Limb Pain	**1,070 (18.04%)**
Radicular Pain Syndrome	804 (13.56%)
Degenerative Disc Disease	266 (4.48%)
CRPS	**605 (10.20%)**
CRPS I	469 (7.91%)
CRPS II	136 (2.29%)
Not Specified	**39 (0.66%)**
Total Patients	**5931 (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 1,730 product performance events reported between June 2004 and October 31, 2020, in patients with spinal cord stimulation systems. These events represent 35.0% of the

total reported events (1,730/4,938), occurred in 828 (14.0%) of the 5,931 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 3,181 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=27).

Any 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 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 219 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=5,931[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	**1,726**	**12.66**	**825 (13.91%)**
Lead Migration/Dislodgement	750	5.50	394 (6.64%)
High Impedance	451	3.31	201 (3.39%)
Lead Fracture	91	0.67	60 (1.01%)
Neurostimulator Unable To Recharge[d]	91	0.67	84 (1.42%)
Device Malfunction[e]	83	0.61	75 (1.26%)
Device Stimulation Issue[f]	50	0.37	29 (0.49%)
Low Impedance	47	0.34	20 (0.34%)
Device Breakage[g]	37	0.27	34 (0.57%)
Extension Fracture	18	0.13	12 (0.20%)
Medical Device Complication[h]	16	0.12	10 (0.17%)
Device Electrical Impedance Issue	13	0.10	9 (0.15%)
Extension Migration	10	0.07	7 (0.12%)
Device Lead Damage	7	0.05	5 (0.08%)
Antenna Cable Breakage	6	0.04	6 (0.10%)
Device Battery Issue	6	0.04	5 (0.08%)
Device Connection Issue	6	0.04	4 (0.07%)
Therapeutic Product Ineffective	6	0.04	5 (0.08%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=5,931[b]
Device Difficult To Use	5	0.04	4 (0.07%)
Device Telemetry Issue	5	0.04	5 (0.08%)
Device Failure[i]	4	0.03	3 (0.05%)
Neurostimulator Migration	3	0.02	3 (0.05%)
Device Charging Issue	2	0.01	2 (0.03%)
Device Loosening	2	0.01	2 (0.03%)
Inadequate Lead Connection	2	0.01	1 (0.02%)
Inappropriate Device Programming	2	0.01	2 (0.03%)
Medical Device Site Erosion	2	0.01	1 (0.02%)
Paraesthesia	2	0.01	1 (0.02%)
Device Kink	1	0.01	1 (0.02%)
Device Material Deterioration	1	0.01	1 (0.02%)
Device Overheating	1	0.01	1 (0.02%)
Extradural Abscess	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%)
Premature Battery Depletion	1	0.01	1 (0.02%)
Sensory Disturbance	1	0.01	1 (0.02%)
Total	**1,730**	**12.69**	**828 (13.96%)**

[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 3,979 patients that used rechargeable SCS neurostimulators in the registry. A total of 2.1% (84/3,979) of patients with a rechargeable SCS neurostimulator experienced a neurostimulator unable to recharge product performance event.

[e] Includes recharging components, charging and other technical related issues.

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

[g] Included external components

[h] This category includes a combination of mechanical and electrical observations.

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

A total of 1,305 (75.4%) of the 1,730 product performance events were related to the lead, 161 (9.3%) were related to "other component", 94 (5.4%) were related to the neurostimulator, 49 (2.8%) were related to "multiple etiologies" (which includes events where at least one device and

one non-device etiology was indicated), 44 (2.5%) were related to recharging process, 40 (2.3%) were related to the extension, 17 (1.0%) were related to programming/stimulation, 9 (0.5%) were related to incisional site/device tract, 6 (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 determined by the physician.

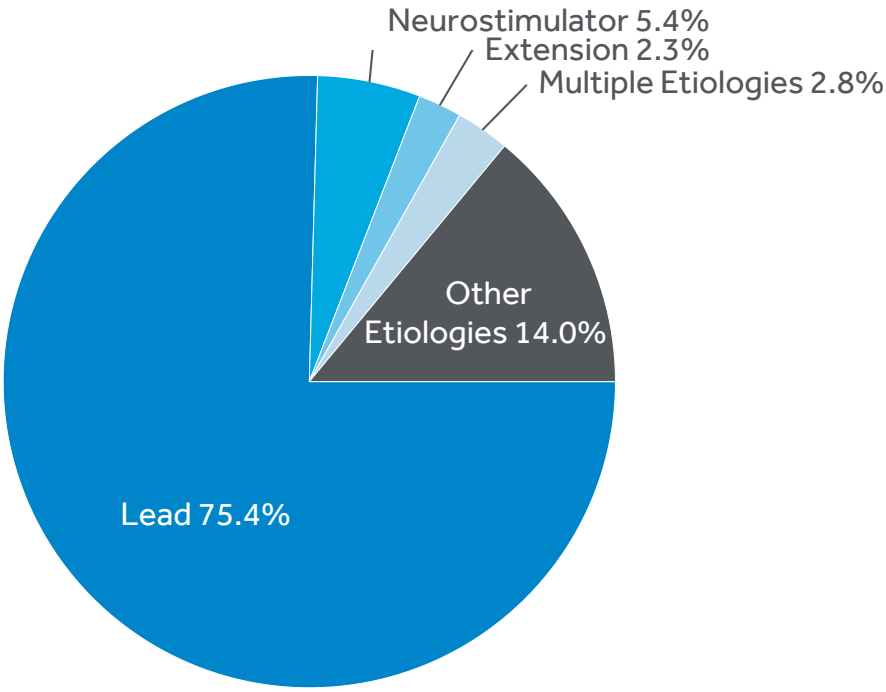


Figure 4.3: Spinal Cord Stimulation System Product Performance Events by Relatedness

Table 4.3 describes the interventions completed for product performance events that required action from the health care provider and thereby, may have resulted in an incremental impact to the patient. Survival estimates presented in previous product performance reports included events where no action was taken. To present survival estimates that may better correlate with patient impact, events where no action was taken have been removed from the device survival estimates presented in this 2020 report. The far-left column lists the top five reported PPEs, and all other reported PPEs are listed under Other. The subsequent columns represent the actions taken by the reporting physician.

Table 4.3: PSTM Product Performance Events by Intervention

Events by Intervention	Surgical Intervention	Reprogramming	Therapy Suspension	Medical or Non-Surgical Intervention [a]	No Action Taken	Total Events
Lead Migration/Dislodgement	579 (77.2%)	88 (11.7%)	19 (2.5%)	14 (1.9%)	50 (6.7%)	**750**
High Impedance	113 (25.1%)	209 (46.3%)	8 (1.8%)	8 (1.8%)	113 (25.1%)	**451**
Lead Fracture	89 (97.8%)	0 (0.0%)	2 (2.2%)	0 (0.0%)	0 (0.0%)	**91**
Neurostimulator Unable To Recharge	32 (35.2%)	4 (4.4%)	3 (3.3%)	46 (50.5%)	6 (6.6%)	**91**
Device Malfunction	17 (20.5%)	6 (7.2%)	3 (3.6%)	50 (60.2%)	7 (8.4%)	**83**
Other [b]	137 (51.9%)	40 (15.2%)	8 (3.0%)	49 (18.6%)	30 (11.4%)	**264**
Total	**967**	**347**	**43**	**167**	**206**	**1730**

[a] Medical or Non-Surgical Therapy contains but is not limited to the following actions: medication adjustment based on disease symptoms, imaging (e.g. MRI or X-ray), other specialist referral.
[b] Other represents all reported PPEs that were not in the top five of occurrence.

4.2.2 Clinical Events Not Related To Product Performance

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

- Enrolled in the PSR since 2013
- 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 4.4: Spinal Cord Stimulation System Clinically Relevant Serious Adverse Events

Event Type	Number of SAE	Patients with SAE n (%) N=3,040	SAE Per 100 Patient Months	Patient with SAE Requiring Surgical Intervention n (%) N=3,040
Infections and infestations	**52**	**52 (1.71%)**	**0.08**	**38 (1.25%)**
Infections - pathogen unspecified	44	44 (1.45%)	0.06	34 (1.12%)
Bacterial infectious disorders	8	8 (0.26%)	0.01	4 (0.13%)
Other SOC Terms ($\leq$1.0% Threshold)	**47**	**42 (1.38%)**	**0.07**	**30 (0.99%)**
Total	**99**	**90 (2.96%)**	**0.15**	**65 (2.14%)**

[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 219 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 47 (21.5%) deaths have been reported in this patient registry study based upon patients receiving therapy for other chronic pain, 33 (15.1%) for radicular pain syndrome, 31 (14.2%) for failed back surgery syndrome (FBSS), 29 (13.2%) for post laminectomy pain, 21 (9.6%) for combination back and leg pain, 13 (5.9%) for CRPS I, 10 (4.6%) for degenerative disc disease, 7 (3.2%) for multiple back operations, 3 (1.4%) for CRPS II, 2 (0.9%) for diabetic neuropathy, 2 (0.9%) for post herpetic neuralgia, 1 (0.5%) for angina, 1 (0.5%) for cervical pain, 1 (0.5%) for traumatic nerve injury, and 18 (8.2%) for other indications. The percentage is based upon the total patient death events and not based upon the rate of occurrence. **Tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 4.5: Spinal Cord Stimulation Patient Deaths by Primary Treatment Indication

Primary Treatment Indication[a]	N (%) of Deaths
Failed Back Pain	**88 (40.18%)**
Failed Back Surgery Syndrome (FBSS)	31 (14.16%)
Post Laminectomy Pain	29 (13.24%)
Combination Back and Leg Pain	21 (9.59%)
Multiple Back Operations	7 (3.20%)
Other Primary Indication	**72 (32.88%)**
Other Chronic Pain	47 (21.46%)
Diabetic Neuropathy	2 (0.91%)
Post Herpetic Neuralgia	2 (0.91%)
Angina	1 (0.46%)
Cervical Pain	1 (0.46%)
Traumatic Nerve Injury	1 (0.46%)
Other Secondary Indication	18 (8.22%)
Trunk and Limb Pain	**43 (19.63%)**
Radicular Pain Syndrome	33 (15.07%)
Degenerative Disc Disease	10 (4.57%)
CRPS	**16 (7.31%)**
CRPS I	13 (5.94%)
CRPS II	3 (1.37%)
Total	**219 (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, 2020, there were 6,507 neurostimulators followed in the registry. The difference between the total number of patients (n=5,931) 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 158,299 months (13,192 years). Table 4.6 provides the number and percentage of neurostimulators by model.

Table 4.6: Spinal Cord Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**4,424 (67.99%)**
RestoreSensor SureScan MRI (97714)	1,377 (21.16%)
Intellis with AdaptiveStim (97715)	926 (14.23%)
PrimeAdvanced SureScan MRI (97702)	740 (11.37%)
PrimeAdvanced (37702)	669 (10.28%)
RestoreSensor (37714)	377 (5.79%)
Itrel 4 (37703)	126 (1.94%)
RestoreAdvanced SureScan MRI (97713)	116 (1.78%)
RestoreUltra SureScan MRI (97712)	92 (1.41%)
Itrel 4 (37704)	1 (0.02%)
No longer manufactured	**2,075 (31.89%)**
RestoreULTRA (37712)	581 (8.93%)
Synergy (7427)	461 (7.08%)
Restore (37711)	447 (6.87%)
RestoreAdvanced (37713)	357 (5.49%)
Itrel 3 (7425)	96 (1.48%)
RestorePrime (37701)	56 (0.86%)
Synergy Versitrel (7427V)	53 (0.81%)
SynergyPlus (7479)	16 (0.25%)
SynergyCompact (7479B)	8 (0.12%)
Other/Unspecified	**8 (0.12%)**
Total	**6,507 (100%)**

4.3.1 Neurostimulator Events

There were 105 product performance-related events with an underlying reported etiology related to spinal cord neurostimulator function. This includes 94 events with a neurostimulator etiology and 11 events with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 78 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 20.6% (384/1,863). 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 105 spinal cord neurostimulator events, 96.2 % (101/105) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 4.7).

Table 4.7: Spinal Cord Stimulation Neurostimulator Product Performance Events by Determination

Product Performance Events	N (%)
RPA Determination	**4 (3.8%)**
Broken Bond Wire	1 (1.0%)
Grommet Loose	1 (1.0%)
Medical Device Complication	1 (1.0%)
No Anomaly Found By RPA	1 (1.0%)
Physician's Determination	**101 (96.2%)**
High Impedance	28 (26.7%)
Neurostimulator Unable To Recharge	24 (22.9%)
Device Malfunction	20 (19.0%)
Lead Migration/Dislodgement	9 (8.6%)
Low Impedance	3 (2.9%)
Medical Device Complication	3 (2.9%)
Device Battery Issue	2 (1.9%)
Device Stimulation Issue	2 (1.9%)
Device Charging Issue	1 (1.0%)
Device Difficult To Use	1 (1.0%)
Device Electrical Impedance Issue	1 (1.0%)
Device Overheating	1 (1.0%)
Device Telemetry Issue	1 (1.0%)
Extension Migration	1 (1.0%)
Medical Device Site Warmth	1 (1.0%)
Neurostimulator Migration	1 (1.0%)
Premature Battery Depletion	1 (1.0%)
Therapeutic Product Ineffective	1 (1.0%)
Total	**105 (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:

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

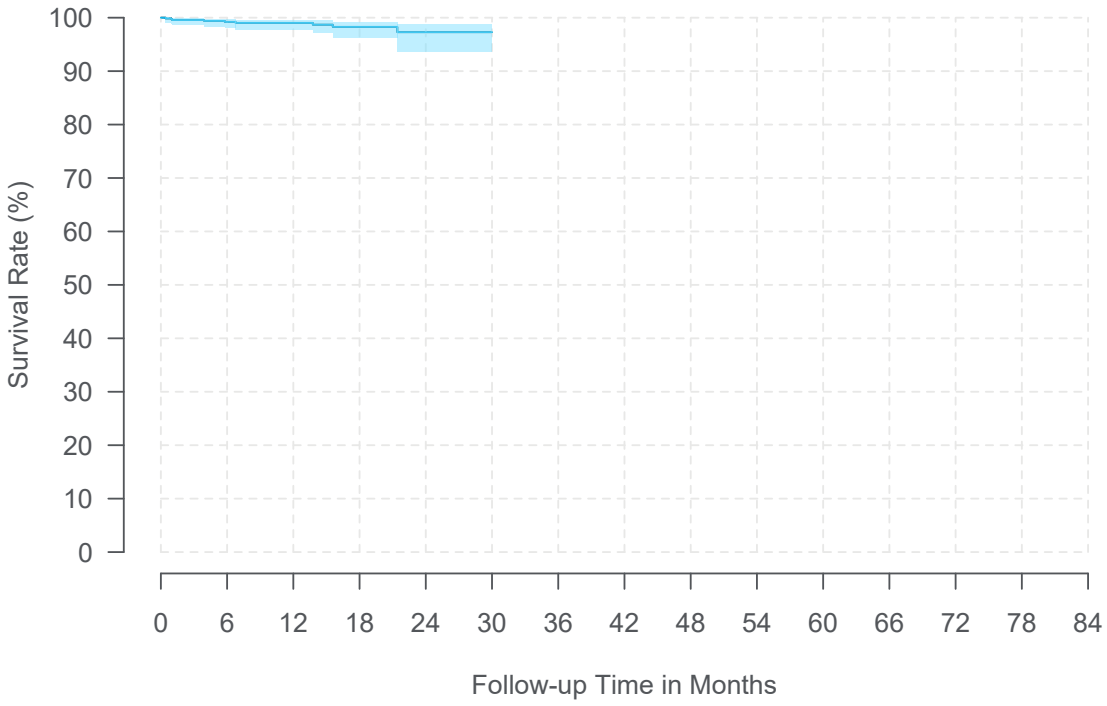
- 4,747 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 1,682 were free from product performance-related events and censoring events, and were censored 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	September 2017
Neurostimulators Enrolled	926
Neurostimulators Currently Active in Study	757
Device Events	9
Median Follow-up Time (Months)	8.3
Cumulative Follow-up Time (Months)	8,974



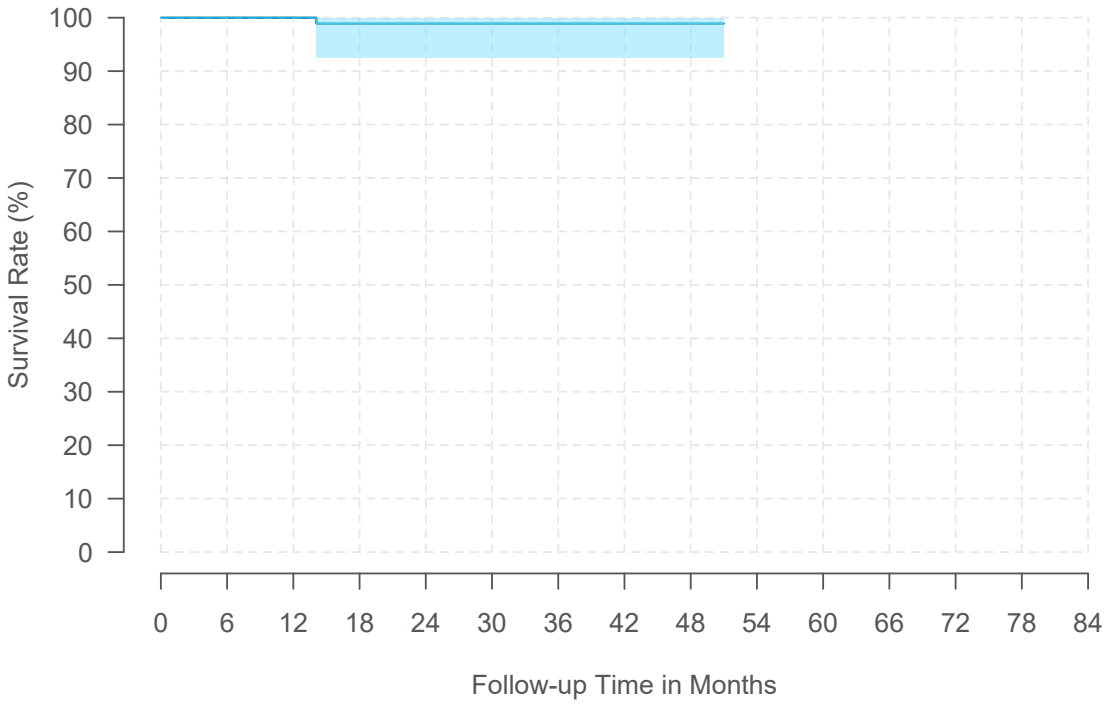
Time Interval	1 Year	2 Years	At 30 Months
Survival (95% CI)	99.0% (97.8%, 99.6%)	97.3% (93.7%, 98.9%)	97.3% (93.7%, 98.9%)
Sample Size	328	57	25

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	4
Device charging issue	1
Device electrical impedance issue	1
Device malfunction	1
Device overheating	1
Lead migration/dislodgement	1
Total	**9**

4.3.2.2 Model Itrel 4

Model Name	Itrel 4 (model 37703)
FDA Approval Date	May 2012
Neurostimulators Enrolled	126
Neurostimulators Currently Active in Study	58
Device Events	1
Median Follow-up Time (Months)	24.0
Cumulative Follow-up Time (Months)	3,516



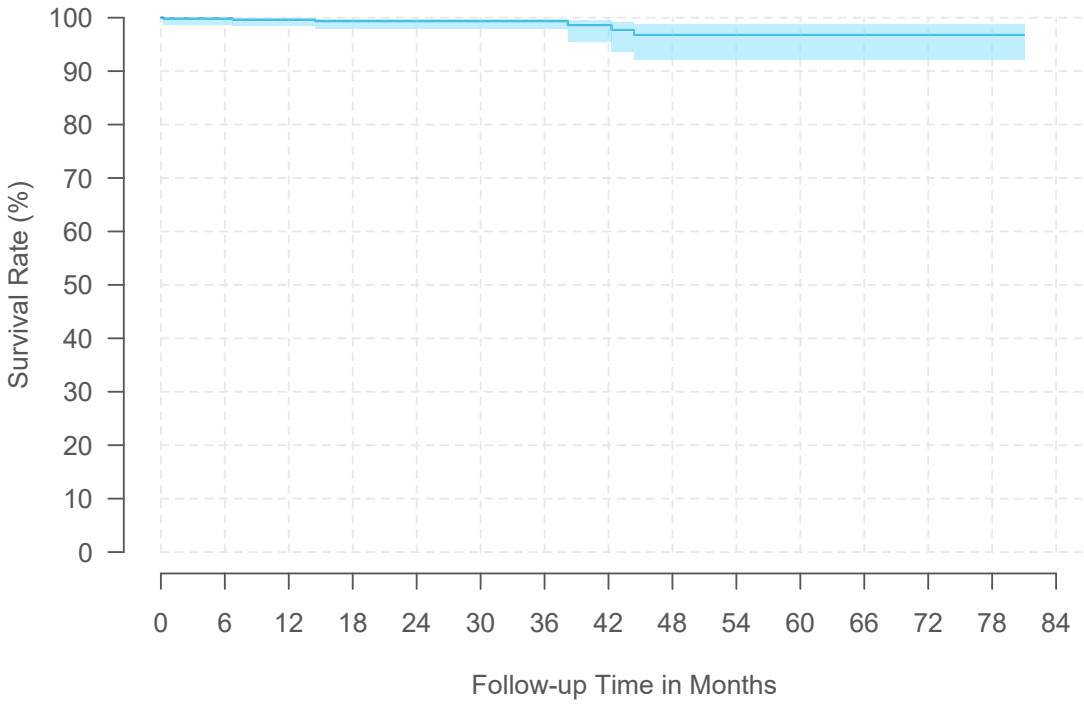
Time Interval	1 Year	2 Years	3 Years	4 Years	At 51 Months
Survival (95% CI)	100.0% (NA)	98.9% (92.4%, 99.8%)	98.9% (92.4%, 99.8%)	98.9% (92.4%, 99.8%)	98.9% (92.4%, 99.8%)
Sample Size	95	62	44	25	21

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
High impedance	1
Total	**1**

4.3.2.3 Model PrimeAdvanced

Model Name	PrimeAdvanced (model 37702)
FDA Approval Date	July 2006
Neurostimulators Enrolled	669
Neurostimulators Currently Active in Study	24
Device Events	6
Median Follow-up Time (Months)	16.0
Cumulative Follow-up Time (Months)	15,308



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%)	99.3% (97.9%, 99.8%)	96.8% (92.0%, 98.7%)	96.8% (92.0%, 98.7%)
Sample Size	393	237	143	94	62

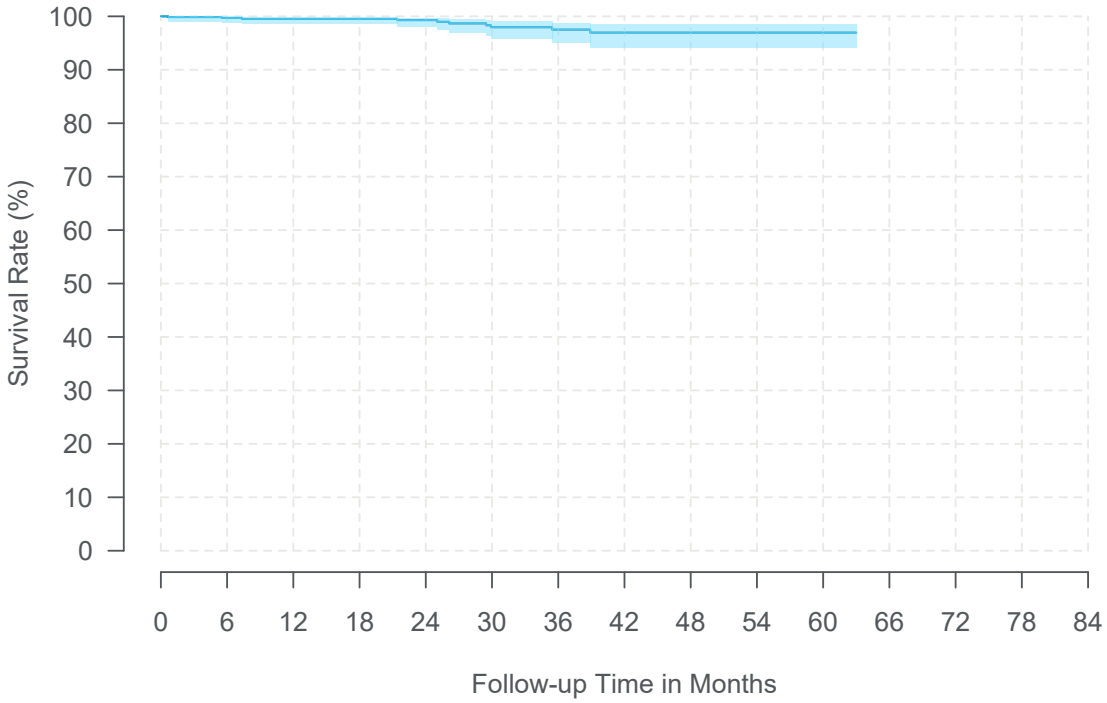
Time Interval	6 Years	At 81 Months			
Survival (95% CI)	96.8% (92.0%, 98.7%)	96.8% (92.0%, 98.7%)			
Sample Size	34	20			

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
Device malfunction	2
High impedance	2
Device stimulation issue	1
Low impedance	1
Total	**6**

4.3.2.4 Model PrimeAdvanced SureScan MRI

Model Name	PrimeAdvanced SureScan MRI (model 97702)
FDA Approval Date	March 2013
Neurostimulators Enrolled	740
Neurostimulators Currently Active in Study	294
Device Events	10
Median Follow-up Time (Months)	23.5
Cumulative Follow-up Time (Months)	19,015



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (98.5%, 99.8%)	99.3% (98.1%, 99.7%)	97.5% (95.1%, 98.8%)	97.0% (94.1%, 98.4%)	97.0% (94.1%, 98.4%)
Sample Size	540	360	213	96	37

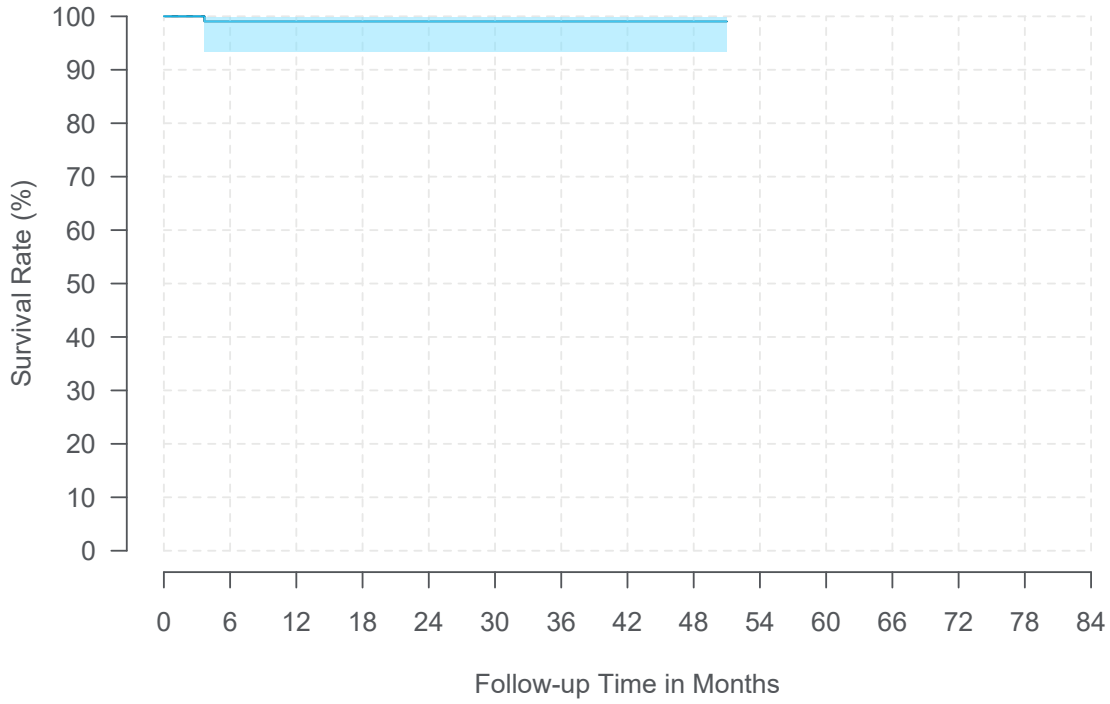
Time Interval	At 63 Months
Survival (95% CI)	97.0% (94.1%, 98.4%)
Sample Size	28

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	6
Device battery issue	1
Lead migration/dislodgement	1
Neurostimulator unable to recharge	1
Premature battery depletion	1
Total	**10**

4.3.2.5 Model RestoreAdvanced SureScan MRI

Model Name	RestoreAdvanced SureScan MRI (model 97713)
FDA Approval Date	March 2013
Neurostimulators Enrolled	116
Neurostimulators Currently Active in Study	33
Device Events	1
Median Follow-up Time (Months)	30.3
Cumulative Follow-up Time (Months)	3,617



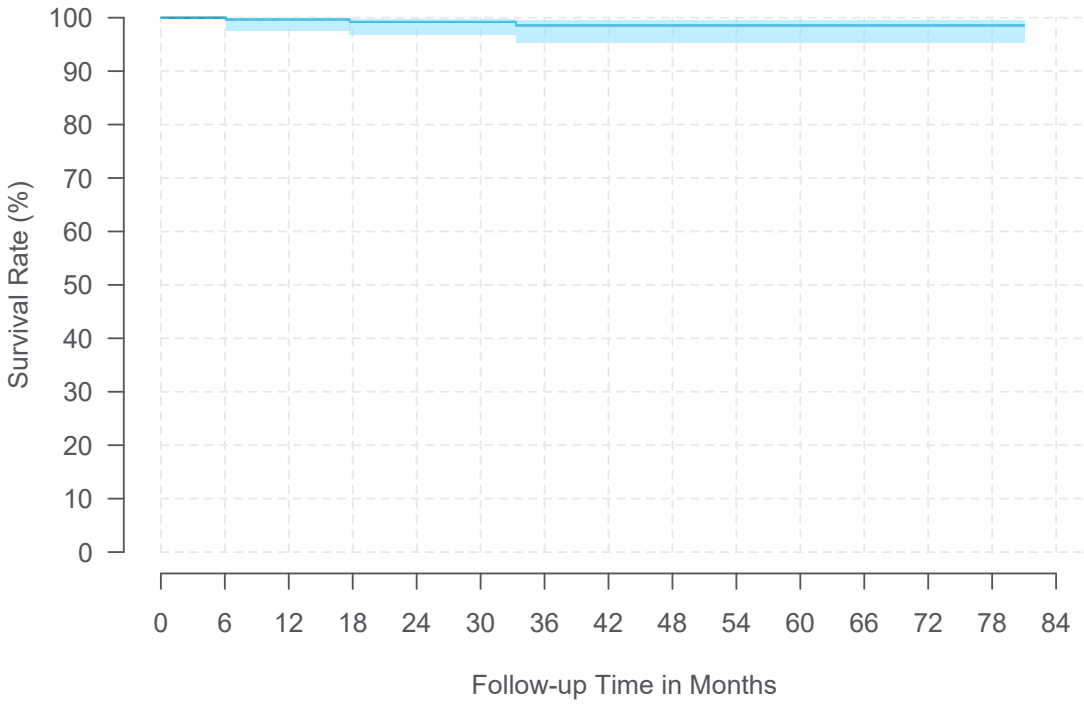
Time Interval	1 Year	2 Years	3 Years	4 Years	At 51 Months
Survival (95% CI)	99.0% (93.4%, 99.9%)	99.0% (93.4%, 99.9%)	99.0% (93.4%, 99.9%)	99.0% (93.4%, 99.9%)	99.0% (93.4%, 99.9%)
Sample Size	89	71	50	24	21

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	377
Neurostimulators Currently Active in Study	37
Device Events	3
Median Follow-up Time (Months)	23.2
Cumulative Follow-up Time (Months)	11,547



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.7% (97.7%, 100%)	99.2% (96.9%, 99.8%)	98.5% (95.3%, 99.6%)	98.5% (95.3%, 99.6%)	98.5% (95.3%, 99.6%)
Sample Size	258	185	135	91	63

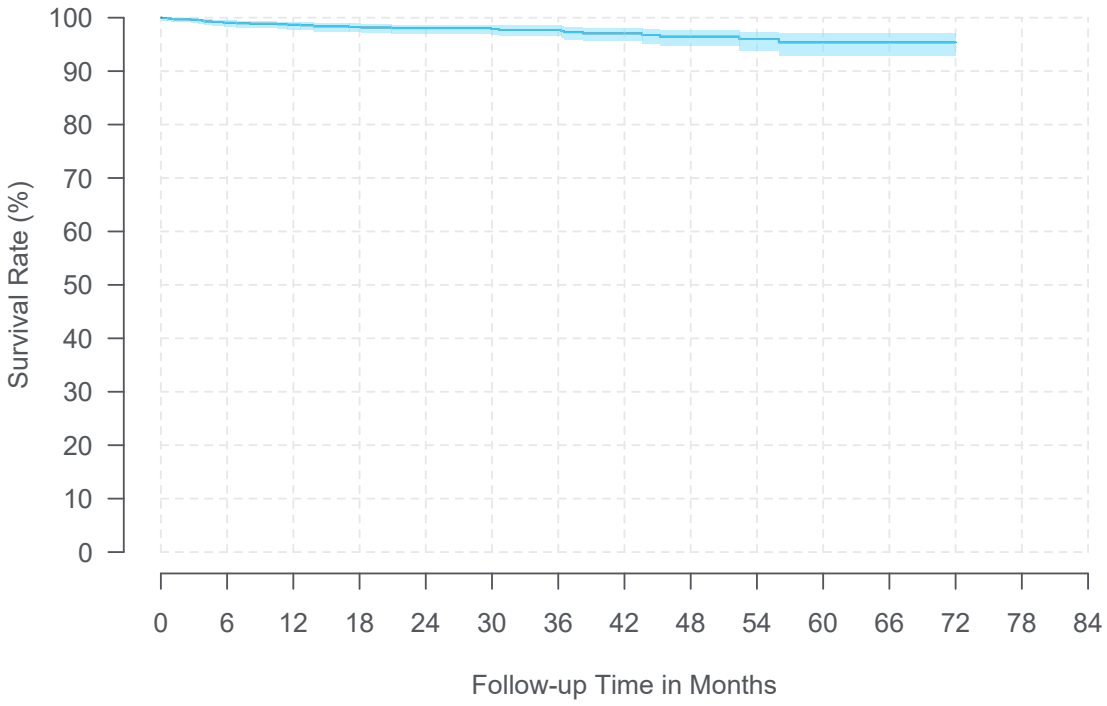
Time Interval	6 Years	At 81 Months			
Survival (95% CI)	98.5% (95.3%, 99.6%)	98.5% (95.3%, 99.6%)			
Sample Size	40	22			

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	2
Device malfunction	1
Total	**3**

4.3.2.7 Model RestoreSensor SureScan MRI

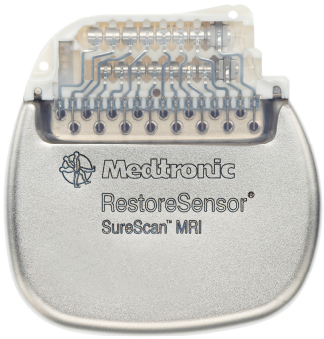
Model Name	RestoreSensor SureScan MRI (model 97714)
FDA Approval Date	March 2013
Neurostimulators Enrolled	1,377
Neurostimulators Currently Active in Study	442
Device Events	31
Median Follow-up Time (Months)	26.1
Cumulative Follow-up Time (Months)	39,678



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.7% (97.9%, 99.2%)	98.0% (97.0%, 98.7%)	97.7% (96.6%, 98.5%)	96.5% (94.7%, 97.6%)	95.4% (92.8%, 97.1%)
Sample Size	1,024	745	471	270	108

Time Interval	6 Years
Survival (95% CI)	95.4% (92.8%, 97.1%)
Sample Size	28

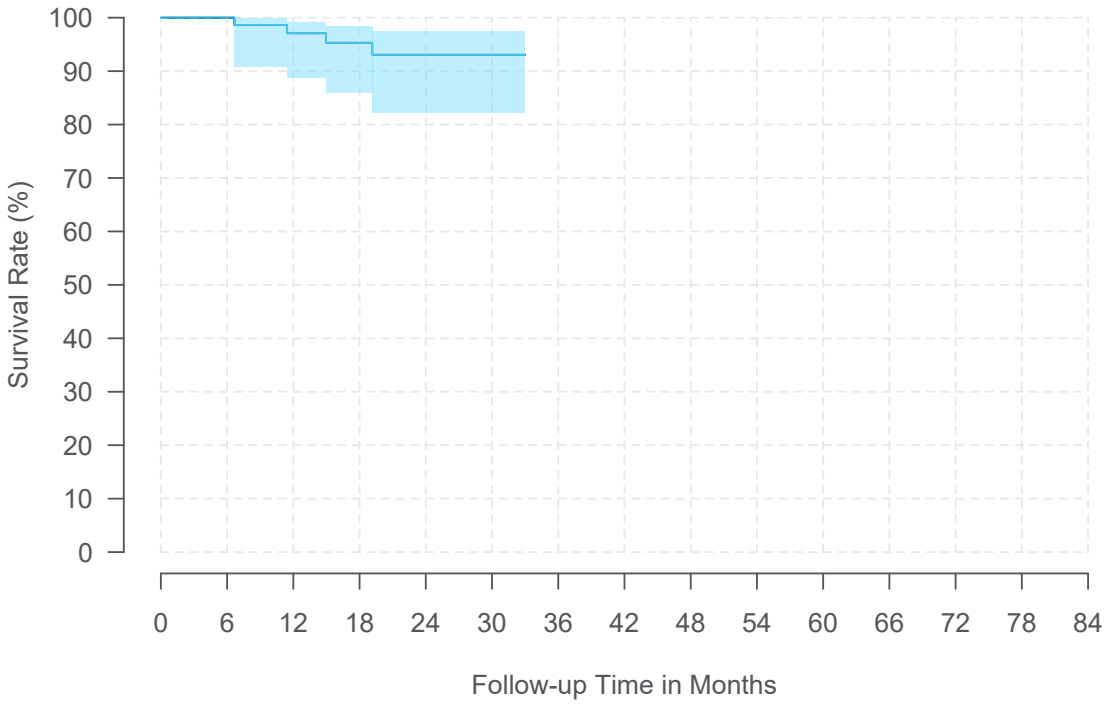
Specification: RestoreSensor SureScan MRI	
Height	54 mm (2.1 in)
Width	54 mm (2.1 in)
Thickness	9 mm (0.4 in)
Volume	22 cc
Battery type	Rechargeable
Expected Battery life	9 years
Maximum Electrodes	16
Amplitude	0 - 10.5 V
Rate	2 - 1200 Hz
Pulse Width	60 - 1000 µsec
Groups	8
Programs	16
Implant Depth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



Neurostimulator Event Summary: RestoreSensor SureScan MRI	N
Neurostimulator unable to recharge	10
Device malfunction	9
Lead migration/dislodgement	5
High impedance	2
Low impedance	2
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	40
Device Events	4
Median Follow-up Time (Months)	18.4
Cumulative Follow-up Time (Months)	1,972



Time Interval	1 Year	2 Years	At 33 Months
Survival (95% CI)	97.1% (88.8%, 99.3%)	93.1% (82.2%, 97.4%)	93.1% (82.2%, 97.4%)
Sample Size	60	35	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 4.8: Spinal Cord Stimulation Primary Cell Neurostimulator Characteristics

Model/Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Itrel 4 (model 37703)	May 2012	126	58	1	24.0	3,516
PrimeAdvanced (model 37702)	July 2006	669	24	6	16.0	15,308
PrimeAdvanced SureScan MRI (model 97702)	March 2013	740	294	10	23.5	19,015

Table 4.9: 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)	100.0% (NA)	98.9% (92.4%, 99.8%)	98.9% (92.4%, 99.8%)	98.9% (92.4%, 99.8%)	
PrimeAdvanced (model 37702)	99.6% (98.5%, 99.9%)	99.3% (97.9%, 99.8%)	99.3% (97.9%, 99.8%)	96.8% (92.0%, 98.7%)	96.8% (92.0%, 98.7%)
PrimeAdvanced SureScan MRI (model 97702)	99.5% (98.5%, 99.8%)	99.3% (98.1%, 99.7%)	97.5% (95.1%, 98.8%)	97.0% (94.1%, 98.4%)	97.0% (94.1%, 98.4%)

Model Name	6 Years				
Itrel 4 (model 37703)					
PrimeAdvanced (model 37702)	96.8% (92.0%, 98.7%)				
PrimeAdvanced SureScan MRI (model 97702)					

Table 4.10: Spinal Cord Stimulation Rechargeable Neurostimulator Characteristics

Model/Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Intellis with AdaptiveStim	September 2017	926	757	9	8.3	8,974
RestoreAdvanced SureScan MRI (model 97713)	March 2013	116	33	1	30.3	3,617
RestoreSensor (model 37714)	November 2011	377	37	3	23.2	11,547
RestoreSensor SureScan MRI (model 97714)	March 2013	1,377	442	31	26.1	39,678
RestoreUltra SureScan MRI (model 97712)	March 2013	92	40	4	18.4	1,972

Table 4.11: 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% (97.8%, 99.6%)	97.3% (93.7%, 98.9%)			
RestoreAdvanced SureScan MRI (model 97713)	99.0% (93.4%, 99.9%)	99.0% (93.4%, 99.9%)	99.0% (93.4%, 99.9%)	99.0% (93.4%, 99.9%)	
RestoreSensor (model 37714)	99.7% (97.7%, 100%)	99.2% (96.9%, 99.8%)	98.5% (95.3%, 99.6%)	98.5% (95.3%, 99.6%)	98.5% (95.3%, 99.6%)
RestoreSensor SureScan MRI (model 97714)	98.7% (97.9%, 99.2%)	98.0% (97.0%, 98.7%)	97.7% (96.6%, 98.5%)	96.5% (94.7%, 97.6%)	95.4% (92.8%, 97.1%)
RestoreUltra SureScan MRI (model 97712)	97.1% (88.8%, 99.3%)	93.1% (82.2%, 97.4%)			

Model Name	6 Years
Intellis with AdaptiveStim	
RestoreAdvanced SureScan MRI (model 97713)	
RestoreSensor (model 37714)	98.5% (95.3%, 99.6%)
RestoreSensor SureScan MRI (model 97714)	95.4% (92.8%, 97.1%)
RestoreUltra SureScan MRI (model 97712)	

4.4 Leads

From June 2004 to the report cut-off date of October 31, 2020, there were 10,507 leads followed in the registry. The difference between the total number of leads (n=10,507) versus the number of neurostimulators (n=6,507) 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 288,607 months (24,051 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 4.12 provides the number and percentage of leads by model.

Table 4.12: Spinal Cord Stimulation Lead Counts by Model

Model Name	N (%)
Currently manufactured	**9,559 (91.0%)**
Vectris SureScan MRI 1x8 Compact (977A2)	4,040 (38.5%)
1x8 Compact (3778)	2,168 (20.6%)
Pisces Standard (3487A)	990 (9.4%)
1x8 Standard (3777)	837 (8.0%)
Pisces Plus (3888)	453 (4.3%)
Specify 5-6-5 (39565)	293 (2.8%)
Pisces Compact (3887)	200 (1.9%)
1x8 SC (3776)	188 (1.8%)
Vectris SureScan MRI 1x8 Subcompact (977A1)	139 (1.3%)
AnkerStim Lead (Approved in Europe, 09100)	119 (1.1%)
Specify SureScan MRI 5-6-5 (977C1)	65 (0.6%)
Specify SureScan MRI 2x8 (977C2)	35 (0.3%)
Specify 2x8 (39286)	32 (0.3%)
No longer manufactured	**686 (6.5%)**
Specify (3998)	157 (1.5%)
Pisces Z Standard (3890)	143 (1.4%)
Pisces Z Compact (3891)	130 (1.2%)
Resume TL (3986A)	108 (1.0%)
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	**262 (2.5%)**
Total	**10,507 (100%)**

Percutaneous leads composed 88.6% (9,313/10,507) of leads in the registry, including 39.8% (4,179/10,507) in the Vectris SureScan lead family, 30.4% (3,193/10,507) in the Pisces-Octad lead family, 15.6% (1,643/10,507) in the Pisces-Quad lead family, and 2.8% (298/10,507) in the Pisces-

Quad LZ lead family; 7.7% (813/10,507) of leads were surgical leads; and 3.6% (381/10,507) of leads were designated as "Other" or were unspecified in the database.

4.4.1 Lead Events

There were 1,331 product performance-related events with an underlying reported etiology related to lead function. This includes 1,305 events with a lead etiology and 26 events with both a lead and other etiology (including device and non-device etiologies). Of these, 981 were the initial product performance event that affected lead survival estimates; the majority were lead migration/dislodgement (n=590), high impedance (n=219), lead fracture (n=78), device stimulation issue (n=42), and low impedance (n=25). There were 909 events in 9,313 (9.8%) percutaneous leads, 45 events in 813 (5.5%) surgical leads, and 27 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:

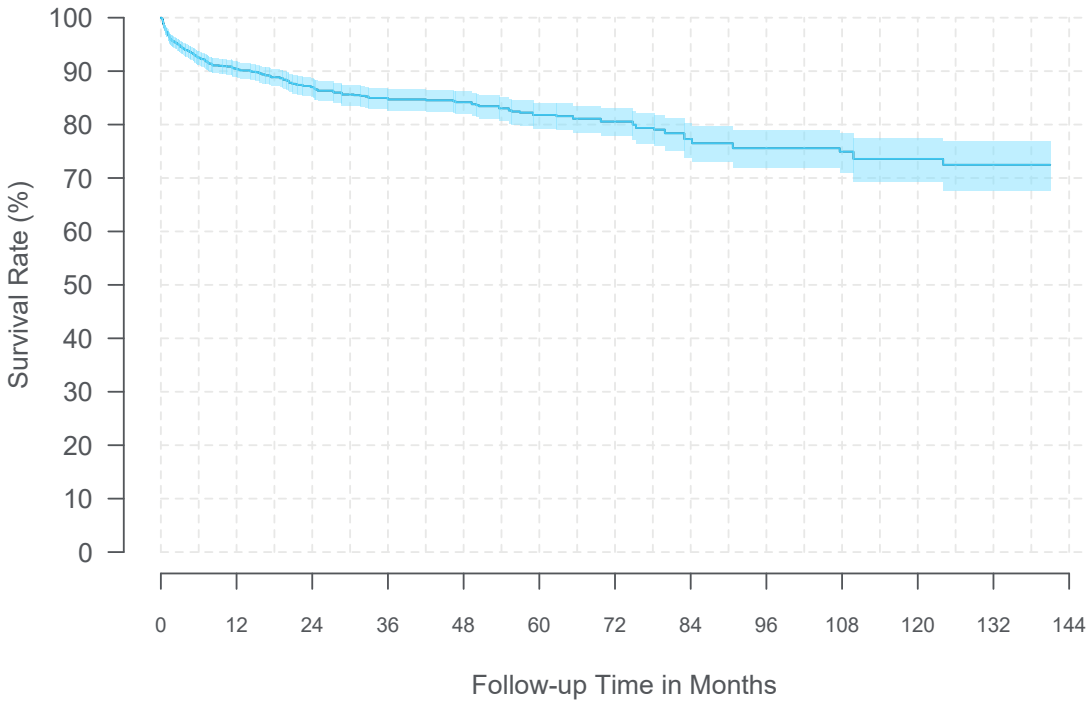
- 981 had follow-up time cut-off due to product performance-related events.
- 6,806 were censored in the survival analysis for the following reasons: patient expired, lead explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,720 were free from product 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	2,168
Leads Currently Active in Study	158
Device Events	261
Median Follow-up Time (Months)	17.9
Cumulative Follow-up Time (Months)	65,703



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	90.4% (88.9%, 91.8%)	87.0% (85.1%, 88.6%)	84.7% (82.6%, 86.6%)	84.2% (82.0%, 86.1%)	81.8% (79.3%, 84.1%)
Sample Size	1,210	799	599	455	376

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	80.6% (77.8%, 83.0%)	77.3% (73.9%, 80.3%)	75.6% (71.8%, 78.9%)	74.9% (71.0%, 78.4%)	73.6% (69.2%, 77.4%)
Sample Size	289	198	144	116	85

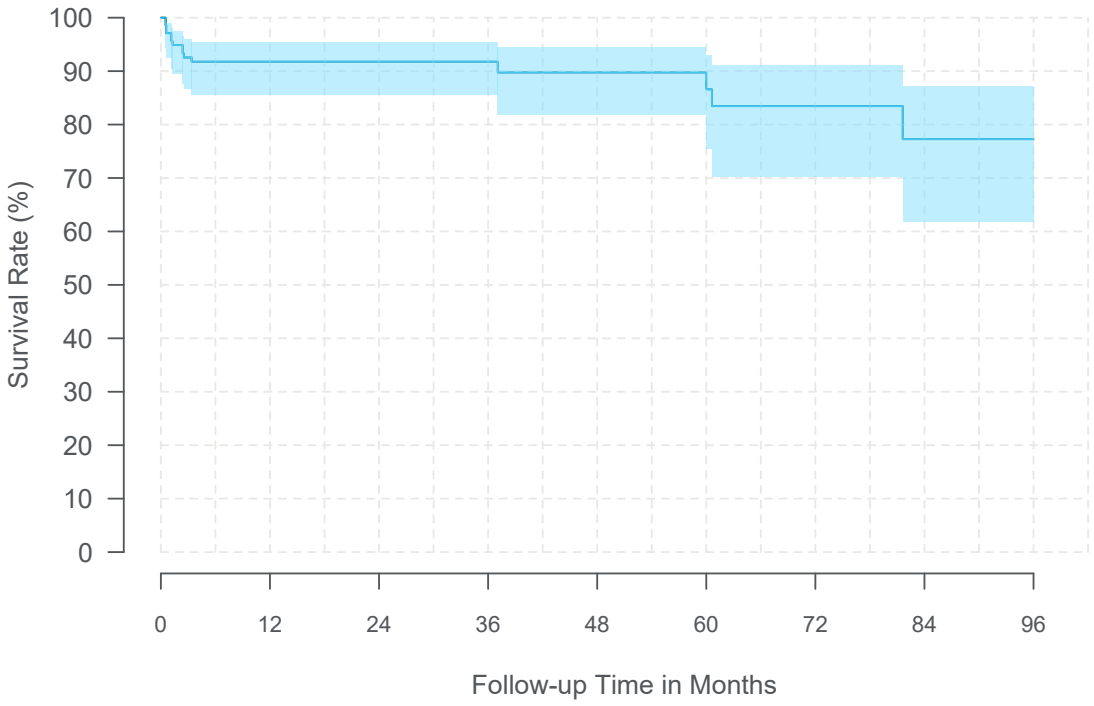
Time Interval	11 Years	At 141 Months			
Survival (95% CI)	72.5% (67.6%, 76.8%)	72.5% (67.6%, 76.8%)			
Sample Size	41	25			

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	203
High impedance	27
Lead fracture	19
Device stimulation issue	6
Medical device complication	4
Medical device site erosion	2
Total	**261**

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	21
Device Events	17
Median Follow-up Time (Months)	14.1
Cumulative Follow-up Time (Months)	5,252



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%)	86.6% (75.4%, 92.9%)
Sample Size	84	62	47	36	27

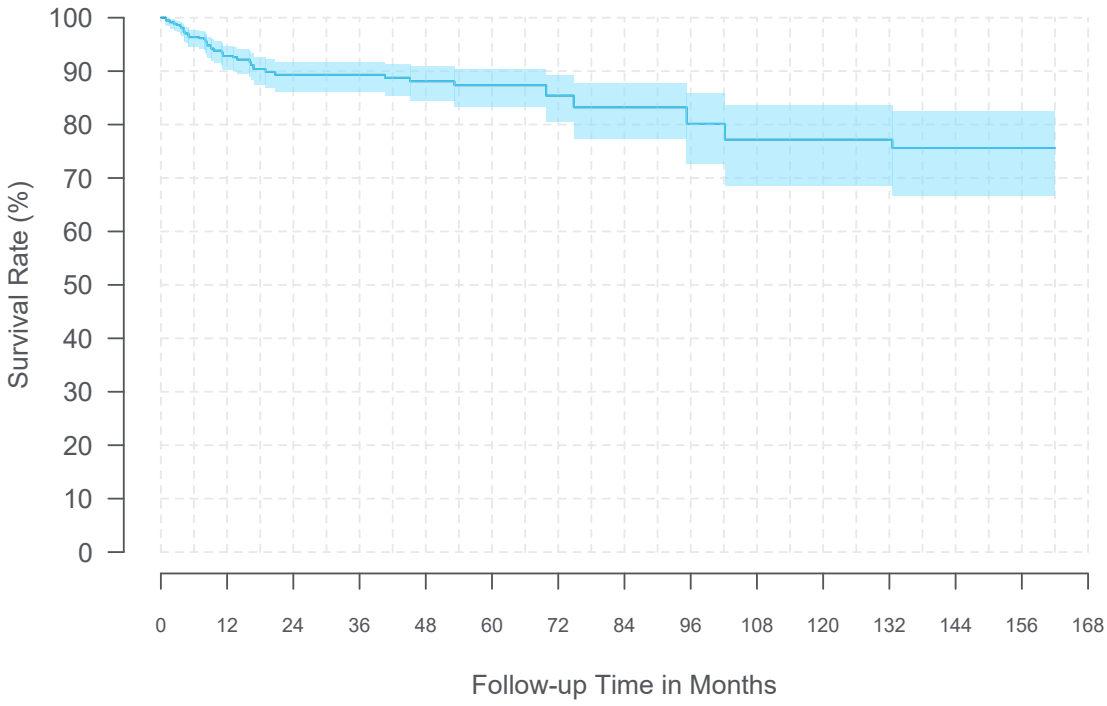
Time Interval	6 Years	7 Years	8 Years		
Survival (95% CI)	83.5% (70.2%, 91.2%)	77.3% (61.8%, 87.1%)	77.3% (61.8%, 87.1%)		
Sample Size	21	22	20		

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	12
High impedance	3
Device stimulation issue	1
Lead fracture	1
Total	**17**

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	81
Device Events	70
Median Follow-up Time (Months)	16.4
Cumulative Follow-up Time (Months)	23,401



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.8% (90.3%, 94.7%)	89.3% (86.2%, 91.8%)	89.3% (86.2%, 91.8%)	88.1% (84.5%, 90.9%)	87.4% (83.4%, 90.4%)
Sample Size	442	287	185	128	102

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	85.4% (80.5%, 89.2%)	83.2% (77.3%, 87.7%)	80.1% (72.7%, 85.8%)	77.2% (68.7%, 83.7%)	77.2% (68.7%, 83.7%)
Sample Size	83	60	51	65	60

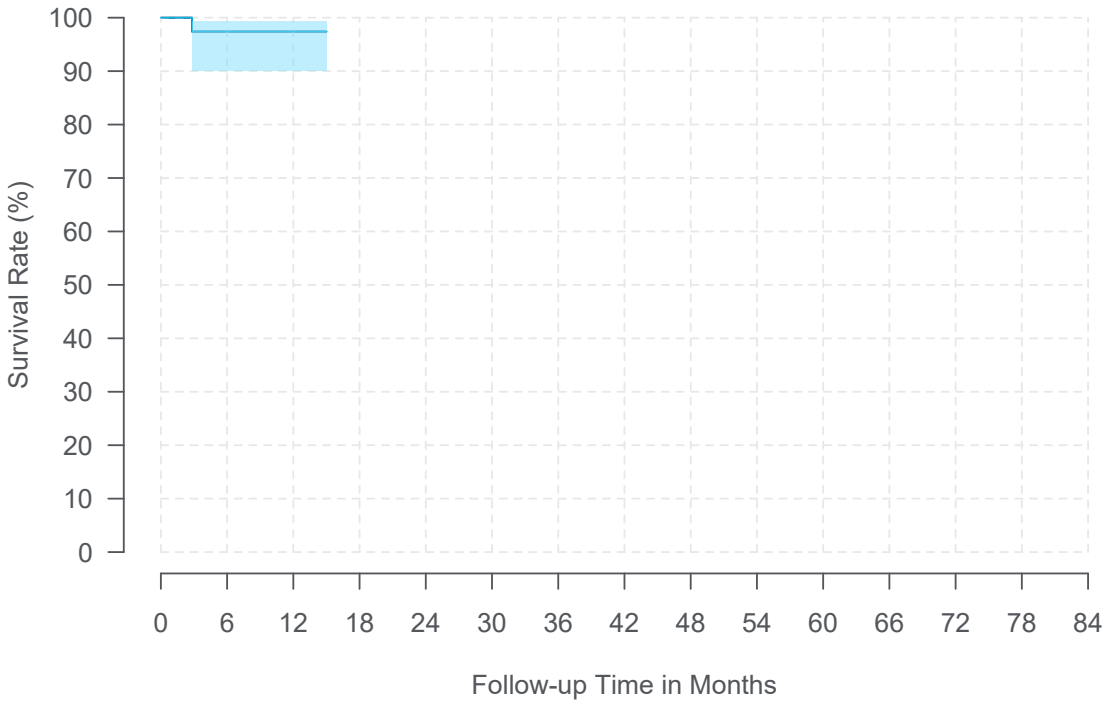
Time Interval	11 Years	12 Years	13 Years	At 162 Months	
Survival (95% CI)	77.2% (68.7%, 83.7%)	75.6% (66.6%, 82.5%)	75.6% (66.6%, 82.5%)	75.6% (66.6%, 82.5%)	
Sample Size	51	41	30	23	

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	41
High impedance	13
Device stimulation issue	7
Lead fracture	3
Device lead damage	2
Device malfunction	2
Low impedance	2
Total	**70**

4.4.2.4 Model AnkerStim

Model Name	AnkerStim (model 09100)
FDA Approval Date	NA
Leads Enrolled	119
Leads Currently Active in Study	98
Device Events	2
Median Follow-up Time (Months)	5.4
Cumulative Follow-up Time (Months)	879



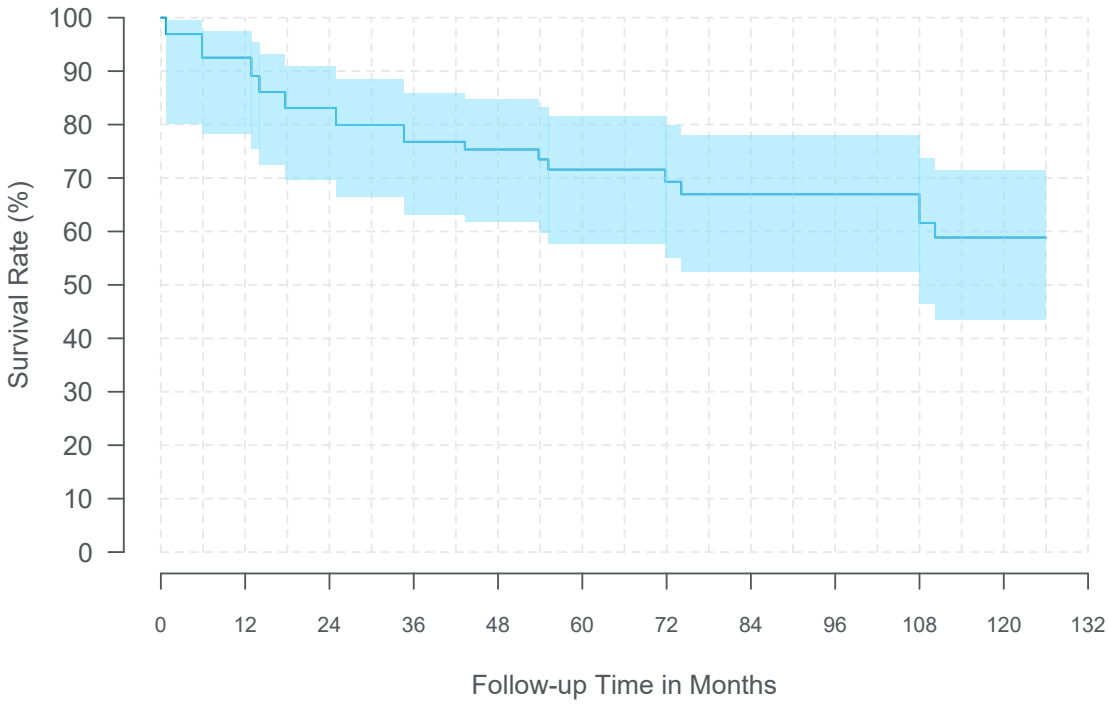
Time Interval	1 Year	At 15 Months
Survival	97.4%	97.4%
(95% CI)	(90.0%, 99.3%)	(90.0%, 99.3%)
Sample Size	32	22

Specification: AnkerStim	
Lead Type	Percutaneous
Lead	
Length (cm)	60
Diameter (mm)	1.3
Electrode	
Number	4
Shape	Cylindrical
Length (mm)	6.0
Individual Surface Area (mm)	24.5
Inter-Electrode Spacing: Edge to Edge (mm)	12.0
Array Length (mm)	60.0

Lead Event Summary: AnkerStim	N
Lead fracture	2
Total	**2**

4.4.2.5 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)	20.1
Cumulative Follow-up Time (Months)	6,937



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	23

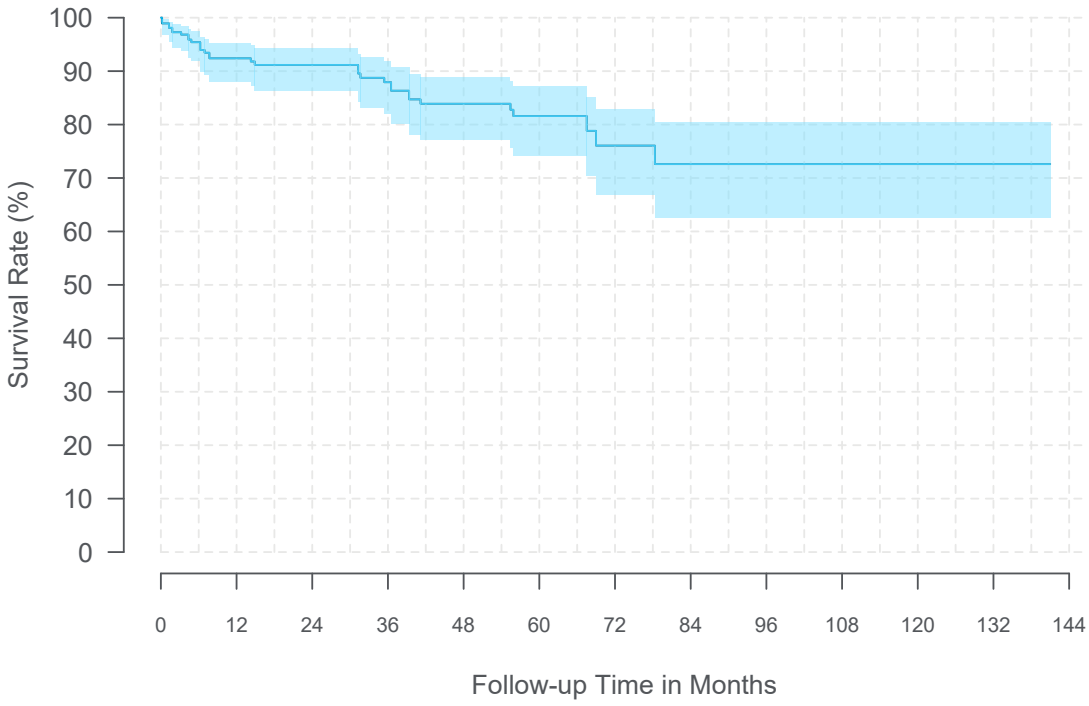
Time Interval	At 126 Months				
Survival (95% CI)	58.9% (43.5%, 71.4%)				
Sample Size	20				

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**

4.4.2.6 Model Pisces Plus

Model Name	Pisces Plus (model 3888)
FDA Approval Date	November 1992
Leads Enrolled	453
Leads Currently Active in Study	58
Device Events	40
Median Follow-up Time (Months)	14.5
Cumulative Follow-up Time (Months)	11,333



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.4% (88.0%, 95.2%)	91.2% (86.4%, 94.3%)	87.9% (82.1%, 92.0%)	83.9% (77.1%, 88.8%)	81.6% (74.1%, 87.1%)
Sample Size	161	119	109	82	66

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	76.1% (66.9%, 83.0%)	72.6% (62.5%, 80.4%)	72.6% (62.5%, 80.4%)	72.6% (62.5%, 80.4%)	72.6% (62.5%, 80.4%)
Sample Size	47	36	34	33	30

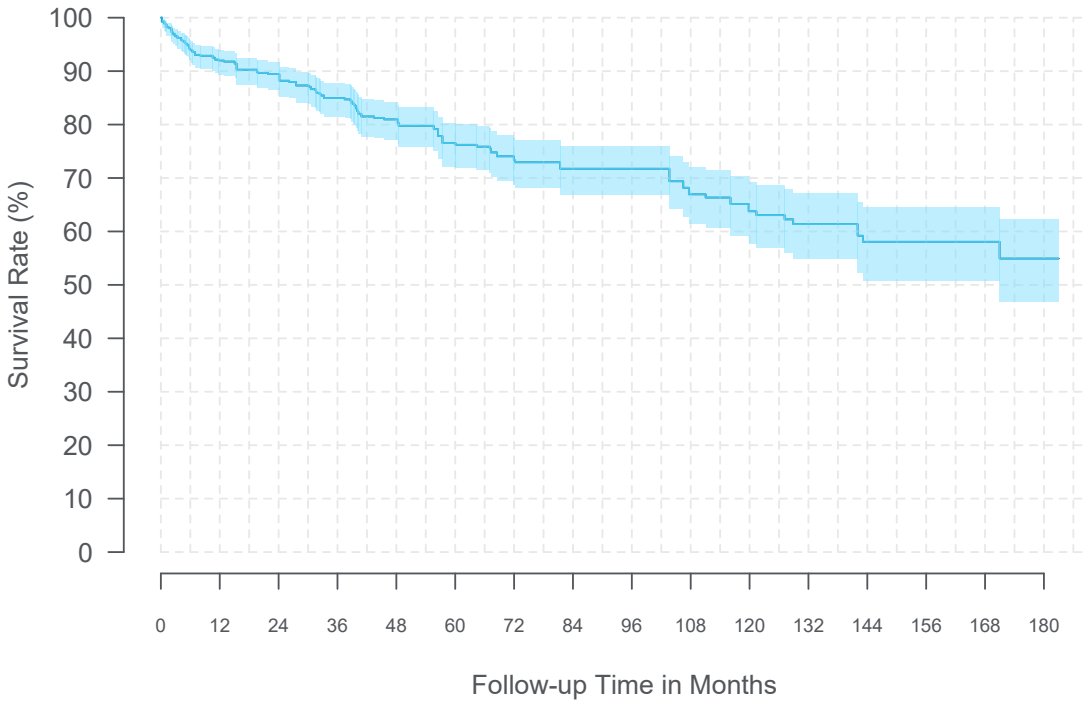
Time Interval	11 Years	At 141 Months			
Survival (95% CI)	72.6% (62.5%, 80.4%)	72.6% (62.5%, 80.4%)			
Sample Size	26	22			

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	27
High impedance	10
Device stimulation issue	2
Lead fracture	1
Total	**40**

4.4.2.7 Model Pisces Standard

Model Name	Pisces Standard (model 3487A)
FDA Approval Date	May 1988
Leads Enrolled	990
Leads Currently Active in Study	74
Device Events	161
Median Follow-up Time (Months)	30.5
Cumulative Follow-up Time (Months)	40,601



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.0% (89.4%, 93.9%)	89.5% (86.6%, 91.7%)	85.0% (81.6%, 87.8%)	81.0% (77.2%, 84.2%)	76.5% (72.2%, 80.3%)
Sample Size	511	423	356	275	229

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	73.3% (68.7%, 77.4%)	71.7% (66.9%, 76.0%)	71.7% (66.9%, 76.0%)	67.0% (61.3%, 71.9%)	63.8% (57.7%, 69.2%)
Sample Size	196	165	129	110	93

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	61.4% (54.9%, 67.2%)	58.1% (50.9%, 64.6%)	58.1% (50.9%, 64.6%)	58.1% (50.9%, 64.6%)	54.9% (46.8%, 62.3%)
Sample Size	63	52	49	39	30

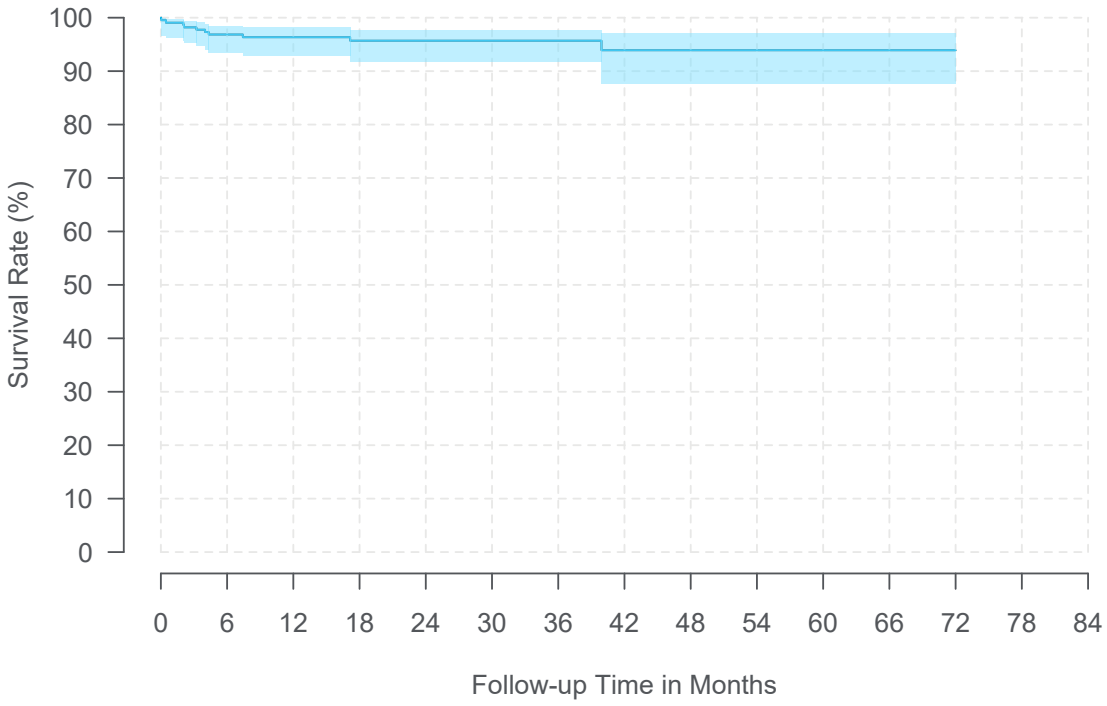
Time Interval	At 183 Months
Survival (95% CI)	54.9% (46.8%, 62.3%)
Sample Size	23

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	69
Lead migration/dislodgement	49
Device stimulation issue	17
Low impedance	15
Lead fracture	8
Inadequate lead connection	2
Device lead damage	1
Total	**161**

4.4.2.8 Model Specify 5-6-5

Model Name	Specify 5-6-5 (model 39565)
FDA Approval Date	June 2007
Leads Enrolled	293
Leads Currently Active in Study	40
Device Events	11
Median Follow-up Time (Months)	21.0
Cumulative Follow-up Time (Months)	7,610



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	96.3% (92.8%, 98.2%)	95.7% (91.8%, 97.8%)	95.7% (91.8%, 97.8%)	93.9% (87.6%, 97.1%)	93.9% (87.6%, 97.1%)
Sample Size	163	115	68	43	26

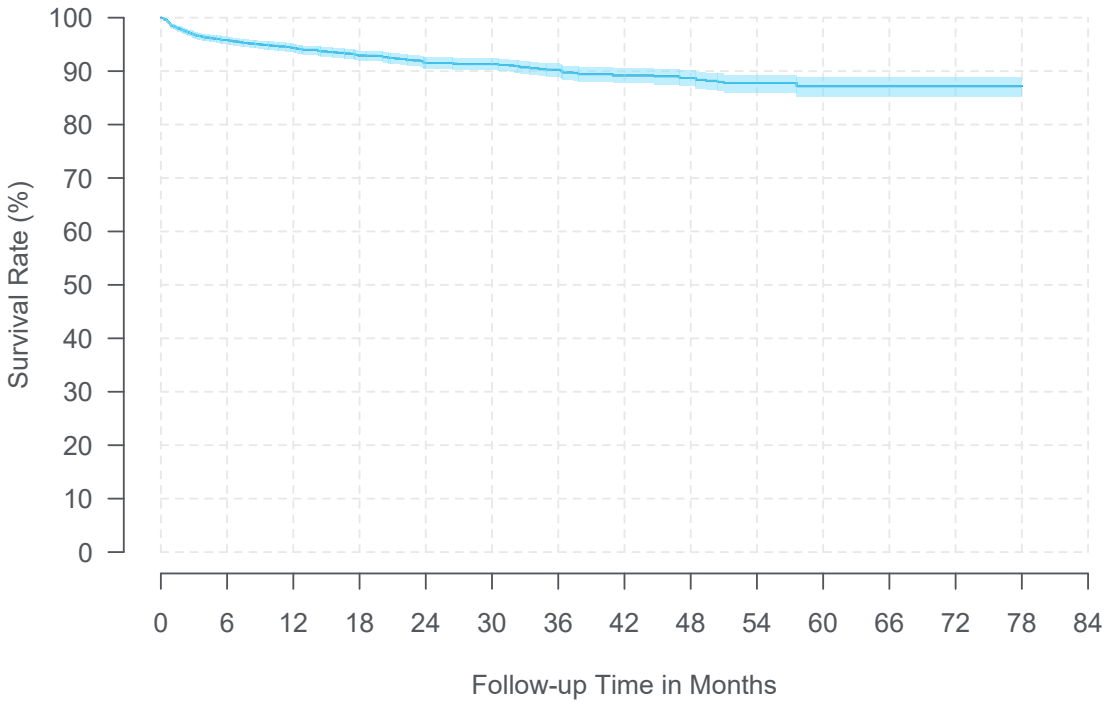
Time Interval	6 Years				
Survival (95% CI)	93.9% (87.6%, 97.1%)				
Sample Size	20				

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
Lead fracture	1
Lead insulation failure	1
Total	**11**

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	4,040
Leads Currently Active in Study	1,964
Device Events	284
Median Follow-up Time (Months)	18.4
Cumulative Follow-up Time (Months)	92,181



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	94.3% (93.4%, 95.1%)	91.5% (90.4%, 92.5%)	90.3% (89.0%, 91.4%)	88.7% (87.2%, 90.1%)	87.2% (85.2%, 88.9%)
Sample Size	2,396	1,492	909	516	252

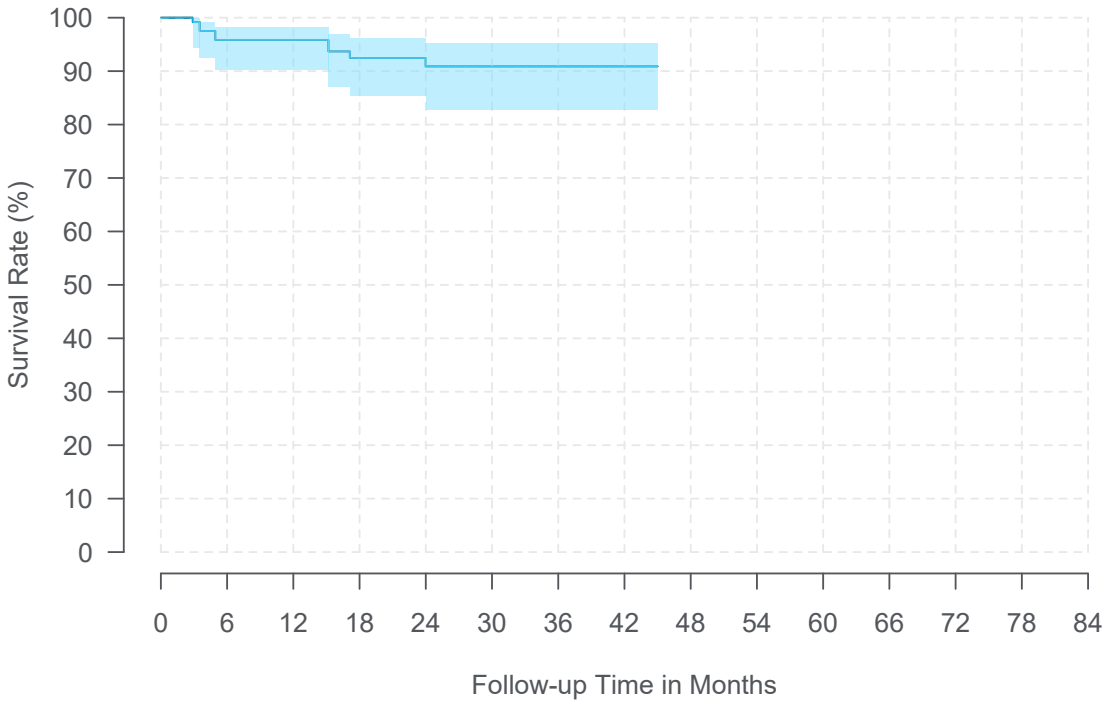
Time Interval	6 Years	At 78 Months			
Survival (95% CI)	87.2% (85.2%, 88.9%)	87.2% (85.2%, 88.9%)			
Sample Size	97	34			

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	204
High impedance	51
Lead fracture	20
Device electrical impedance issue	4
Device difficult to use	2
Device malfunction	1
Low impedance	1
Therapeutic product ineffective	1
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	139
Leads Currently Active in Study	42
Device Events	9
Median Follow-up Time (Months)	18.7
Cumulative Follow-up Time (Months)	3,429



Time Interval	1 Year	2 Years	3 Years	At 45 Months
Survival (95% CI)	95.8% (90.3%, 98.2%)	90.9% (82.9%, 95.3%)	90.9% (82.9%, 95.3%)	90.9% (82.9%, 95.3%)
Sample Size	90	57	38	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	6
Lead fracture	2
High impedance	1
Total	**9**

4.4.3 Lead Summary

Table 4.13: Spinal Cord Stimulation Percutaneous Lead Characteristics

Model/Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
1x8 Compact (model 3778)	April 2005	2,168	158	261	17.9	65,703
1x8 SC (model 3776)	November 2005	188	21	17	14.1	5,252
1x8 Standard (model 3777)	April 2005	837	81	70	16.4	23,401
AnkerStim Lead (Approved in Europe): 09100	NA	119	98	2	5.4	879
Pisces Compact (model 3887)	January 1997	200	46	24	20.1	6,937
Pisces Plus (model 3888)	November 1992	453	58	40	14.5	11,333
Pisces Standard (model 3487A)	May 1988	990	74	161	30.5	40,601
Vectris SureScan MRI 1x8 Compact (model 977A2)	March 2013	4,040	1,964	284	18.4	92,181
Vectris SureScan MRI 1x8 Subcompact (model 977A1)	March 2013	139	42	9	18.7	3,429

Table 4.14: 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)	90.4% (88.9%, 91.8%)	87.0% (85.1%, 88.6%)	84.7% (82.6%, 86.6%)	84.2% (82.0%, 86.1%)	81.8% (79.3%, 84.1%)
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%)	86.6% (75.4%, 92.9%)
1x8 Standard (model 3777)	92.8% (90.3%, 94.7%)	89.3% (86.2%, 91.8%)	89.3% (86.2%, 91.8%)	88.1% (84.5%, 90.9%)	87.4% (83.4%, 90.4%)
AnkerStim Lead (Approved in Europe): 09100	97.4% (90.0%, 99.3%)				
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)	92.4% (88.0%, 95.2%)	91.2% (86.4%, 94.3%)	87.9% (82.1%, 92.0%)	83.9% (77.1%, 88.8%)	81.6% (74.1%, 87.1%)
Pisces Standard (model 3487A)	92.0% (89.4%, 93.9%)	89.5% (86.6%, 91.7%)	85.0% (81.6%, 87.8%)	81.0% (77.2%, 84.2%)	76.5% (72.2%, 80.3%)
Vectris SureScan MRI 1x8 Compact (model 977A2)	94.3% (93.4%, 95.1%)	91.5% (90.4%, 92.5%)	90.3% (89.0%, 91.4%)	88.7% (87.2%, 90.1%)	87.2% (85.2%, 88.9%)
Vectris SureScan MRI 1x8 Subcompact (model 977A1)	95.8% (90.3%, 98.2%)	90.9% (82.9%, 95.3%)	90.9% (82.9%, 95.3%)		

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
1x8 Compact (model 3778)	80.6% (77.8%, 83.0%)	77.3% (73.9%, 80.3%)	75.6% (71.8%, 78.9%)	74.9% (71.0%, 78.4%)	73.6% (69.2%, 77.4%)
1x8 SC (model 3776)	83.5% (70.2%, 91.2%)	77.3% (61.8%, 87.1%)	77.3% (61.8%, 87.1%)		
1x8 Standard (model 3777)	85.4% (80.5%, 89.2%)	83.2% (77.3%, 87.7%)	80.1% (72.7%, 85.8%)	77.2% (68.7%, 83.7%)	77.2% (68.7%, 83.7%)
AnkerStim Lead (Approved in Europe): 09100					
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)	76.1% (66.9%, 83.0%)	72.6% (62.5%, 80.4%)	72.6% (62.5%, 80.4%)	72.6% (62.5%, 80.4%)	72.6% (62.5%, 80.4%)
Pisces Standard (model 3487A)	73.3% (68.7%, 77.4%)	71.7% (66.9%, 76.0%)	71.7% (66.9%, 76.0%)	67.0% (61.3%, 71.9%)	63.8% (57.7%, 69.2%)
Vectris SureScan MRI 1x8 Compact (model 977A2)	87.2% (85.2%, 88.9%)				
Vectris SureScan MRI 1x8 Subcompact (model 977A1)					

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
1x8 Compact (model 3778)	72.5% (67.6%, 76.8%)				
1x8 SC (model 3776)					
1x8 Standard (model 3777)	77.2% (68.7%, 83.7%)	75.6% (66.6%, 82.5%)	75.6% (66.6%, 82.5%)		
AnkerStim Lead (Approved in Europe): 09100					
Pisces Compact (model 3887)					
Pisces Plus (model 3888)	72.6% (62.5%, 80.4%)				
Pisces Standard (model 3487A)	61.4% (54.9%, 67.2%)	58.1% (50.9%, 64.6%)	58.1% (50.9%, 64.6%)	58.1% (50.9%, 64.6%)	54.9% (46.8%, 62.3%)
Vectris SureScan MRI 1x8 Compact (model 977A2)					
Vectris SureScan MRI 1x8 Subcompact (model 977A1)					

Table 4.15: Spinal Cord Stimulation Surgical Lead Characteristics

Model/Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Specify 5-6-5 (model 39565)	June 2007	293	40	11	21.0	7,610

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

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Specify 5-6-5 (model 39565)	96.3% (92.8%, 98.2%)	95.7% (91.8%, 97.8%)	95.7% (91.8%, 97.8%)	93.9% (87.6%, 97.1%)	93.9% (87.6%, 97.1%)

Model Name	6 Years
Specify 5-6-5 (model 39565)	93.9% (87.6%, 97.1%)

4.5 Extensions

From June 2004 to the report cut-off date of October 31, 2020, there were 3,584 extensions followed in the registry. The difference between the total number of extensions (n=3,584) versus neurostimulators (n=6,507) were due to the fact that some systems did not use an extension. The aggregate prospective follow-up time for all extensions was 109,291 months (9,108 years). An extension is a set of thin wires with a protective coating that connects the neurostimulator to the lead. Table 4.17 provides the number and percentage of extensions by model.

Table 4.17: Spinal Cord Stimulation Extension Counts by Model

Model Name	N (%)
Currently manufactured	**2,481 (69.2%)**
1x8 (37081)	1,511 (42.2%)
Bifurcated Stretch-Coil (37082)	643 (17.9%)
Single Stretch-Coil (37083)	327 (9.1%)
No longer manufactured	**1,081 (30.2%)**
Low Profile Quad (7489)	758 (21.1%)
Quadripolar in-line (7495)	279 (7.8%)
Synergy bifurcated 1x8 (7472)	26 (0.7%)
Quadripolar (7496)	9 (0.3%)
Synergy 1x8 (7471)	9 (0.3%)
Other/Unspecified	**22 (0.6%)**
Total	**3,584 (100%)**

4.5.1 Extension Events

There were 50 product performance-related events with an underlying reported etiology related to extension function. This includes 40 events with an extension etiology and 10 events with both an extension and other etiology (including device and non-device etiologies). Of these, 36 were the initial product performance event that affected extension survival estimates; the majority were extension fracture (n=17) and extension migration (n=8).

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:

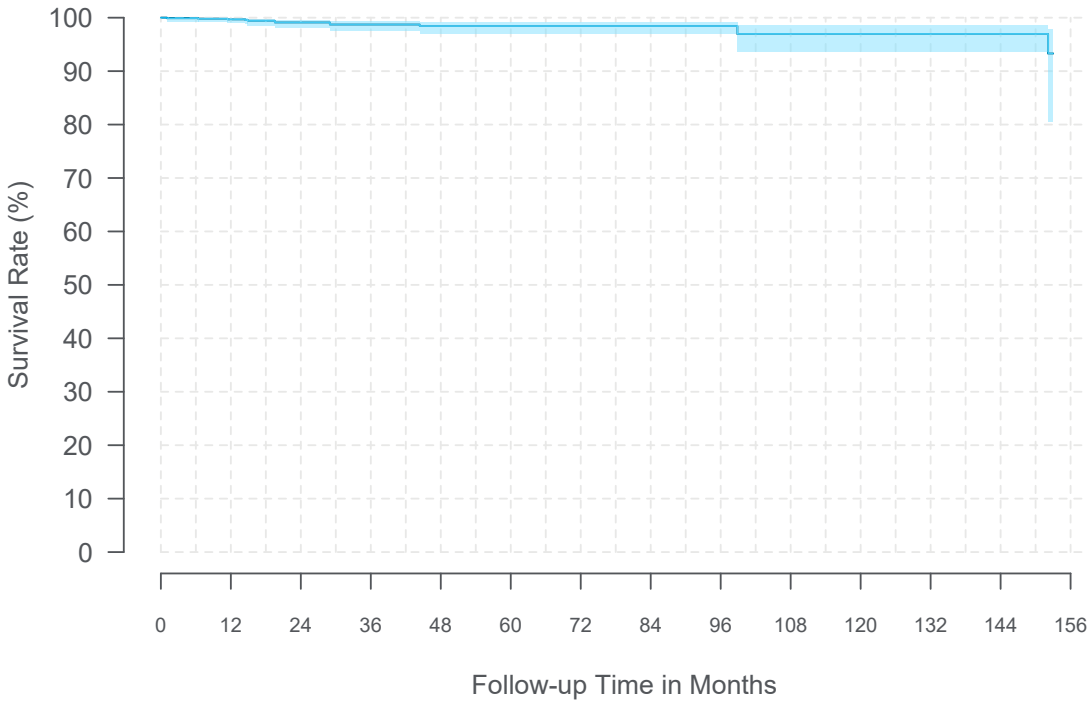
- 36 had follow-up time cut-off due to product performance-related events.
- 2,936 were censored in the survival analysis for the following reasons: patient expired, extension explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 612 were free from 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	1,511
Extensions Currently Active in Study	330
Device Events	14
Median Follow-up Time (Months)	20.0
Cumulative Follow-up Time (Months)	45,764



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.7% (99.0%, 99.9%)	99.1% (98.1%, 99.6%)	98.7% (97.5%, 99.3%)	98.4% (97.0%, 99.2%)	98.4% (97.0%, 99.2%)
Sample Size	827	556	399	328	272

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	98.4% (97.0%, 99.2%)	98.4% (97.0%, 99.2%)	98.4% (97.0%, 99.2%)	97.0% (93.6%, 98.6%)	97.0% (93.6%, 98.6%)
Sample Size	222	174	147	111	91

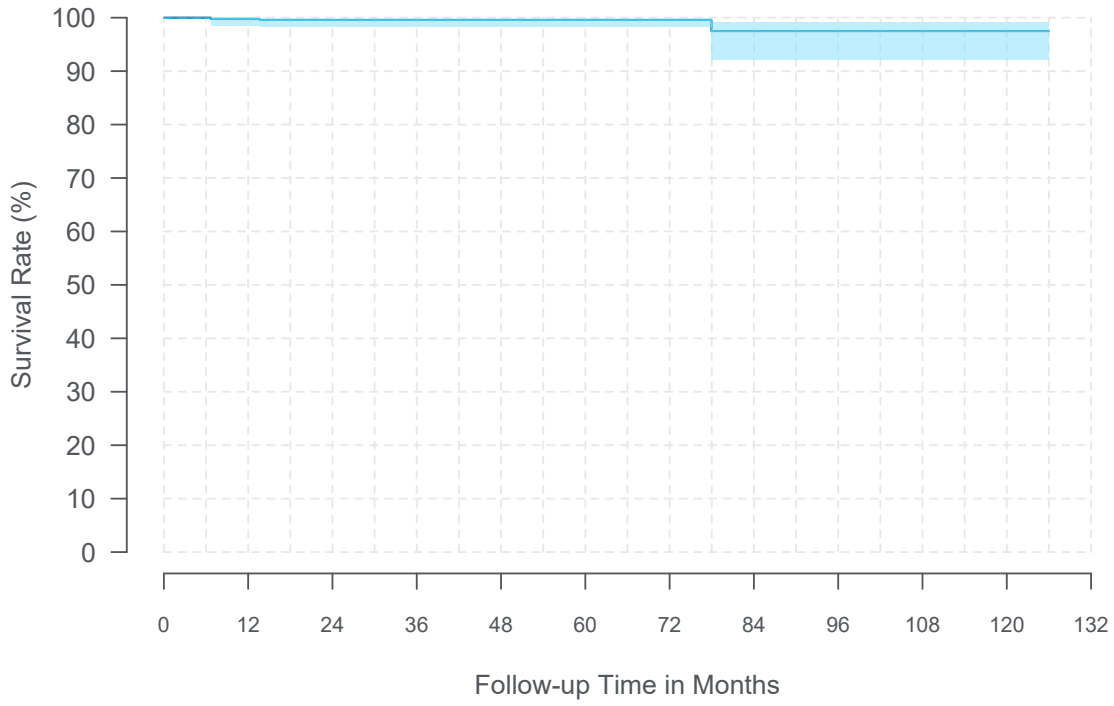
Time Interval	11 Years	12 Years	At 153 Months		
Survival (95% CI)	97.0% (93.6%, 98.6%)	97.0% (93.6%, 98.6%)	93.3% (80.5%, 97.8%)		
Sample Size	63	34	23		

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	4
Extension migration	2
Low impedance	1
Total	**14**

4.5.2.2 Model Bifurcated Stretch-Coil Extension

Model Name	Bifurcated Stretch-Coil Extension (model 37082)
FDA Approval Date	March 2006
Extensions Enrolled	643
Extensions Currently Active in Study	45
Device Events	4
Median Follow-up Time (Months)	23.2
Cumulative Follow-up Time (Months)	22,370



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	433	309	217	160	132

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	99.6% (98.2%, 99.9%)	97.5% (92.1%, 99.2%)	97.5% (92.1%, 99.2%)	97.5% (92.1%, 99.2%)	97.5% (92.1%, 99.2%)
Sample Size	107	83	60	48	34

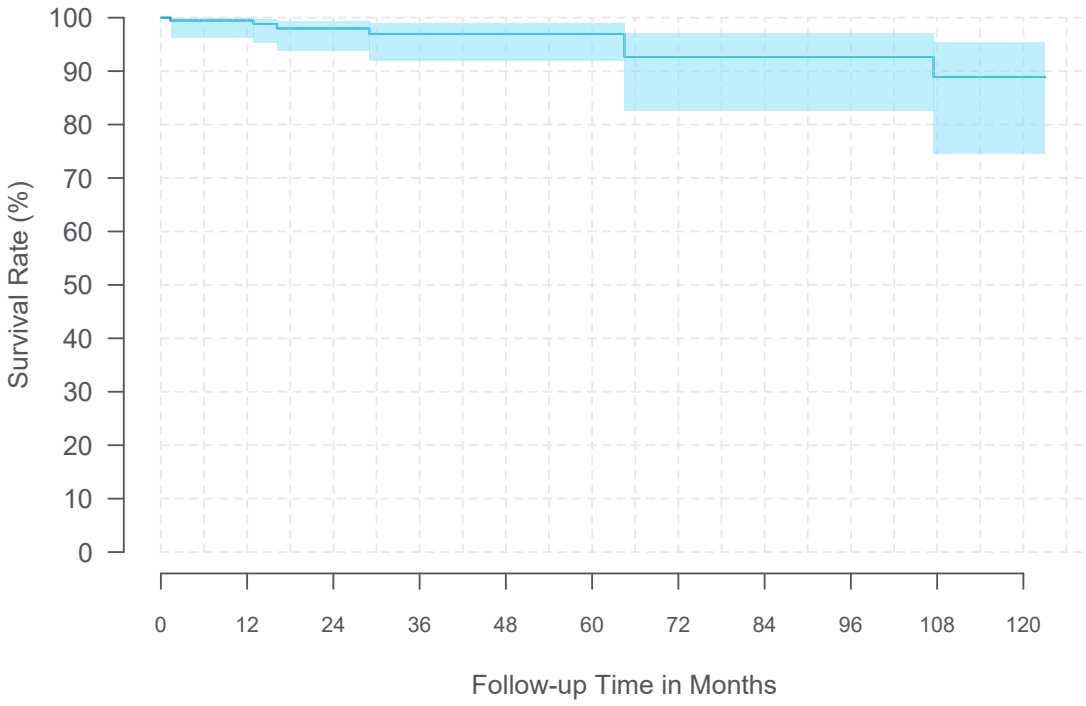
Time Interval	At 126 Months
Survival (95% CI)	97.5% (92.1%, 99.2%)
Sample Size	24

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 Single Stretch-Coil Extension

Model Name	Single Stretch-Coil Extension (model 37083)
FDA Approval Date	September 2005
Extensions Enrolled	327
Extensions Currently Active in Study	114
Device Events	10
Median Follow-up Time (Months)	12.9
Cumulative Follow-up Time (Months)	8,321



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (96.3%, 99.9%)	98.0% (93.8%, 99.4%)	97.0% (91.9%, 98.9%)	97.0% (91.9%, 98.9%)	97.0% (91.9%, 98.9%)
Sample Size	155	114	71	58	45

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	92.7% (82.6%, 97.0%)	92.7% (82.6%, 97.0%)	92.7% (82.6%, 97.0%)	88.9% (74.5%, 95.4%)	88.9% (74.5%, 95.4%)
Sample Size	33	32	27	23	21

Time Interval	At 123 Months
Survival (95% CI)	88.9% (74.5%, 95.4%)
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	4
Device failure	1
Total	**10**

4.5.3 Extension Summary

Table 4.18: Spinal Cord Stimulation Extension Characteristics

Model/Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
1x8 Extension (model 37081)	April 2005	1,511	330	14	20	45,764
Bifurcated Stretch-Coil Extension (model 37082)	March 2006	643	45	4	23.2	22,370
Single Stretch-Coil Extension (model 37083)	September 2005	327	114	10	12.9	8,321

Table 4.19: 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%)	99.1% (98.1%, 99.6%)	98.7% (97.5%, 99.3%)	98.4% (97.0%, 99.2%)	98.4% (97.0%, 99.2%)
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%)
Single Stretch-Coil Extension (model 37083)	99.5% (96.3%, 99.9%)	98.0% (93.8%, 99.4%)	97.0% (91.9%, 98.9%)	97.0% (91.9%, 98.9%)	97.0% (91.9%, 98.9%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
1x8 Extension (model 37081)	98.4% (97.0%, 99.2%)	98.4% (97.0%, 99.2%)	98.4% (97.0%, 99.2%)	97.0% (93.6%, 98.6%)	97.0% (93.6%, 98.6%)
Bifurcated Stretch-Coil Extension (model 37082)	99.6% (98.2%, 99.9%)	97.5% (92.1%, 99.2%)	97.5% (92.1%, 99.2%)	97.5% (92.1%, 99.2%)	97.5% (92.1%, 99.2%)
Single Stretch-Coil Extension (model 37083)	92.7% (82.6%, 97.0%)	92.7% (82.6%, 97.0%)	92.7% (82.6%, 97.0%)	88.9% (74.5%, 95.4%)	88.9% (74.5%, 95.4%)

Model Name	11 Years	12 Years			
1x8 Extension (model 37081)	97.0% (93.6%, 98.6%)	97.0% (93.6%, 98.6%)			
Bifurcated Stretch-Coil Extension (model 37082)					
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, 2020. Forty-nine 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.

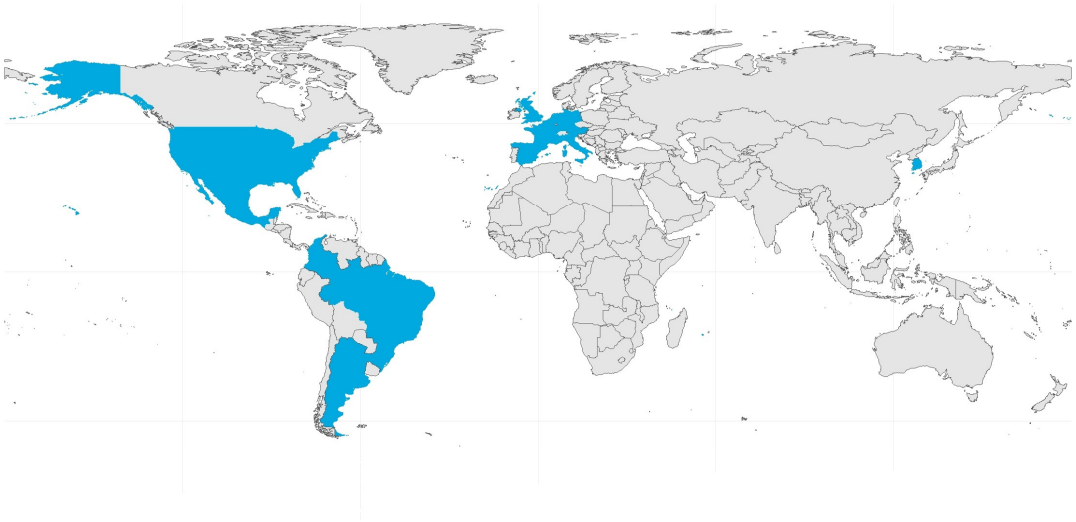


Figure 5.1: Countries with Deep Brain Stimulation Therapy Patients in Registry (Highlighted)

5.1.2 Patients

Of the 2,760 deep brain stimulation patients enrolled, the primary indications for implant were as follows: 60.9% were implanted for the treatment of Parkinson's Disease, 24.2% were implanted for the treatment of essential tremor, 9.1% were implanted for the treatment of dystonia, 1.4% were implanted for the treatment of obsessive compulsive disorder, 1.2% were implanted for the

treatment of epilepsy, 2.5% were implanted for the treatment of other indications, and 0.6% 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).

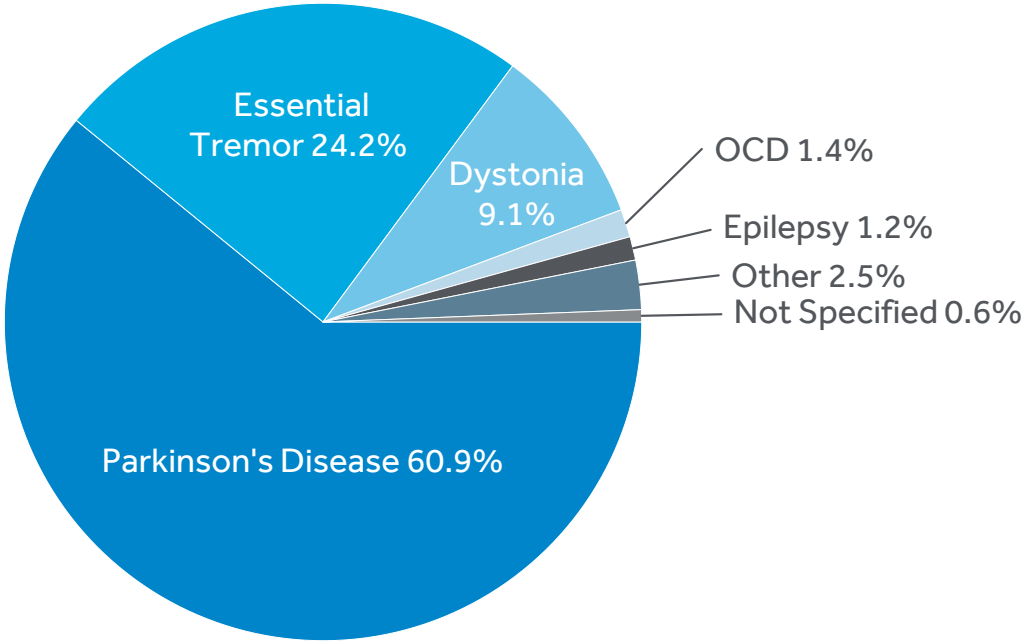


Figure 5.2: Deep Brain Stimulation Primary Treatment Indications

Table 5.1: Deep Brain Stimulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Parkinson's Disease	1,681 (60.9%)
Essential Tremor	669 (24.2%)
Dystonia	252 (9.1%)
OCD	39 (1.4%)
Epilepsy	33 (1.2%)
Other	69 (2.5%)
Not Specified	17 (0.6%)
Total Patients	**2,760(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 390 product performance events reported between July 2009 and October 31, 2020, in patients with deep brain stimulation systems. These events represent 22.6% of the total reported events (390/1,729), occurred in 241 of the 2,760 (8.7%) total patients enrolled, and are presented graphically within this report (e.g. events per patient years as well as survival curves). Of the remaining 1,339 reported events 218 were serious (not product performance related) and 1,121 were non-serious (not product performance related). Serious non-product performance related events (n=218) are described in Table 5.4. Non serious non-product performance related (n=1,121) 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 269 deaths reported for patients followed in the PSR with deep brain stimulation systems (see Table 5.5), 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=2,760[b]
RPA Determination	**3**	**0.03**	**3 (0.11%)**
Premature Battery Depletion	3	0.03	3 (0.11%)
Physician's Determination	**387**	**4.40**	**239 (8.66%)**
High Impedance	190	2.16	113 (4.09%)
Lead Migration/Dislodgement	41	0.47	30 (1.09%)
Device Malfunction	26	0.3	21 (0.76%)
Low Impedance	25	0.28	17 (0.62%)
Lead Fracture	22	0.25	18 (0.65%)
Extension Migration	17	0.19	9 (0.33%)
Neurostimulator Unable To Recharge[c]	13	0.15	13 (0.47%)
Extension Fracture	11	0.13	8 (0.29%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=2,760[b]
Medical Device Complication	8	0.09	6 (0.22%)
Premature Battery Depletion	6	0.07	6 (0.22%)
Device Breakage	5	0.06	5 (0.18%)
Medical Device Site Infection	4	0.05	3 (0.11%)
Device Connection Issue	2	0.02	2 (0.07%)
Device Lead Issue	2	0.02	2 (0.07%)
Device Material Issue	2	0.02	1 (0.04%)
Electromagnetic Interference	2	0.02	2 (0.07%)
Other[d]	11	0.13	11 (0.40%)
Total	**390**	**4.44**	**241 (8.73%)**

[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 13 patients that used rechargeable neurostimulators for DBS in the registry. A total of 2.4% (13/533) 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 185 (47.4%) of the 390 product performance events were related to the lead, 75 (19.2%) were related to the extension, 64 (16.4%) were related to the neurostimulator, 15 (3.8%) were related to multiple etiologies, which includes events where at least one device and one non-device etiology was indicated, 27 (6.9%) were related to other component, 9 (2.3%) were related to surgery/anesthesia, 6 (1.5%) were related to recharging process, 4 (1.0%) were related to incisional site/device tract, 4 (1.0%) were related to programming/stimulation, 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.

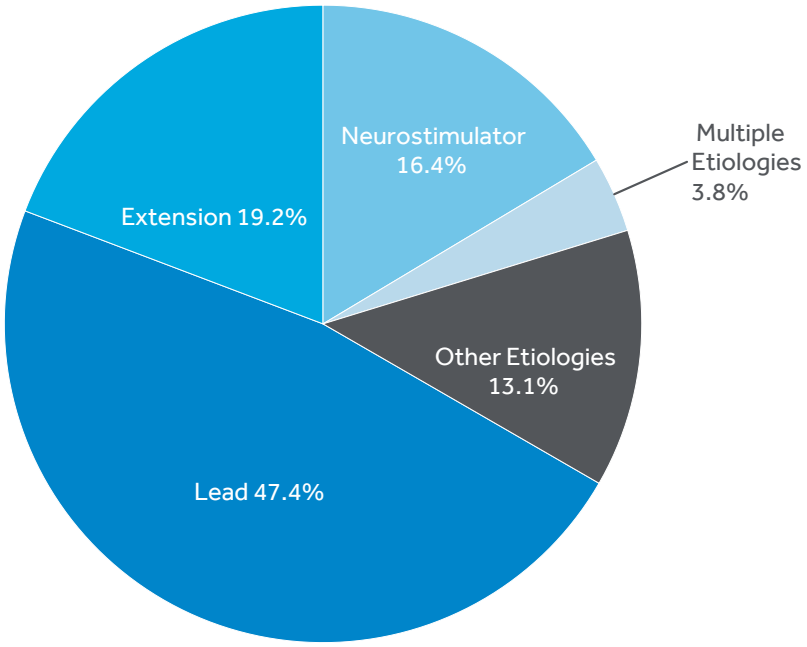


Figure 5.3: Deep Brain Stimulation System Product Performance Events by Relatedness

Table 5.3 describes the interventions completed for product performance events that required action from the health care provider and thereby, may have resulted in an incremental impact to the patient. Survival estimates presented in previous product performance reports included events where no action was taken. To present survival estimates that may better correlate with patient impact, events where no action was taken have been removed from the device survival estimates presented in this 2020 report. The far-left column lists the top five reported PPEs, and all other reported PPEs are listed under Other. The subsequent columns represent the actions taken by the reporting physician.

Table 5.3: DBS Product Performance Events by Intervention

Events by Intervention	Surgical Intervention	Reprogramming	Medical or Non-Surgical Intervention [a]	Therapy Suspension	No Action Taken	Total Events
High Impedance	73 (38.4%)	46 (24.2%)	11 (5.8%)	2 (1.1%)	58 (30.5%)	**190**
Lead Migration/Dislodgement	33 (80.5%)	6 (14.6%)	0 (0.0%)	0 (0.0%)	2 (4.9%)	**41**
Device Malfunction	5 (19.2%)	5 (19.2%)	10 (38.5%)	1 (3.8%)	5 (19.2%)	**26**
Low Impedance	7 (28.0%)	6 (24.0%)	0 (0.0%)	3 (12.0%)	9 (36.0%)	**25**
Lead Fracture	18 (81.8%)	3 (13.6%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	**22**
Other [b]	58 (67.4%)	4 (4.7%)	18 (20.9%)	2 (2.3%)	4 (4.7%)	**86**
Total	**194**	**70**	**39**	**8**	**79**	**390**

[a] Medical or Non-Surgical Therapy contains but is not limited to the following actions: medication adjustment based on disease symptoms, imaging (e.g. MRI or X-ray), other specialist referral.

[b] Other represents all reported PPEs that were not in the top five of occurrence.

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=1,577)
- Categorized as serious adverse events
- Occurred with a System Organ Class (SOC) threshold ≥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 5.4: Deep Brain Stimulation System Clinical Events Not Related To Product Performance

Event Type	Number of SAE	Patients with SAE n (%)[a] N=1,577	SAE Per 100 Patient Months	Patient with SAE Requiring Surgical Intervention n (%) N=1,577
Infections and infestations	**91**	**75 (4.76%)**	**0.17**	**69 (4.38%)**
Infections - pathogen unspecified	81	67 (4.25%)	0.15	61 (3.87%)
Bacterial infectious disorders	10	10 (0.63%)	0.02	8 (0.51%)
Nervous system disorders	**44**	**40 (2.54%)**	**0.08**	**4 (0.25%)**
Central nervous system vascular disorders	17	17 (1.08%)	0.03	1 (0.06%)
Movement disorders (incl parkinsonism)	14	14 (0.89%)	0.03	1 (0.06%)
Neurological disorders NEC	8	8 (0.51%)	0.01	2 (0.13%)
Other[b]	5	5 (0.32%)	0.01	0 (0.00%)
General disorders and administration site conditions	**36**	**34 (2.16%)**	**0.07**	**21 (1.33%)**
Complications associated with device	27	26 (1.65%)	0.05	21 (1.33%)
General system disorders NEC	6	6 (0.38%)	0.01	0 (0.00%)
Other[b]	3	3 (0.19%)	0.01	0 (0.00%)
Other SOC Terms (<1.0% Threshold)	**47**	**46 (2.92%)**	**0.09**	**20 (1.27%)**
Total	**218**	**177 (11.22%)**	**0.41**	**106 (6.72%)**

[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 269 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 220 (81.8%) deaths have been reported in this patient registry study based upon patients receiving therapy for Parkinson's Disease, 35 (13.0%) for essential tremor, 11 (4.1%) for dystonia, 1 (0.4%) for OCD, and 2 (0.7%) for other indication, (see Table 5.5). The percentage is based upon the total patient death events and not based upon the rate of occurrence. **Tables depicted without**

a patient denominator should not be interpreted using other numbers within this report to calculate event rates.

Table 5.5: Deep Brain Stimulation System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths	Mean Age of Death in Years
Parkinson's Disease	220 (81.8%)	73.0
Essential Tremor	35 (13.0%)	74.3
Dystonia	11 (4.1%)	50.5
OCD	1 (0.4%)	70.4
Other	2 (0.7%)	76.6
Total	**269 (100%)**	**72.4**

[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, 2020, there were 4,292 neurostimulators followed in the registry. The difference between the total number of patients (n=2,760) versus the number of neurostimulators (n=4,292) 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 113,625 months (9,469 years). Table 5.6 provides the number and percentage of neurostimulators by model.

Table 5.6: Deep Brain Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	
Activa PC	2,562 (59.7%)
Activa SC	1,031 (24.0%)
Activa RC	547 (12.7%)
Percept PC	41 (1.0%)
No longer manufactured	
Other/Unspecified[a]	32 (0.7%)
Soletra	67 (1.6%)
Total	**4,292 (100%)**

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

5.3.1 Neurostimulator Events

Of the total of 390 product performance-related events, there were 66 product performance-related events with an underlying reported etiology related to neurostimulator function. This includes 64 events with a neurostimulator etiology and 2 events with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 47 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 4.6% (81/1,751). 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 66 neurostimulator events, 95.5 % (63/66) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 5.7).

Table 5.7: Deep Brain Stimulation Neurostimulator Product Performance Events by Determination

Product Performance Events	N (%)
RPA Determination	**3 (4.5%)**
Premature Battery Depletion	3 (4.5%)
Physician's Determination	**63 (95.5%)**
High Impedance	32 (48.5%)
Device Malfunction	10 (15.2%)
Premature Battery Depletion	6 (9.1%)
Low Impedance	5 (7.6%)
Electromagnetic Interference	2 (3.0%)
Extension Migration	2 (3.0%)
Device Issue	1 (1.5%)
Device Lead Issue	1 (1.5%)
Medical Device Site Infection	1 (1.5%)
Neurostimulator Unable To Recharge	1 (1.5%)
Paraesthesia	1 (1.5%)
Wound Infection	1 (1.5%)
Total	**66 (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:

- 47 had follow-up time cut-off due to product performance-related events.
- 2,623 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.

- 1,622 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.

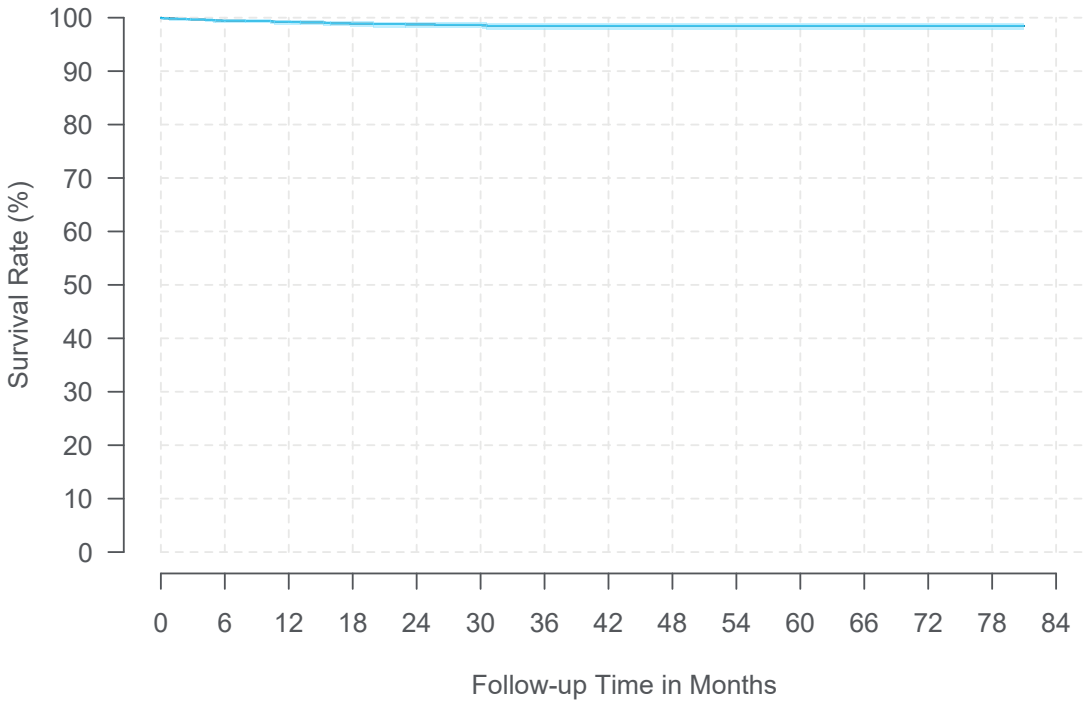
5.3.2 Neurostimulator Models

The following figures and tables represent neurostimulator survival and 95% confidence intervals where at least 20 neurostimulators contributed to each 3-month interval. The Percept PC model is not shown due to insufficient data.

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	2,562
Neurostimulators Currently Active in Study	947
Device Events	32
Median Follow-up Time (Months)	24.6
Cumulative Follow-up Time (Months)	68,974



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.2% (98.8%, 99.5%)	98.7% (98.1%, 99.2%)	98.5% (97.8%, 99.0%)	98.5% (97.8%, 99.0%)	98.5% (97.8%, 99.0%)
Sample Size	1,856	1,306	793	386	147

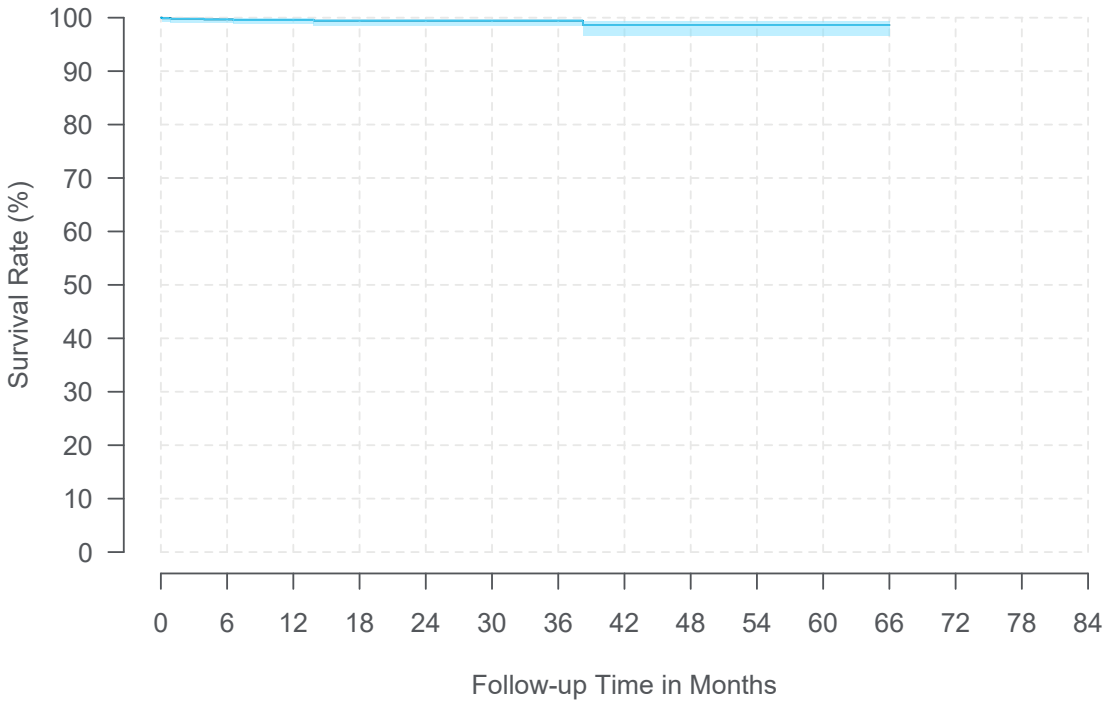
Time Interval	6 Years	At 81 Months			
Survival (95% CI)	98.5% (97.8%, 99.0%)	98.5% (97.8%, 99.0%)			
Sample Size	51	26			

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	15
Premature battery depletion	8
Device malfunction	5
Device issue	1
Electromagnetic interference	1
Low impedance	1
Medical device site infection	1
Total	**32**

5.3.2.2 Model Activa SC

Model Name	Activa SC
FDA Approval Date	January 2011
Neurostimulators Enrolled	1,031
Neurostimulators Currently Active in Study	278
Device Events	7
Median Follow-up Time (Months)	24.5
Cumulative Follow-up Time (Months)	26,584



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (98.8%, 99.8%)	99.4% (98.6%, 99.8%)	99.4% (98.6%, 99.8%)	98.6% (96.7%, 99.4%)	98.6% (96.7%, 99.4%)
Sample Size	744	520	284	125	45

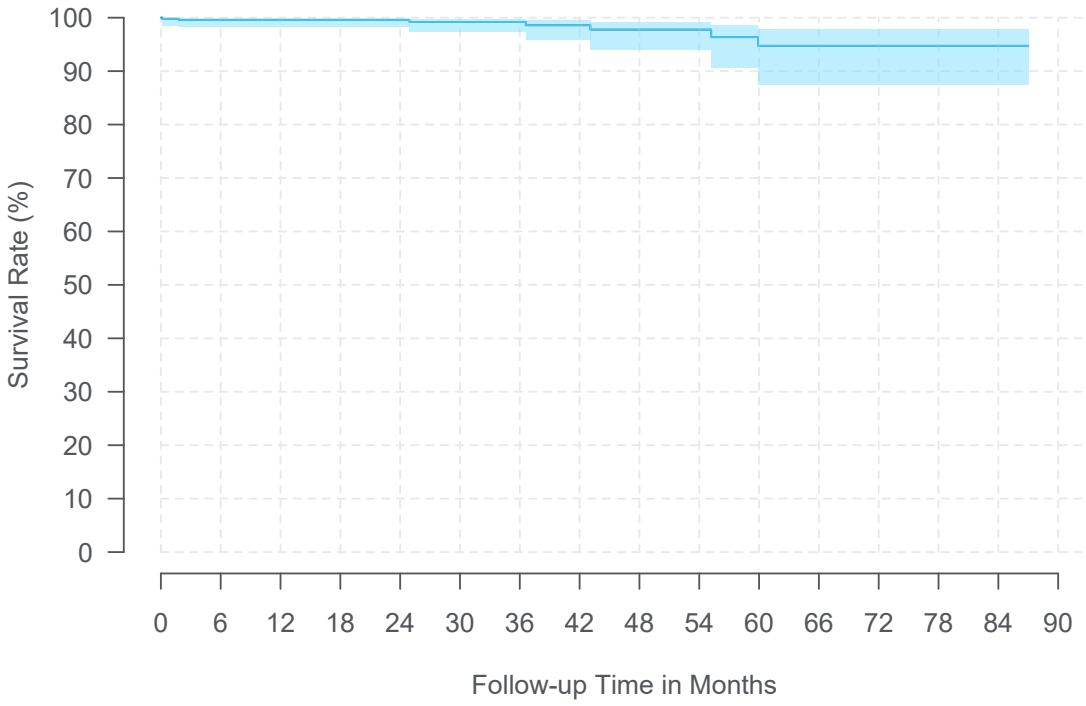
Time Interval	At 66 Months
Survival (95% CI)	98.6% (96.7%, 99.4%)
Sample Size	31

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	3
Device lead issue	1
Low impedance	1
Premature battery depletion	1
Wound infection	1
Total	**7**

5.3.2.3 Model Activa RC

Model Name	Activa RC
FDA Approval Date	March 2009
Neurostimulators Enrolled	547
Neurostimulators Currently Active in Study	351
Device Events	8
Median Follow-up Time (Months)	23.6
Cumulative Follow-up Time (Months)	15,201



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (98.3%, 99.9%)	99.6% (98.3%, 99.9%)	99.2% (97.4%, 99.8%)	97.8% (94.1%, 99.2%)	94.7% (87.4%, 97.8%)
Sample Size	371	265	174	91	57

Time Interval	6 Years	7 Years	At 87 Months		
Survival (95% CI)	94.7% (87.4%, 97.8%)	94.7% (87.4%, 97.8%)	94.7% (87.4%, 97.8%)		
Sample Size	41	22	20		

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
Extension migration	2
High impedance	2
Neurostimulator unable to recharge	1
Paraesthesia	1
Total	**8**

5.3.3 Neurostimulator Summary

Table 5.8: 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	2,562	947	32	24.6	68,974
Activa SC	January 2011	1,031	278	7	24.5	26,584
Activa RC	March 2009	547	351	8	23.6	15,201

Table 5.9: Deep Brain Stimulation Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years	6 Years	7 Years
Activa PC	99.2% (98.8%, 99.5%)	98.7% (98.1%, 99.2%)	98.5% (97.8%, 99.0%)	98.5% (97.8%, 99.0%)	98.5% (97.8%, 99.0%)	98.5% (97.8%, 99.0%)	
Activa SC	99.6% (98.8%, 99.8%)	99.4% (98.6%, 99.8%)	99.4% (98.6%, 99.8%)	98.6% (96.7%, 99.4%)	98.6% (96.7%, 99.4%)		
Activa RC	99.6% (98.3%, 99.9%)	99.6% (98.3%, 99.9%)	99.2% (97.4%, 99.8%)	97.8% (94.1%, 99.2%)	94.7% (87.4%, 97.8%)	94.7% (87.4%, 97.8%)	94.7% (87.4%, 97.8%)

5.4 Leads

From July 2009 to the report cut-off date of October 31, 2020, there were 4,673 leads followed in the registry. The difference between the total number of leads (n=4,673) versus neurostimulators (n=4,292) 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 180,372 months (15,031 years). Table 5.10 provides the number and percentage of leads by model.

Table 5.10: Deep Brain Stimulation Lead Counts by Model

Model Name	N (%)
3389 (compact electrode spacing)	2,618 (56.0%)
3387 (standard electrode spacing)	1,986 (42.5%)
3391 (large electrodes and wide spacing)	54 (1.2%)
Other/Unspecified[a]	15 (0.3%)
Total	**4,673 (100%)**

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

5.4.1 Lead Events

Of the total of 390 product performance-related events, there were 194 product performance-related events with an underlying reported etiology related to lead function. This includes 185 events with a lead etiology and 9 events with both a lead and other etiology (including device and non-device etiologies). Of these, 122 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:

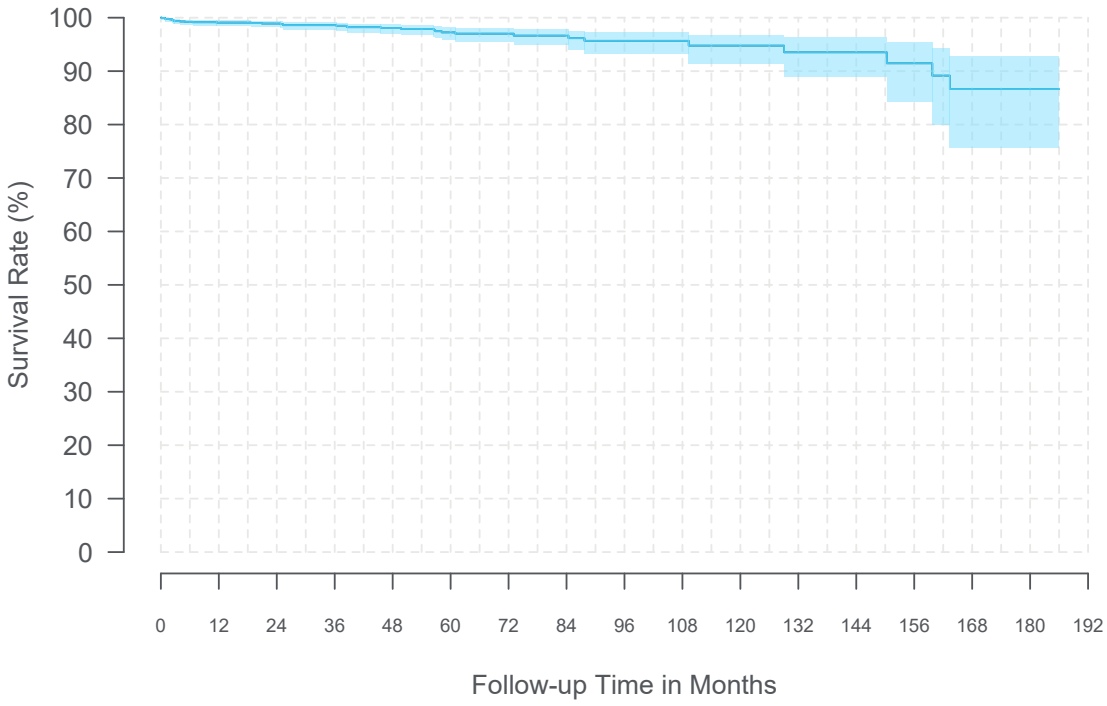
- 122 had follow-up time cut-off due to product performance-related events.
- 1,979 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,572 were free 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	1,986
Leads Currently Active in Study	1,071
Device Events	38
Median Follow-up Time (Months)	34.0
Cumulative Follow-up Time (Months)	73,121



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.1% (98.5%, 99.5%)	98.9% (98.2%, 99.3%)	98.6% (97.8%, 99.1%)	98.1% (97.0%, 98.7%)	97.3% (95.8%, 98.2%)
Sample Size	1,320	1,012	804	583	417

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	97.0% (95.5%, 98.0%)	96.6% (94.9%, 97.8%)	95.7% (93.2%, 97.2%)	95.7% (93.2%, 97.2%)	94.8% (91.4%, 96.8%)
Sample Size	266	212	137	103	90

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	93.5% (88.9%, 96.3%)	93.5% (88.9%, 96.3%)	91.5% (84.4%, 95.4%)	86.6% (75.8%, 92.9%)	86.6% (75.8%, 92.9%)
Sample Size	72	48	37	34	30

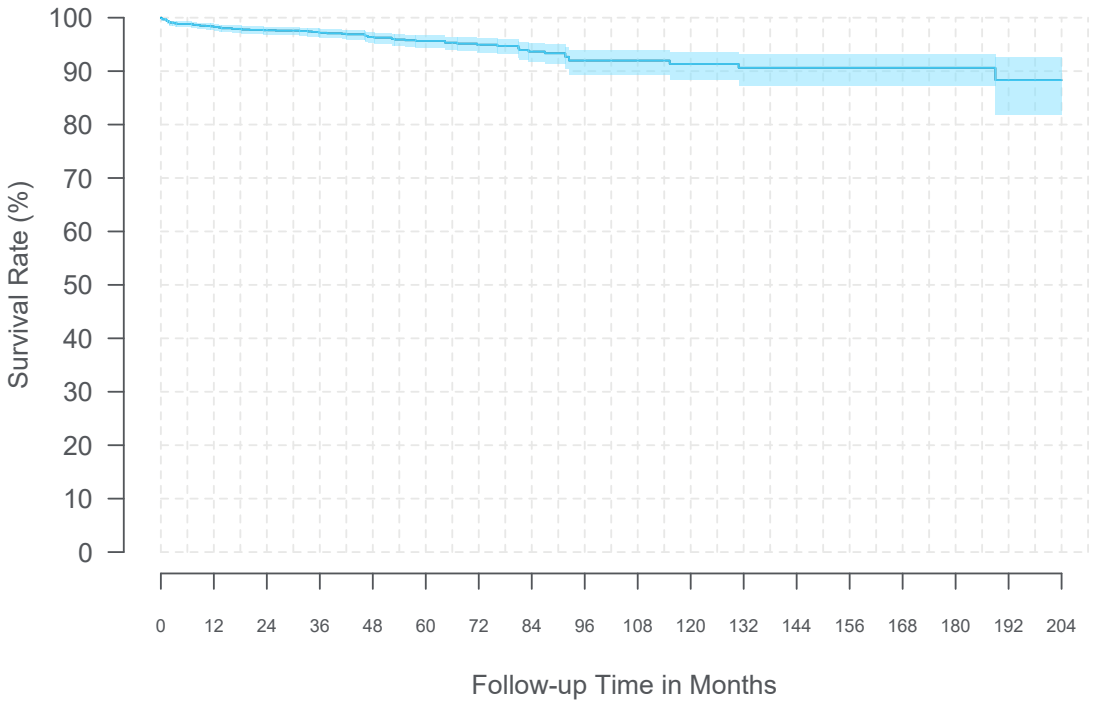
Time Interval	At 186 Months
Survival (95% CI)	86.6% (75.8%, 92.9%)
Sample Size	22

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	20
Lead migration/dislodgement	8
Low impedance	5
Lead fracture	3
Device lead issue	1
Medical device complication	1
Total	**38**

5.4.2.2 Model 3389

Model Name	3389
FDA Approval Date	September 1999
Leads Enrolled	2,618
Leads Currently Active in Study	1,502
Device Events	80
Median Follow-up Time (Months)	39.4
Cumulative Follow-up Time (Months)	105,076



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.3% (97.6%, 98.8%)	97.6% (96.8%, 98.3%)	97.2% (96.3%, 97.9%)	96.4% (95.3%, 97.2%)	95.6% (94.4%, 96.6%)
Sample Size	1,692	1,413	1,157	892	638

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	94.9% (93.5%, 96.1%)	93.7% (91.7%, 95.2%)	92.0% (89.4%, 93.9%)	92.0% (89.4%, 93.9%)	91.3% (88.4%, 93.5%)
Sample Size	450	325	247	168	141

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)
Sample Size	130	102	82	67	48

Time Interval	16 Years	17 Years			
Survival (95% CI)	88.3% (81.8%, 92.6%)	88.3% (81.8%, 92.6%)			
Sample Size	37	22			

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	40
Lead migration/dislodgement	19
Lead fracture	12
Low impedance	3
Device material issue	2
Medical device site infection	2
Device malfunction	1
Lead insulation failure	1
Total	**80**

5.4.3 Lead Summary

Table 5.11: 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	1,986	1,071	38	34	73,121
3389	September 1999	2,618	1,502	80	39.4	105,076

Table 5.12: Deep Brain Stimulation Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
3387	99.1% (98.5%, 99.5%)	98.9% (98.2%, 99.3%)	98.6% (97.8%, 99.1%)	98.1% (97.0%, 98.7%)	97.3% (95.8%, 98.2%)
3389	98.3% (97.6%, 98.8%)	97.6% (96.8%, 98.3%)	97.2% (96.3%, 97.9%)	96.4% (95.3%, 97.2%)	95.6% (94.4%, 96.6%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
3387	97.0% (95.5%, 98.0%)	96.6% (94.9%, 97.8%)	95.7% (93.2%, 97.2%)	95.7% (93.2%, 97.2%)	94.8% (91.4%, 96.8%)
3389	94.9% (93.5%, 96.1%)	93.7% (91.7%, 95.2%)	92.0% (89.4%, 93.9%)	92.0% (89.4%, 93.9%)	91.3% (88.4%, 93.5%)

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
3387	93.5% (88.9%, 96.3%)	93.5% (88.9%, 96.3%)	91.5% (84.4%, 95.4%)	86.6% (75.8%, 92.9%)	86.6% (75.8%, 92.9%)
3389	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)	90.6% (87.3%, 93.1%)

Model Name	16 Years	17 Years			
3387					
3389	88.3% (81.8%, 92.6%)	88.3% (81.8%, 92.6%)			

5.5 Extensions

From July 2009 to the report cut-off date of October 31, 2020, there were 4,752 extensions followed in the registry. The difference between the total number of extensions (n=4,752) versus neurostimulators (n=4,292) 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 177,871 months (14,823 years). The table below provides the number and percentage of extensions by model. Table 5.13 provides the number and percentage of extensions by model.

Table 5.13: Deep Brain Stimulation Extension Counts by Model

Model Name	N (%)
Currently manufactured	
37085/37086 (quadripolar stretch)	4,141 (87.1%)
Other/Unspecified[a]	115 (2.4%)
No longer manufactured	
7482[b] (quadripolar)	496 (10.4%)
Total	**4,752 (100%)**

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

5.5.1 Extension Events

Of the total of 390 product performance-related events, there were 79 product performance-related events with an underlying reported etiology related to extension function. This includes 75 events with an extension etiology and 4 events with both an extension and other etiology (including device and non-device etiologies). Of these, 66 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:

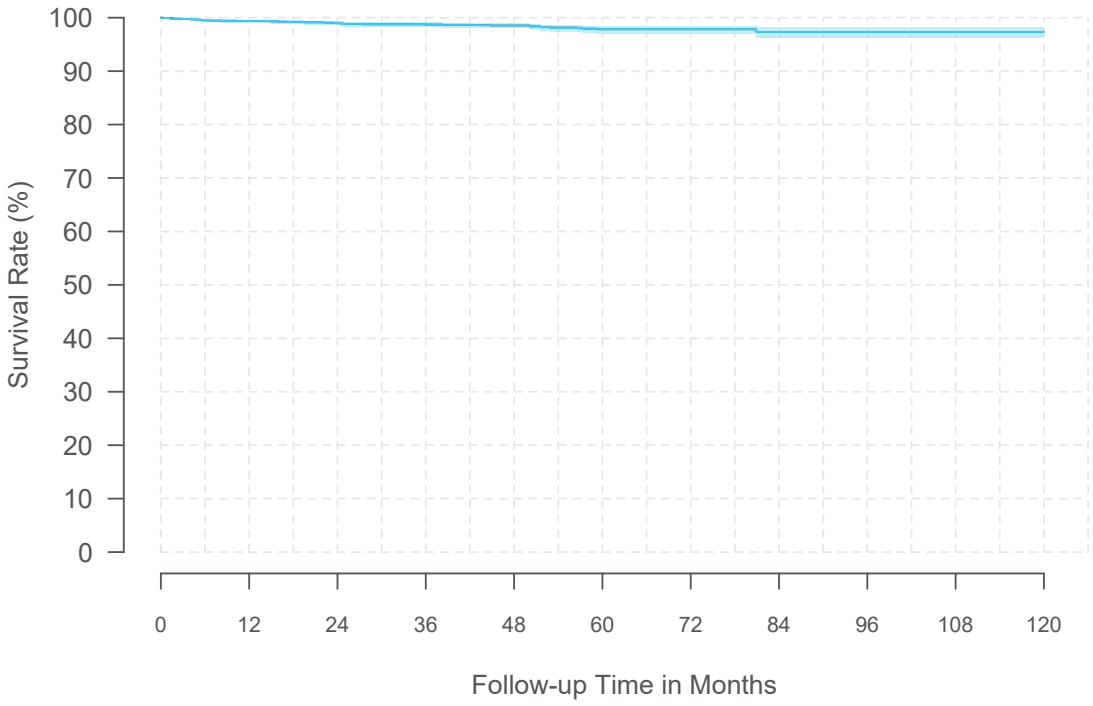
- 66 had follow-up time cut-off due to product performance-related events.
- 2,057 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,629 were free 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

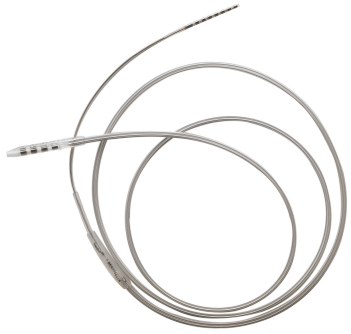
Model Name	37085/37086
FDA Approval Date	March 2009
Extensions Enrolled	4,141
Extensions Currently Active in Study	2,372
Device Events	54
Median Follow-up Time (Months)	33.8
Cumulative Follow-up Time (Months)	150,685



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.4% (99.1%, 99.6%)	99.0% (98.6%, 99.3%)	98.7% (98.2%, 99.1%)	98.5% (98.0%, 98.9%)	97.8% (97.1%, 98.4%)
Sample Size	3,004	2,408	1,909	1,357	871

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	97.8% (97.1%, 98.4%)	97.3% (96.2%, 98.1%)	97.3% (96.2%, 98.1%)	97.3% (96.2%, 98.1%)	97.3% (96.2%, 98.1%)
Sample Size	549	321	148	60	22

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	24
Extension migration	13
Extension fracture	7
Low impedance	4
Medical device complication	4
Device malfunction	1
Lead migration/dislodgement	1
Total Extension Events	**54**

5.5.3 Extension Summary

Table 5.14: 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	4,141	2,372	54	33.8	150,685

Table 5.15: Deep Brain Stimulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
37085/37086	99.4% (99.1%, 99.6%)	99.0% (98.6%, 99.3%)	98.7% (98.2%, 99.1%)	98.5% (98.0%, 98.9%)	97.8% (97.1%, 98.4%)
Model Name	**6 Years**	**7 Years**	**8 Years**	**9 Years**	**10 Years**
37085/37086	97.8% (97.1%, 98.4%)	97.3% (96.2%, 98.1%)	97.3% (96.2%, 98.1%)	97.3% (96.2%, 98.1%)	97.3%

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, 2020. Twenty-four centers in North America, South America, and Europe have enrolled and contributed patients to the sacral neuromodulation systems section of this report.

6.1.2 Patients

Of the 1,314 sacral neuromodulation patients enrolled, the primary indications for implant were as follows: 43.4% were implanted for the treatment of urinary urge incontinence, 29.0% were implanted for the treatment of urgency-frequency, 13.2% were implanted for the treatment of urinary retention, 7.4% were implanted for the treatment of fecal incontinence, 2.6% 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).

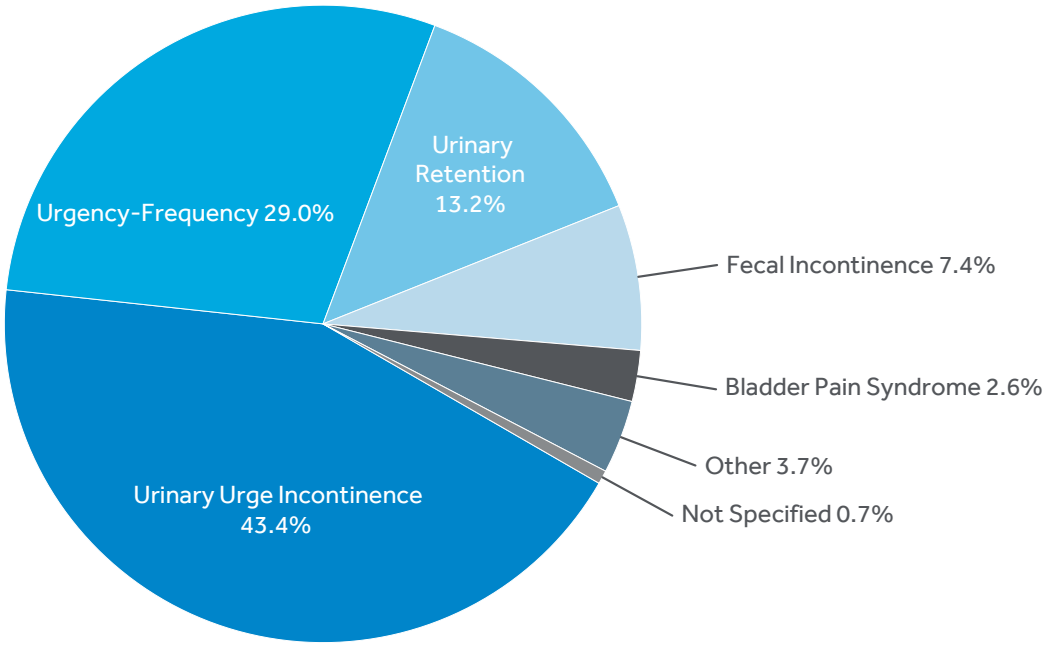


Figure 6.1: Sacral Neuromodulation Primary Treatment Indications

Table 6.1: Sacral Neuromodulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Urinary Urge Incontinence	570 (43.4%)
Urgency-Frequency	381 (29.0%)
Urinary Retention	174 (13.2%)
Fecal Incontinence	97 (7.4%)
Bladder Pain Syndrome	34 (2.6%)
Other	49 (3.7%)
Not Specified	9 (0.7%)
Total Patients	**1,314 (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 183 product performance events reported between April 2010 and October 31, 2020, in patients with sacral neuromodulation systems. These events represent 20.4% of the total reported events (183/895), occurred in 142 (10.8%) of the 1,314 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 683 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=29).

Any 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 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 40 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=1,314[b]
RPA Determination	**0**	**0.00**	**0 (0.00%)**
Physician's Determination	**183**	**6.12**	**142 (10.81%)**
High Impedance	62	2.07	48 (3.65%)
Lead Migration/Dislodgement	39	1.30	34 (2.59%)
Lead Fracture	21	0.70	19 (1.45%)
Device Lead Issue	18	0.60	13 (0.99%)
Device Malfunction[c]	13	0.43	12 (0.91%)
Low Impedance	10	0.33	9 (0.68%)
Device Battery Issue	5	0.17	4 (0.30%)
Device Electrical Impedance Issue	3	0.10	2 (0.15%)
Device Failure	2	0.07	1 (0.08%)
Device Issue	2	0.07	1 (0.08%)
Neurostimulator Migration	2	0.07	2 (0.15%)
Device Lead Damage	1	0.03	1 (0.08%)
Device Placement At Incorrect Location	1	0.03	1 (0.08%)
Device Stimulation Issue	1	0.03	1 (0.08%)
Device Telemetry Issue	1	0.03	1 (0.08%)
Neurostimulator Unable To Recharge	1	0.03	1 (0.08%)
Therapeutic Product Ineffective	1	0.03	1 (0.08%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%) N=1,314[b]
Total	**183**	**6.12**	**142 (10.81%)**

[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] See Neurostimulator Event Summary Tables for additional details on device malfunctions by model.

A total of 127 (69.4%) of 183 product performance events were related to the lead only, 35 (19.1%) related to neurostimulator 2 (1.1%) related to the extension only, 5 (2.7%) related to multiple etiologies (which includes events where at least one device and one non-device etiology was indicated), and 14 (7.7%) related to other etiologies. Relatedness is determined by the physician.

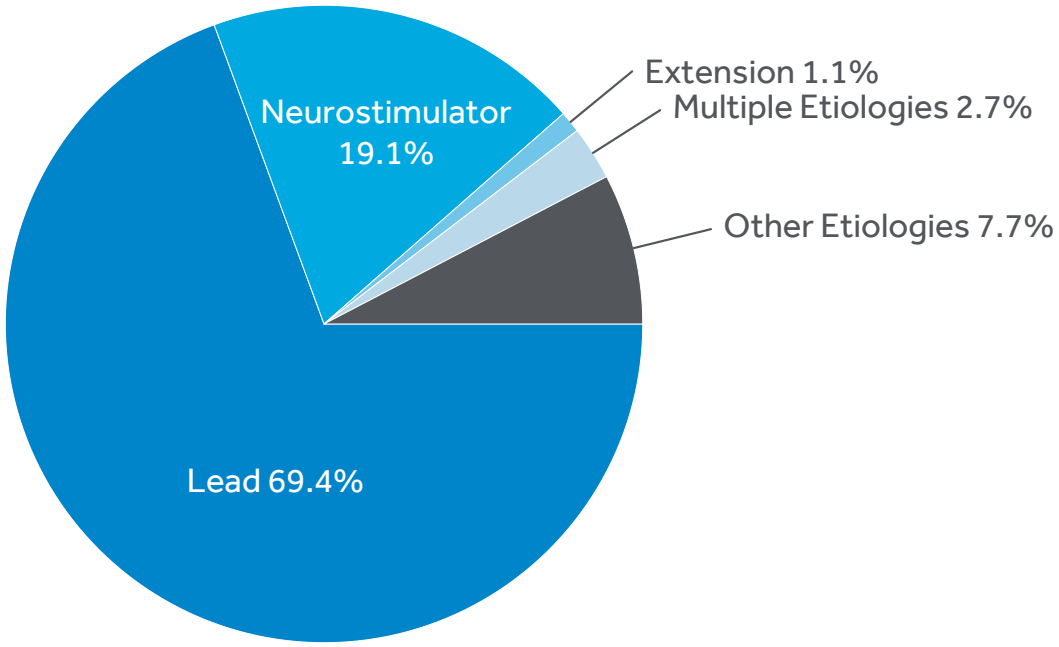


Figure 6.2: Sacral Neuromodulation System Product Performance Events by Relatedness

Table 6.3 describes the interventions completed for product performance events that required action from the health care provider and thereby, may have resulted in an incremental impact to the patient. Survival estimates presented in previous product performance reports included events where no action was taken. To present survival estimates that may better

correlate with patient impact, events where no action was taken have been removed from the device survival estimates presented in this 2020 report. The far-left column lists the top five reported PPEs, and all other reported PPEs are listed under Other. The subsequent columns represent the actions taken by the reporting physician.

Table 6.3: Sacral Neuromodulation System Product Performance Events by Intervention

Events by Intervention	Surgical Intervention	Reprogramming	Therapy Suspension	Medical or Non-Surgical Intervention [a]	No Action Taken	Total Events
High Impedance	31 (50.0%)	24 (38.7%)	0 (0.0%)	0 (0.0%)	7 (11.3%)	**62**
Lead Migration/Dislodgement	27 (69.2%)	5 (12.8%)	0 (0.0%)	1 (2.6%)	6 (15.4%)	**39**
Lead Fracture	12 (57.1%)	3 (14.3%)	0 (0.0%)	3 (14.3%)	3 (14.3%)	**21**
Device Lead Issue	8 (44.4%)	5 (27.8%)	2 (11.1%)	0 (0.0%)	3 (16.7%)	**18**
Device Malfunction	5 (38.5%)	3 (23.1%)	2 (15.4%)	1 (7.7%)	2 (15.4%)	**13**
Other [b]	17 (56.7%)	7 (23.3%)	1 (3.3%)	1 (3.3%)	4 (13.3%)	**30**
Total	**100**	**47**	**5**	**6**	**25**	**183**

[a] Medical or Non-Surgical Therapy contains but is not limited to the following actions: medication adjustment based on disease symptoms, imaging (e.g. MRI or X-ray), other specialist referral.

[b] Other represents all reported PPEs that were not in the top five of occurrence.

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
- 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 6.4: Sacral Neuromodulation System Clinical Events Not Related To Product Performance

Event Type	Number of SAE	Patients with SAE n (%) N=1,004	SAE Per 100 Patient Months	Patient with SAE Requiring Surgical Intervention n (%) N=1,004
Infections and infestations	**8**	**8 (0.80%)**	**0.034**	**6 (0.60%)**
Infections - pathogen unspecified	7	7 (0.70%)	0.030	5 (0.50%)
Other[a]	1	1 (0.10%)	0.004	1 (0.10%)
Other SOC Terms (<0.5% Threshold)	**1**	**1 (0.10%)**	**0.004**	**1 (0.10%)**
Total	**9**	**9 (0.90%)**	**0.038**	**7 (0.70%)**

[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 40 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. **Tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 6.5: Sacral Neuromodulation System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Urgency-Frequency	17 (42.5%)
Urinary Urge Incontinence	10 (25.0%)
Urinary Retention	7 (17.5%)
Fecal Incontinence	1 (2.5%)
Other	5 (12.5%)
Total	**40 (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, 2020, there were 1,324 neurostimulators followed in the registry. The difference between the total number of patients (n=1,314) versus the total number of neurostimulators (n=1,324) is due to the fact that some patients were subsequently re-implanted.

In total, 7.6% (101/1,324) of neurostimulators were InterStim, and 91.6% (1213/1,324) were InterStim II. The aggregate prospective follow-up time for all neurostimulators was 34,823 months (2,902 years).

Table 6.6: Sacral Neuromodulation Neurostimulator Counts by Model

Model Name	N (%)
InterStim II	1213 (91.6%)
InterStim	101 (7.6%)
InterStim Micro	10 (0.8%)
Total	**1,324 (100%)**

6.3.1 Neurostimulator Events

There were 37 product performance-related events with an underlying reported etiology related to neurostimulator function. This includes 35 events with a neurostimulator etiology and 2 events with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 29 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 14.5% (46/317). 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 37 neurostimulator events, 100.0 % (37/37) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 6.7).

Table 6.7: Sacral Neuromodulation Neurostimulator PPE by Determination

Product Performance Events	N (%)
Physician's Determination	**37 (100%)**
High Impedance	10 (27.0%)
Device Malfunction[a]	9 (24.3%)
Device Lead Issue	5 (13.5%)
Device Battery Issue	4 (10.8%)
Lead Migration/Dislodgement	2 (5.4%)
Device Electrical Impedance Issue	1 (2.7%)
Device Failure	1 (2.7%)
Device Issue	1 (2.7%)
Device Stimulation Issue	1 (2.7%)
Neurostimulator Migration	1 (2.7%)
Neurostimulator Unable To Recharge	1 (2.7%)
Therapeutic Product Ineffective	1 (2.7%)

[a] See Neurostimulator Event Summary Tables for additional details on device malfunction 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:

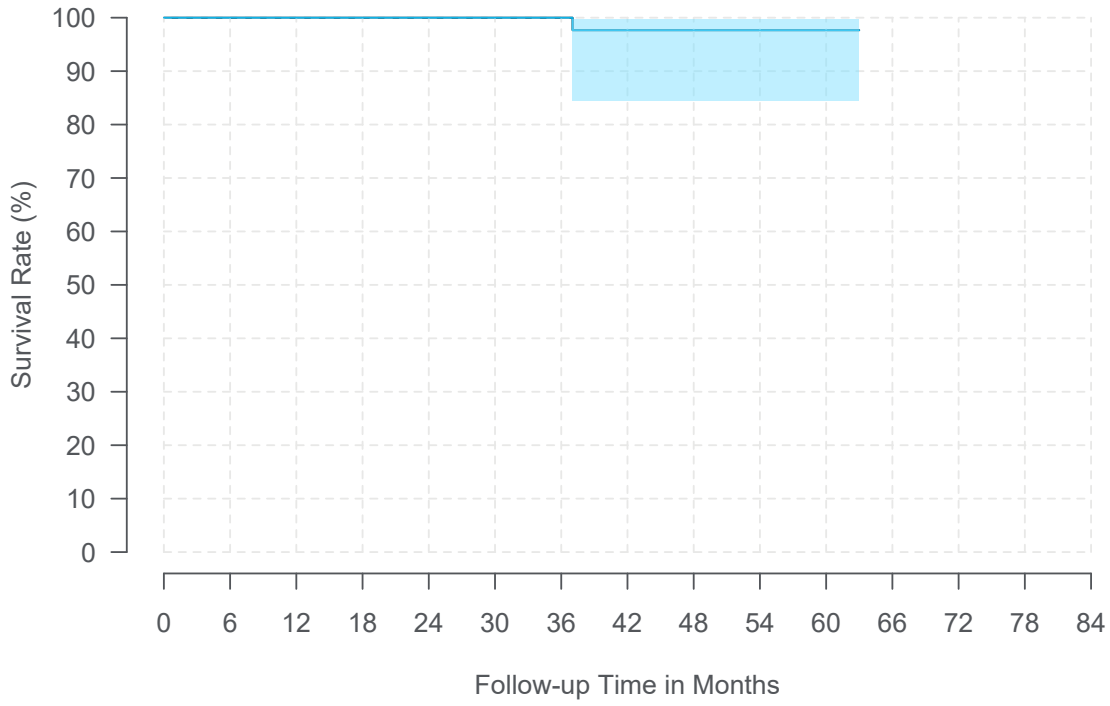
- 29 had follow-up time cut-off due to product performance-related events.
- 683 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 612 were free from 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. The InterStim Micro model is not shown due to the insufficient data.

6.3.2.1 Model 3023

Model Name	InterStim
FDA Approval Date	July 1998
Neurostimulators Enrolled	101
Neurostimulators Currently Active in Study	16
Device Events	2
Median Follow-up Time (Months)	27.3
Cumulative Follow-up Time (Months)	3,564



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	100.0% (NA)	100.0% (NA)	100.0% (NA)	97.6% (84.4%, 99.7%)	97.6% (84.4%, 99.7%)
Sample Size	70	59	42	29	20

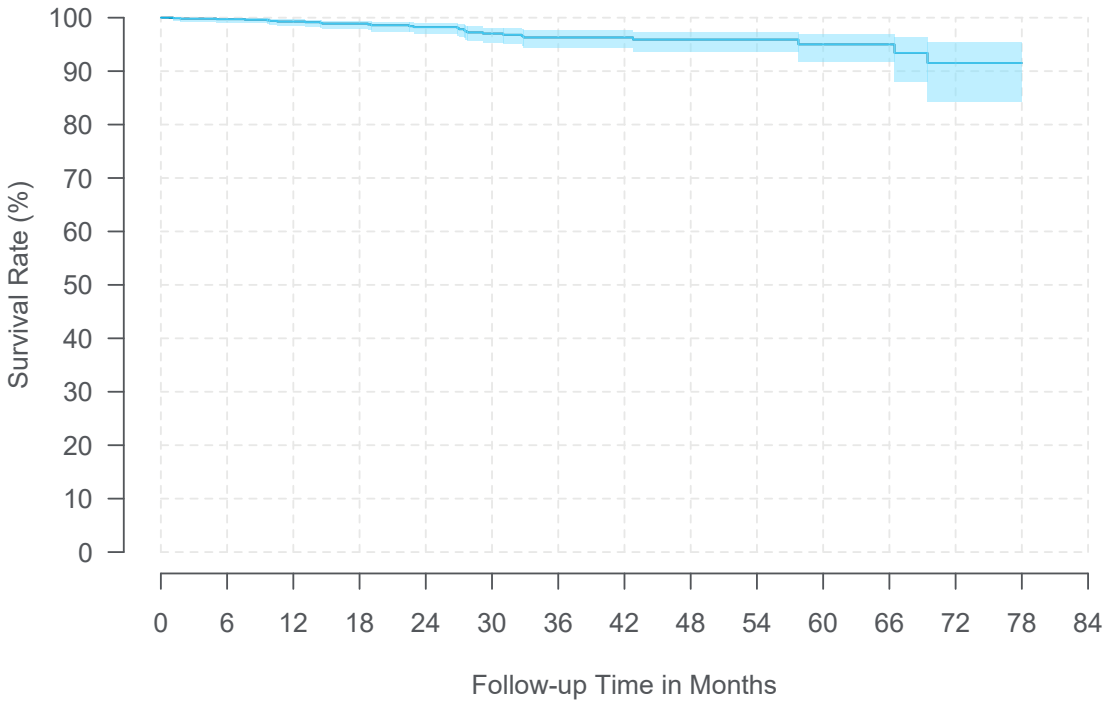
Time Interval	At 63 Months
Survival (95% CI)	97.6% (84.4%, 99.7%)
Sample Size	20

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
High Impedance	1
Total	**2**

6.3.2.2 Model 3058

Model Name	InterStim II
FDA Approval Date	June 2006
Neurostimulators Enrolled	1,213
Neurostimulators Currently Active in Study	592
Device Events	27
Median Follow-up Time (Months)	20.8
Cumulative Follow-up Time (Months)	31,259



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.3% (98.5%, 99.7%)	98.2% (97.0%, 99.0%)	96.3% (94.4%, 97.6%)	95.9% (93.8%, 97.3%)	95.0% (91.9%, 97.0%)
Sample Size	834	538	344	193	95

Time Interval	6 Years	At 78 Months			
Survival (95% CI)	91.5% (84.3%, 95.5%)	91.5% (84.3%, 95.5%)			
Sample Size	41	24			

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	7
Device Lead Issue	3
Device Battery Issue	2
Lead Migration/Dislodgement	2
Device Electrical Impedance Issue	1
Device Failure	1
Device Issue	1
Device Stimulation Issue	1
Neurostimulator Migration	1
Therapeutic Product Ineffective	1
Total	**27**

6.3.3 Neurostimulator Summary

Table 6.8: Sacral Neuromodulation Neurostimulator Characteristics

Model Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
InterStim	July 1998	101	16	2	27.3	3,564
InterStim II	June 2006	1,213	592	27	20.8	31,259

Table 6.9: Sacral Neuromodulation Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years	6 Years
InterStim	100.0%	100.0%	100.0%	97.6%	97.6%	
	(NA)	(NA)	(NA)	(84.4%, 99.7%)	(84.4%, 99.7%)	
InterStim II	99.3%	98.2%	96.3%	95.9%	95.0%	91.5%
	(98.5%, 99.7%)	(97.0%, 99.0%)	(94.4%, 97.6%)	(93.8%, 97.3%)	(91.9%, 97.0%)	(84.3%, 95.5%)

6.4 Leads

From April 2010 to the report cut-off date of October 31, 2020, there were 1,273 leads followed in the registry. The difference between the total number of leads (n=1,273) versus the total number of neurostimulators (n=1,324) 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 34,983 months (2,915 years). Table 6.10 provides the number and percentage of leads by model.

Table 6.10: Sacral Neuromodulation Lead Counts by Model

Model Name	N (%)
Currently manufactured	**1,167 (91.7%)**
InterStim Quad Lead Tined (3889)	1,141 (89.6%)
InterStim SureScan MRI Lead (978B1)	16 (1.3%)
InterStim SureScan MRI Lead (978A1)	10 (0.8%)
No longer manufactured	**105 (8.2%)**
InterStim Extended Electrode Quad Lead Tined (3093)	100 (7.9%)
InterStim Quad Lead (3080)	3 (0.2%)
InterStim Extended Electrode Quad Lead (3092)	2 (0.2%)
Other/Unspecified	**1 (0.1%)**
Total	**1,273 (100%)**

6.4.1 Lead Events

There were 130 product performance-related events with an underlying reported etiology related to lead function. This includes 127 events with a lead etiology and 3 events with both a lead and other etiology (including device and non-device etiologies). Of these, 102 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:

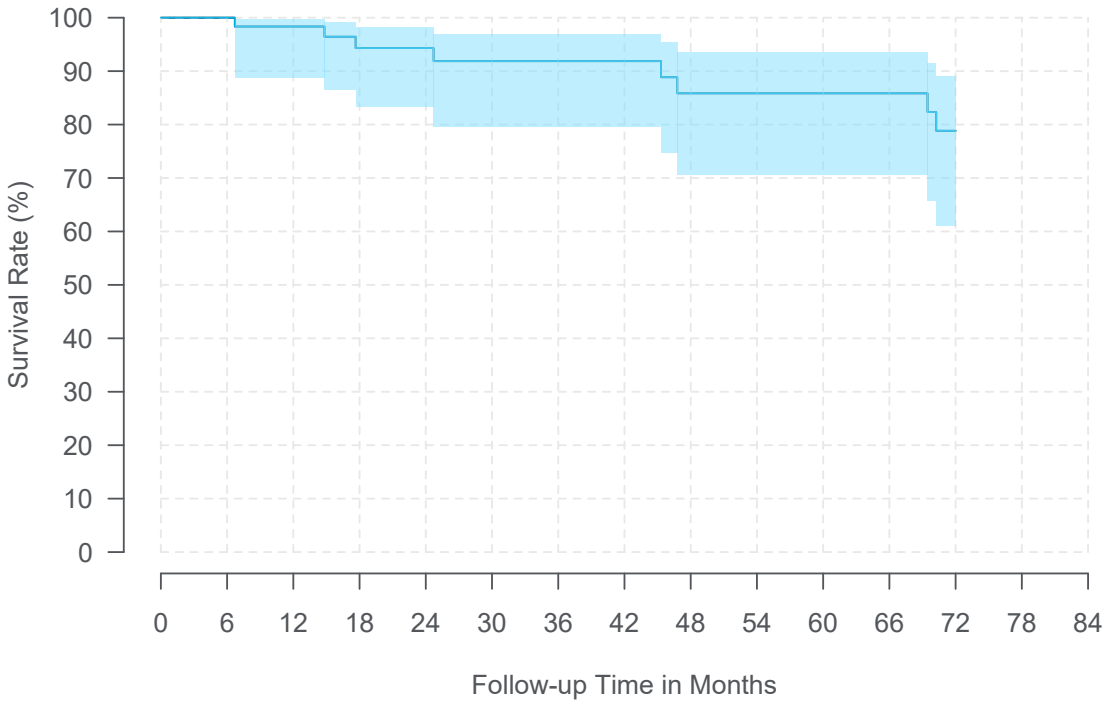
- 102 had follow-up time cut-off due to product performance-related events.
- 569 were censored in the survival analysis for the following reasons: patient expired, lead explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 602 were free from product 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. The SureScan MRI lead models 978A1 and 978B1 are not shown due to the insufficient data.

6.4.2.1 Model 3093

Model Name	InterStim Extended Electrode Quad Lead Tined
FDA Approval Date	September 2002
Leads Enrolled	100
Leads Currently Active in Study	32
Device Events	10
Median Follow-up Time (Months)	25.1
Cumulative Follow-up Time (Months)	3,380



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.3% (88.8%, 99.8%)	94.3% (83.3%, 98.1%)	91.9% (79.5%, 96.9%)	85.8% (70.5%, 93.5%)	85.8% (70.5%, 93.5%)
Sample Size	51	38	30	28	26

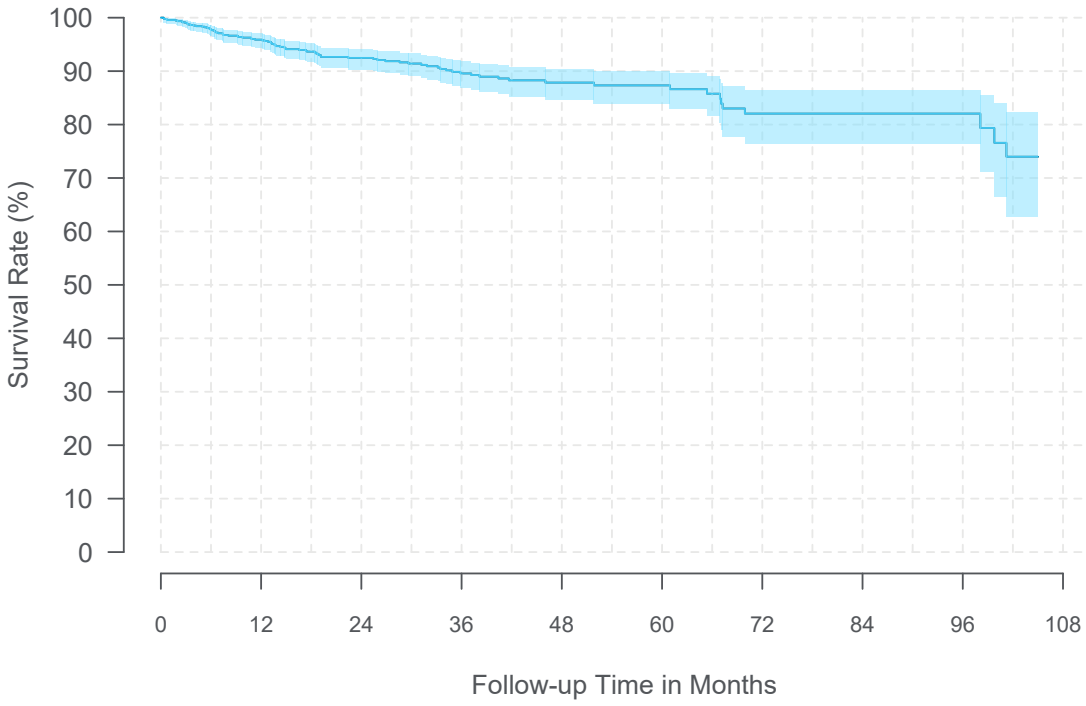
Time Interval	6 Years				
Survival (95% CI)	78.8% (61.1%, 89.1%)				
Sample Size	21				

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 Lead Issue	2
Device Electrical Impedance Issue	1
Device Lead Damage	1
Device Placement At Incorrect Location	1
Lead Fracture	1
Lead Migration/Dislodgement	1
Total	**10**

6.4.2.2 Model 3889

Model Name	InterStim Quad Lead Tined
FDA Approval Date	September 2002
Leads Enrolled	1,141
Leads Currently Active in Study	557
Device Events	90
Median Follow-up Time (Months)	21.9
Cumulative Follow-up Time (Months)	31,452



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	95.9% (94.4%, 97.0%)	92.5% (90.4%, 94.1%)	89.6% (86.8%, 91.7%)	87.9% (84.7%, 90.4%)	87.3% (84.0%, 90.0%)
Sample Size	740	478	311	194	123

Time Interval	6 Years	7 Years	8 Years	At 105 Months	
Survival (95% CI)	82.1% (76.4%, 86.5%)	82.1% (76.4%, 86.5%)	82.1% (76.4%, 86.5%)	74.0% (62.7%, 82.3%)	
Sample Size	84	48	34	22	

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	13
Device Lead Issue	8
Low Impedance	5
Device Battery Issue	1
Device Electrical Impedance Issue	1
Device Failure	1
Device Issue	1
Device Malfunction	1
Total	**90**

6.4.3 Lead Summary

Table 6.11: Sacral Neuromodulation Lead Characteristics

Model Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
InterStim Extended Electrode Quad Lead Tined (model 3093)	September 2002	100	32	10	25.1	3,380
InterStim Quad Lead Tined (model 3889)	September 2002	1,141	557	90	21.9	31,452

Table 6.12: 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% (88.8%, 99.8%)	94.3% (83.3%, 98.1%)	91.9% (79.5%, 96.9%)	85.8% (70.5%, 93.5%)	85.8% (70.5%, 93.5%)
InterStim Quad Lead Tined (model 3889)	95.9% (94.4%, 97.0%)	92.5% (90.4%, 94.1%)	89.6% (86.8%, 91.7%)	87.9% (84.7%, 90.4%)	87.3% (84.0%, 90.0%)

Model Name	6 Years	7 Years	8 Years		
InterStim Extended Electrode Quad Lead Tined (model 3093)	78.8% (61.1%, 89.1%)				
InterStim Quad Lead Tined (model 3889)	82.1% (76.4%, 86.5%)	82.1% (76.4%, 86.5%)	82.1% (76.4%, 86.5%)		

6.5 Extensions

From April 2010 to the report cut-off date of October 31, 2020, 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=1,324) 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 3,730 months (311 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:

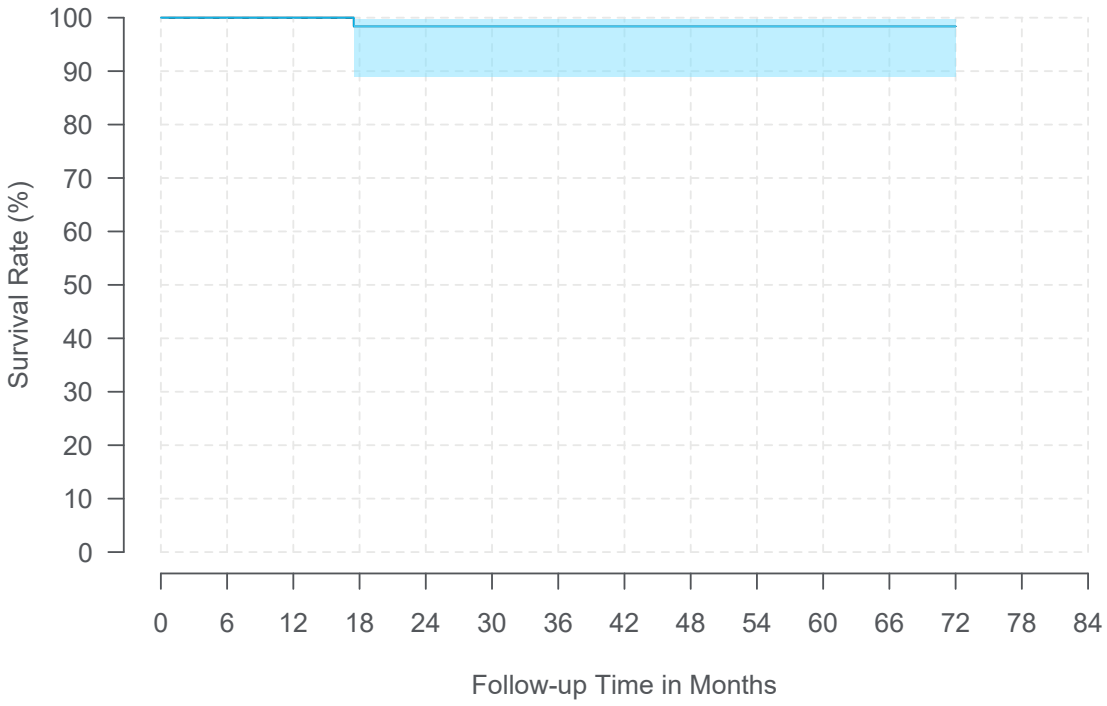
- 1 had follow-up time cut-off due to product performance-related events.
- 81 were censored in the survival analysis for the following reasons: patient expired, extension explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 20 were free from product 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	20
Device Events	1
Median Follow-up Time (Months)	27.2
Cumulative Follow-up Time (Months)	3,730



Time Interval	1 Year	2 Years	3 Years	4 Years	5 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%)	98.4% (89.0%, 99.8%)
Sample Size	64	51	33	23	21

Time Interval	6 Years
Survival (95% CI)	98.4% (89.0%, 99.8%)
Sample Size	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 6.13: Sacral Neuromodulation Extension Characteristics

Model Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Device Events	Median Follow-up Time (Months)	Cumulative Follow-up Time (Months)
Quadripolar extension (model 3095)	July 1998	102	20	1	27.2	3,730

Table 6.14: Sacral Neuromodulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years	6 Years
Quadripolar extension (model 3095)	100.0% (NA)	98.4% (89.0%, 99.8%)	98.4% (89.0%, 99.8%)	98.4% (89.0%, 99.8%)	98.4% (89.0%, 99.8%)	98.4% (89.0%, 99.8%)