PRODUCT PERFORMANCE REPORT

SUMMARY OF DATA FROM THE MEDTRONIC POST-MARKET REGISTRY

2018

v.1.0 04Mar2019

Medtronic
Further, Together

Contents

1 Overview

1.1 Registry Background

Medtronic uses a prospective, long-term multi-center registry to monitor the performance of certain products at selected centers titled the Product Surveillance Registry (PSR). This 2018 Product Performance Report 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 was created by Medtronic to monitor the performance of commercially available infusion and spinal cord stimulation systems. These systems were initiated into the registry in August 2003 and June 2004, respectively. Prior to the development of the registry, Medtronic Neuromodulation typically evaluated patient and product outcomes by retrospectively analyzing data from Returned Product Analysis (RPA) and complaints data. The registry allows Medtronic to prospectively capture valuable real-world information that can be used in conjunction with these retrospective and passive data sources. This information is used to guide future product development efforts aimed at improving product reliability and quality. The data are also used to measure progress toward improving product performance to fulfill regulatory requirements. In addition, data from the registry provide information about the treatment practices of physicians using these therapies.

This registry was initially designed to track performance of the Medtronic implantable targeted drug delivery systems (infusion pumps and catheters). These surgically-placed devices deliver prescribed medication directly to the fluid around the spinal cord for the treatment of chronic pain or severe spasticity.

The Medtronic spinal cord stimulation systems (spinal cord neurostimulators, leads, and extensions) for pain indications were later added to the registry. Implanted spinal cord neurostimulators send electrical impulses to the spinal cord.

In July 2009, the Medtronic deep brain stimulation systems (deep brain neurostimulators, leads, and extensions) were included in the registry. Deep brain stimulation (DBS) uses a surgically implanted neurostimulator to deliver electrical stimulation to targeted areas in the brain.

In April 2010, the Medtronic sacral neuromodulation systems (neurostimulators, leads, and extensions) were added to the registry. This implantable system sends electrical pulses through

a lead to the sacral nerves to modulate the neural activity that influences the behavior of the pelvic floor, lower urinary tract, urinary and anal sphincters, and colon.

The registry has collected data from centers across the United States, Europe, and South America. There have been 71 centers that have contributed data for targeted drug delivery systems, 82 centers for spinal cord stimulation systems, 38 centers for deep brain stimulation, and 20 centers for sacral neuromodulation. 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 11th Annual Medtronic Neurostimulation and Targeted Drug Delivery Systems 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 Systems therapies, we believe that performance reporting is even more important. We strive for better performance with every new product 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 17,366 patients in our ongoing post-market registry. The registry has enrolled 52,879 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 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, Data Science
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 the Product Performance Report.

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1.5 Trademarks of Medtronic, Inc.

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

2 Methodology

2.1 Event Classification

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

- Implanted or external components,
- Implant or modification procedure, or
- Infusion or stimulation therapy.

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

In early versions of the protocol for infusion and spinal cord stimulation systems, an event was reportable only if it required a surgical intervention, led to therapy abandonment, or resulted in death. This event threshold was expanded for infusion and spinal cord stimulation systems in April 2010 in order to capture additional adverse event data.

Additionally, since the protocol expansion, the seriousness (per ISO 14155-1) of adverse events has been assessed and reported by the registry investigators.

For centers participating in the PSR protocol of the registry, specific therapy relevant events are also collected and include:

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

By design, not all adverse events experienced by patients during participation were reported in the registry because the registry is primarily focused on understanding the long term reliability and performance of Medtronic implanted systems.

All events reported in the registry are coded using version 21.0 of the Medical Dictionary for Regulatory Activities (MedDRA) and combined by related terms. Medtronic own coding system for events related to implanted neuromodulation systems, which do not exist in the MedDRA dictionary, was integrated with the MedDRA dictionary.

2.1.1 Registry Definitions

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

- **Adverse Event:** any death or undesirable experience (associated with signs, symptoms, illnesses, or other medical events) occurring to the patient that appears or worsens during the clinical study and is possibly related to the device, procedure, and/or therapy.
- **Device Event:** an issue with any of the implantable or external system components.
- **Therapy Relevant Event:** a specific event type for deep brain stimulation therapies which are collected regardless of relatedness to the device, procedure, or therapy.

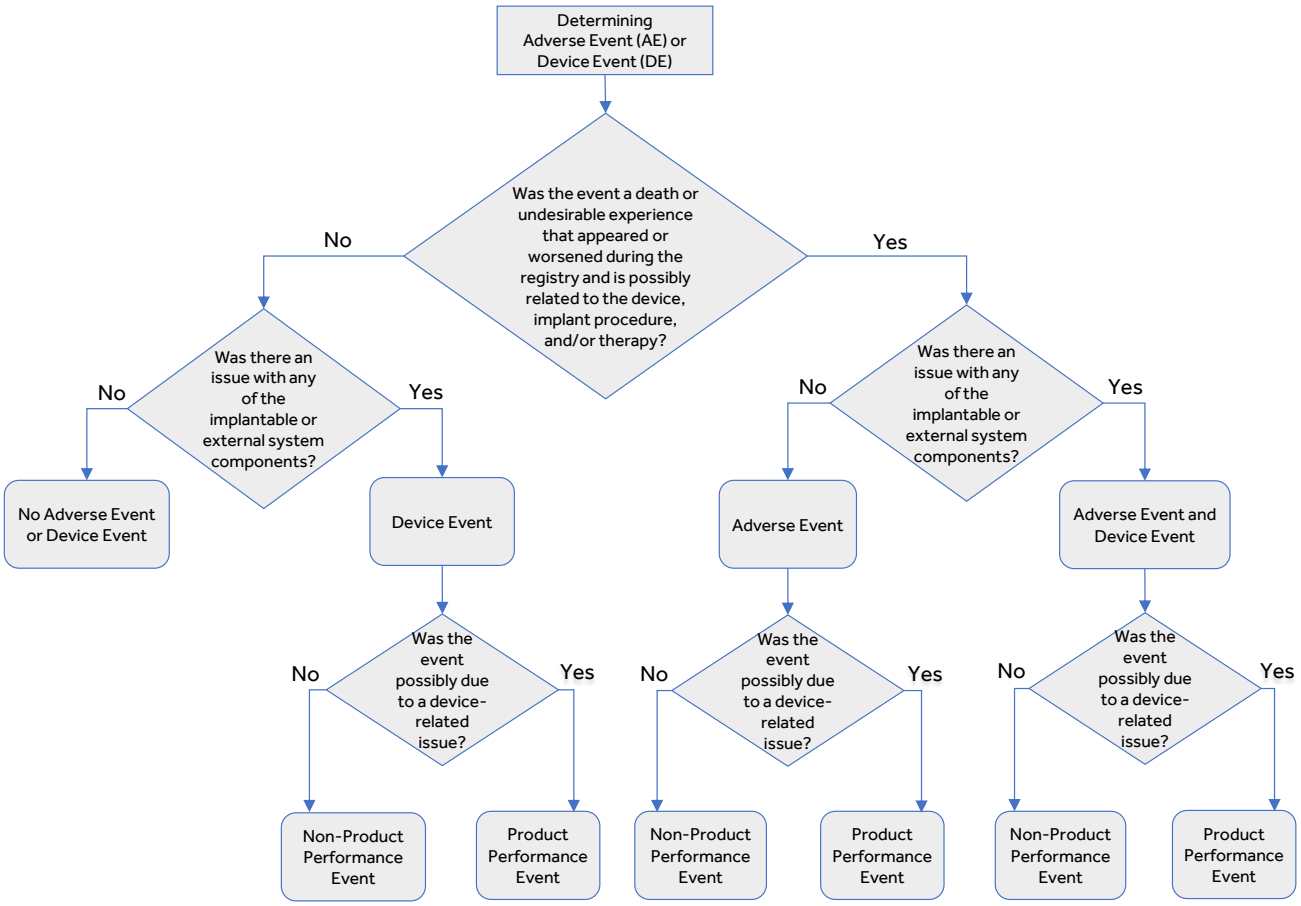


Figure 2.1: Adverse Event/Device Event Flowchart

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 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, that possibly resulted from or was related to the implant procedure, or modification between implant and procedure, therapy, or delivery of therapy, and cannot be classified as product performance-related.

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 2 or more devices.

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).

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.

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, 2018. Seventy-one centers, in North America, Europe and South America, enrolled patients and contributed patient data to the targeted drug delivery systems section of this report.

3.1.2 Patients

There were 8,444 total targeted drug delivery system patients enrolled through October 31, 2018. In Table 3.1 and Figure 3.1, 57.4% 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 22.3% for treatment of spasticity, and 17.8% 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.

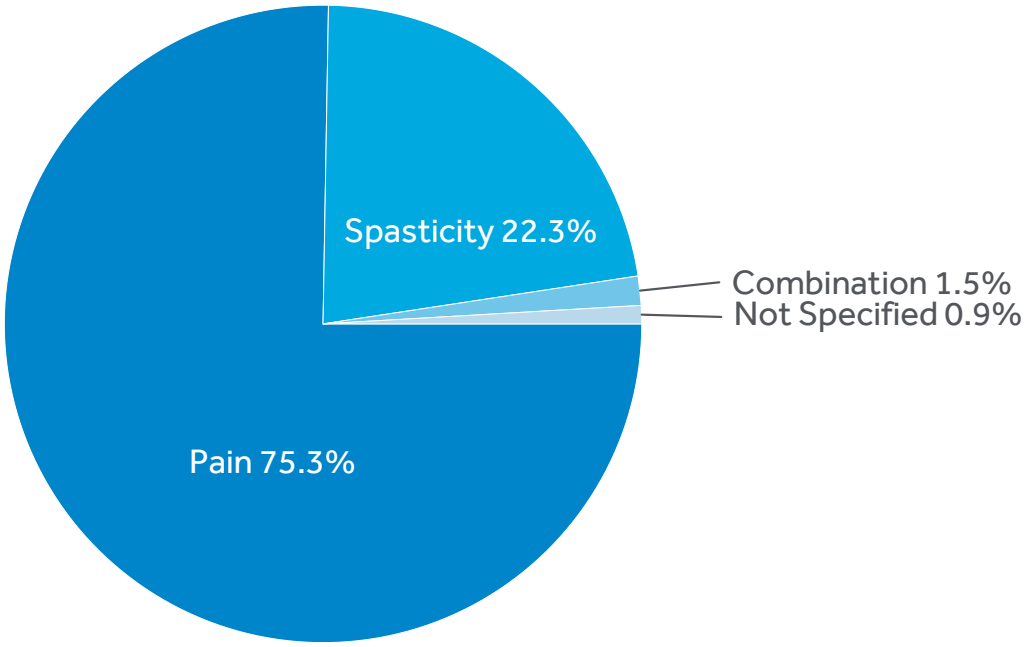


Figure 3.1: Targeted Drug Delivery Primary Treatment Indications

Table 3.1: Targeted Drug Delivery Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Pain	**6,356 (75.3%)**
Non-malignant pain	4,850 (57.4%)
Malignant pain	1,505 (17.8%)
Pain, Not specified	1 (0.0%)
Spasticity	**1,885 (22.3%)**
Combination	**125 (1.5%)**
Non-malignant pain & Spasticity	123 (1.5%)
Malignant pain & Chemotherapy	1 (0.0%)
Non-malignant pain & Chemotherapy	1 (0.0%)
Not Specified[b]	**78 (0.9%)**
Total Patients	**8,444 (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	531
Abdominal/Visceral	340
Extremity	224
Pelvic	207
Thoracic	170
Head/Neck	90
Other	116
Not Specified	441
Total Sites of Pain[a]	**2,119**

[a] In 1,506 patients with indications of malignant pain and a combination of malignant pain and chemotherapy.

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

Non-Malignant Pain: Sub-Indications	Enrolled Patients (%)
Back Pain with Leg Pain	1,533 (30.8%)
Back Pain without Leg Pain	1,456 (29.3%)
General Neuropathic Condition	223 (4.5%)
CRPS I[a]	159 (3.2%)
Peripheral Neuropathy	81 (1.6%)
Joint Pain/Arthritis	69 (1.4%)
General Nociceptive Condition	48 (1.0%)
CRPS II[a]	36 (0.7%)
Osteoporosis	20 (0.4%)
Other	394 (7.9%)
Not Specified	955 (19.2%)
Total Patients[b]	**4,974**

[a] CRPS is complex regional pain syndrome.

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

Table 3.4: Targeted Drug Delivery Spasticity: Sub-Indications

Spasticity: Sub-Indications	Pediatrics (%) (<18 years)	Adults (%) (>= 18 years)	All Patients (%)
Cerebral Palsy	326 (77.1%)	208 (13.1%)	534 (26.6%)
Multiple Sclerosis	0 (0.0%)	510 (32.2%)	510 (25.4%)
Spinal Cord Injury	7 (1.7%)	291 (18.4%)	298 (14.8%)
Brain Injury	34 (8.0%)	112 (7.1%)	146 (7.3%)
Stroke	1 (0.2%)	80 (5.0%)	81 (4.0%)
Other	11 (2.6%)	154 (9.7%)	165 (8.2%)
Not Specified	44 (10.4%)	230 (14.5%)	274 (13.6%)
Total Patients[a]	**423**	**1,585**	**2,008**

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

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. However, product labeling varies by geography, so local Medtronic representative for region-specific product labeling should be contacted.

3.2 Event Summary

There were 1,927 product performance events reported between August 7, 2003 and October 31, 2018, in patients with targeted drug delivery systems. These events represent 23.9% of the total reported events (1,927/8,068). These events occurred in 1,256 (14.9%) of the 8,444 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 6,117 non-product performance events that were collected to understand patient experience (clinical signs and symptoms) with the targeted drug delivery systems (see Table 3.6). 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=24).

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 3.5 and Table 3.10 to Table 3.14 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 2,102 deaths reported for patients with targeted drug delivery systems (see Table 3.7). 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 and Table 3.6 include combined data from these versions of the protocol.

3.2.1 Product Performance Events

Table 3.5: Targeted Drug Delivery System Product Performance Events

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%)[b]
RPA Determination	**250**	**0.94**	**226 (2.68%)**
Pump Motor Stall[c]	131	0.49	125 (1.48%)
Corrosion And/Or Gear Wear	28	0.10	28 (0.33%)
Laboratory Overinfusion Finding[d]	23	0.09	23 (0.27%)
Confirmed Overinfusion[e]	11	0.04	5 (0.06%)
Reduced Battery Performance	10	0.04	10 (0.12%)
Battery High Resistance	9	0.03	9 (0.11%)
Deformed Pump Tube	8	0.03	7 (0.08%)
Reservoir Access Issues Due To Residue	7	0.03	6 (0.07%)
Motor Feedthrough Anomaly	6	0.02	6 (0.07%)
Hole In Pump Tube	2	0.01	1 (0.01%)
Other[f]	13	0.05	13 (0.15%)
Not Coded[g]	2	0.01	2 (0.02%)
Physician's Determination	**1,677**	**6.28**	**1,129 (13.37%)**
Catheter Occlusion	356	1.33	317 (3.75%)
Catheter Dislodgement	323	1.21	275 (3.26%)
Catheter Break/Cut	223	0.84	198 (2.34%)
Catheter Kink	187	0.70	164 (1.94%)
Pump Motor Stall[h]	96	0.36	77 (0.91%)
Device Malfunction[i]	89	0.33	82 (0.97%)
Catheter Related Complication	84	0.31	78 (0.92%)
Catheter Leakage	62	0.23	59 (0.70%)
Pump Reservoir Volume Discrepancy	55	0.21	41 (0.49%)
Catheter Disconnection At Pump	46	0.17	45 (0.53%)
Pump Unable To Enter/Withdraw From Catheter Access Port	30	0.11	24 (0.28%)
Pump Underinfusion	19	0.07	16 (0.19%)
Device Difficult To Use	17	0.06	17 (0.20%)
Pump Connector Break/Cut	17	0.06	16 (0.19%)
Medical Device Complication[j]	16	0.06	14 (0.17%)
Device Issue[k]	9	0.03	9 (0.11%)
Catheter Disconnection Between Catheter Segments	7	0.03	7 (0.08%)
Catheter Access Port Issue	6	0.02	6 (0.07%)
Device Breakage	6	0.02	6 (0.07%)
Catheter Damage	5	0.02	5 (0.06%)
Device Alarm Issue	4	0.01	4 (0.05%)
Device Connection Issue	3	0.01	3 (0.04%)
Pump Not Infusing	3	0.01	3 (0.04%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%)[b]
Device Damage	2	0.01	2 (0.02%)
Physician Reported Overinfusion[l]	2	0.01	2 (0.02%)
Other[f]	10	0.04	10 (0.12%)
Total	**1,927**	**7.22**	**1,256 (14.87%)**

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

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

[c] Of the 131 RPA determined motor stalls, 129 had a pump etiology and 2 had other etiologies. Motor stall count does not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. The SynchroMed II pump is designed to temporarily stop the rotor of the pump motor and suspend drug infusion for the duration of the MRI exposure for patient safety.

[d] Includes pumps where a physician reported a device related event not meeting the definition for confirmed overinfusion.

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

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

[g] Sites were queried for additional event information and could not be coded at this time.

[h] Of the 96 physician determined motor stalls, 88 had a pump etiology; 1 had another etiology and 7 had an MRI etiology. Of the 7 with MRI etiology, 1 pump was replaced and 6 remain active in the patients. Motor stall count does not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. The SynchroMed II pump is designed to temporarily stop the rotor of the pump motor and suspend drug infusion for the duration of the MRI exposure for patient safety.

[i] Includes 57 PTM malfunctions, 9 unexpectedly locked out of PTM, 5 pump malfunctions, 2 pump reset occurred, 3 PTM unable to sync with pump, 3 PTM displayed incorrect alarm date, 3 pump in stopped mode, 1 clinician programmer malfunction, 1 patient felt pump not working, 1 unspecific difficulties with PTM, 1 PTM bonding issue, 1 possibly due to antenna, 1 suspected rotor problem, 1 possible pump malfunction.

[j] Includes 4 worn catheter connector, 2 possible corrosion of catheter due to concentration of drug, 1 metal clips on sutureless connector appear bent, 1 pump unable to interrogate/program, 1 pump in safe state, 1 worn proximal connector, 1 telemetry was stopped secondary to error code, 1 worn catheter, 1 sutureless connector failure, 1 pump beeped, 1 wear and tear of connector pin, 1 pocket of air detected in dye study.

[k] Includes 6 unable to activate PTM, 2 PTM Error Codes and 1 de-coupled PTM.

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

A total of 1,350 (70.1%) of the 1,927 product performance events were related to the catheter. This includes 1,340 (69.5%) with a catheter etiology and 10 events with both a catheter and other etiology (including device and non-device etiologies). There were 441 (22.9%) events

related to the pump. This includes 435 (22.6%) with a pump etiology and 6 events with both a pump and other etiology (including device and non-device etiologies). There were 114 (5.9%) related to other component and 38 (2.0%) related to other etiologies. Relatedness is reported by the physician.

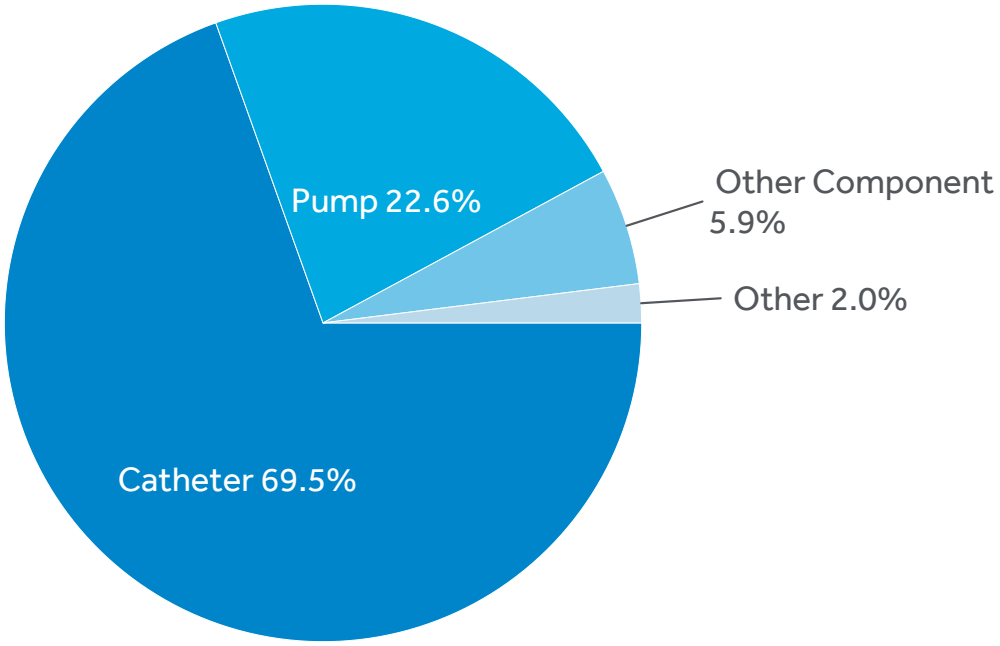


Figure 3.2: Targeted Drug Delivery System Product Performance Events by Relatedness

3.2.2 Non-Product Performance Events

Adverse events and device events that were not related to a product performance event are categorized in Table 3.6 by event group term. These events do not include deaths (see Section 3.2.3) or normal battery depletions. As explained in the Methodology section of this report, this registry's event reporting has evolved over time. Therefore, the event counts are strictly the sum of the events collected up to the October 31, 2018 data cut-off. **All tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 3.6: Targeted Drug Delivery System Non-Product Performance Events

Non-Product Performance Events	Event Counts
Therapeutic and nontherapeutic effects (excluding toxicity)	**2,114**
Adverse Drug Reaction	1,599
Therapeutic Product Ineffective	153
Drug Withdrawal Syndrome	140
Withdrawal Syndrome	79
Inadequate Analgesia	71
Therapeutic Response Decreased	58
Therapy Non-Responder	6
Other[a]	8
Complications associated with device	**1,153**
Medical Device Site Pain	634
Medical Device Site Extravasation	260
Medical Device Site Erosion	43
Medical Device Site Discomfort	39
Medical Device Site Erythema	38
Medical Device Site Haematoma	31
Medical Device Site Swelling	19
Medical Device Site Haemorrhage	12
Medical Device Site Irritation	10
Medical Device Complication	8
Medical Device Discomfort	8
Medical Device Site Inflammation	8
Medical Device Site Rash	6
Drug-Related Pump Anomaly	5
Medical Device Site Oedema	5
Other[a]	27

...continued

Non-Product Performance Events	Event Counts
Device issues[b]	**528**
Pump Inversion	202
Pump Migration	99
Pump Reservoir Volume Discrepancy	78
Device Malfunction	70
Device Issue	22
Pump Reservoir Issue	14
Catheter Break/Cut	9
Device Extrusion	8
Pump Unable To Enter/Withdraw From Catheter Access Port	6
Other[a]	20
Infections - pathogen unspecified	**374**
Medical Device Site Infection	250
Wound Infection	58
Meningitis	23
Infection	16
Catheter Site Infection	8
Medical Device Site Abscess	5
Other[a]	14
General system disorders NEC	**315**
Pain	213
Oedema Peripheral	64
Oedema	15
Asthenia	6
Other[a]	17
Neurological disorders NEC	**308**
Cerebrospinal Fluid Leakage	121
Hypoaesthesia	70
Somnolence	40
Paraesthesia	17
Hyperaesthesia	15
Sedation	11
Clonus	6
Dizziness	6
Lethargy	5
Other[a]	17

...continued

Non-Product Performance Events	Event Counts
Procedural related injuries and complications NEC	**230**
Wound Dehiscence	85
Seroma	44
Post Lumbar Puncture Syndrome	37
Sedation Complication	13
Procedural Headache	10
Anaesthetic Complication	5
Pseudomeningocele	5
Suture Related Complication	5
Other[a]	26
Administration site reactions	**224**
Catheter Site Pain	133
Catheter Site Fibrosis	18
Inflammatory Mass (Possible)	18
Inflammatory Mass (Confirmed)	13
Catheter Site Extravasation	8
Catheter Site Swelling	8
Catheter Site Granuloma	5
Catheter Site Mass	5
Other[a]	16
Medication errors and other product use errors and issues	**107**
Device Difficult To Use	94
Other[a]	13
Headaches	**63**
Headache	63
No Anomaly Found By RPA	**61**
No Anomaly Found By RPA[c]	61
Overdoses and underdoses NEC	**61**
Overdose	59
Other[a]	2
Musculoskeletal and connective tissue disorders NEC	**60**
Back Pain	33
Pain In Extremity	13
Other[a]	14
Muscle disorders	**46**
Muscular Weakness	35
Muscle Spasms	10
Other[a]	1

...continued

Non-Product Performance Events	Event Counts
Urinary tract signs and symptoms	**45**
Urinary Retention	27
Dysuria	10
Other[a]	8
Gastrointestinal signs and symptoms	**39**
Nausea	20
Vomiting	10
Abdominal Pain	6
Other[a]	3
Neuromuscular disorders	**39**
Muscle Spasticity	32
Other[a]	7
Bacterial infectious disorders	**30**
Medical Device Site Cellulitis	18
Other[a]	12
Tissue disorders NEC	**30**
Impaired Healing	28
Other[a]	2
Epidermal and dermal conditions	**28**
Pruritus	8
Erythema	7
Other[a]	13
Injuries NEC	**24**
Wound Secretion	11
Other[a]	13
Psychiatric disorders NEC	**23**
Mental Status Changes	22
Other[a]	1
Exposures, chemical injuries and poisoning	**21**
Toxicity To Various Agents	21
Respiratory disorders NEC	**17**
Respiratory Depression	6
Other[a]	11
Skin appendage conditions	**16**
Hyperhidrosis	16
Gastrointestinal motility and defaecation conditions	**14**
Constipation	14
Allergic conditions	**12**
Drug Hypersensitivity	6
Hypersensitivity	6

...continued

Non-Product Performance Events	Event Counts
Decreased and nonspecific blood pressure disorders and shock	**9**
Hypotension	7
Other[a]	2
Spinal cord and nerve root disorders	**9**
Other[a]	9
Mental impairment disorders	**8**
Memory Impairment	6
Other[a]	2
Disturbances in thinking and perception	**7**
Hallucination	5
Other[a]	2
Genitourinary tract disorders NEC	**6**
Genitourinary Symptom	6
Skin and subcutaneous tissue disorders NEC	**6**
Skin Erosion	6
Structural brain disorders	**6**
Subdural Hygroma	6
Central nervous system infections and inflammations	**5**
Arachnoiditis	5
Other[a]	**79**
Total	**6,117**

[a] Composed of event codes with fewer than 5 events each.

[b] Device issues count does not include temporary motor stalls that may be expected (e.g. due to MRI) and recovered within a 24-hour period. The SynchroMed II pump is designed to temporarily stop the rotor of the pump motor and suspend drug infusion for the duration of the MRI exposure for patient safety.

[c] The results reported herein reflect the finding from the Returned Product Analysis (RPA) on the products that were returned with a suspected device issue.

3.2.3 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 2,102 patients in the registry had expired. As with previous reports, no deaths were were reported as a direct result of a product performance event. One death was reported by the physician as possibly related to the intrathecal medications in a patient who expired due to pulmonary embolism. A second death was reported by the physician as due to acute respiratory failure following a device procedure, and was assessed by Medical Safety as probably related to the device and implant procedure. A third death was reported by the physician as possibly related to

the intrathecal medication in a patient who expired due to probable arteriosclerotic cardiovascular disease. Medical Safety assessed this event as unassessable due to incomplete information.

Since 2003, a total of 1,212 (57.7%) deaths have been reported in this patient registry study based upon patients receiving therapy for malignant pain, 677 (32.2%) for non-malignant pain, 198 (9.4%) for spasticity, 9 (0.4%) for non-malignant pain & spasticity, and 6 (0.3%) for not specified primary indication (see Table 3.7). The percentage is based upon the total patient death events and not based upon the rate of occurrence. As mentioned previously, **all tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 3.7: Targeted Drug Delivery System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Malignant pain	1,212 (57.7%)
Non-malignant pain	677 (32.2%)
Spasticity	198 (9.4%)
Non-malignant pain & Spasticity	9 (0.4%)
Not Specified	6 (0.3%)
Total	**2,102 (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, 2018, there were 10,378 pumps followed in the registry. The difference between the total number of patients (n=8,444) 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 313,001 months (26,083 years). Table 3.8 provides the number and percentage of pumps by model.

3.3.1 SynchroMed II Design Change: Pump Enhancements

Design changes to the SynchroMed II 20mL and 40mL 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 3.8 provides the number and percentage of pumps by model and pump enhancement.

Table 3.8: Targeted Drug Delivery Pump Counts by Model and Pump Enhancement

	Model Name	N (%)
Currently manufactured	**SynchroMed II 40 mL**	**5,563 (60.5%)**
	Pre-enhancements	4,630 (50.4%)
	GW3/FT enhancements	530 (5.8%)
	GW3/FT/DLC enhancements	380 (4.1%)
	Unknown[a]	23 (0.3%)
	SynchroMed II 20 mL	**3,628 (39.5%)**
	Pre-enhancements	2,961 (32.2%)
	GW3/FT enhancements	362 (3.9%)
	GW3/FT/DLC enhancements	303 (3.3%)
	Unknown[a]	2 (0.0%)
No longer manufactured	**SynchroMed EL 18 mL**	**1,146 (5.8%)**
	SynchroMed EL 10 mL	**34 (0.2%)**
	SynchroMed Classic	**5 (0.0%)**
	Other	**2 (0.0%)**
	Total	**10,378 (100%)**

[a] Sites were queried for additional pump information and could not be coded at this time.

3.3.2 Pump Events

There were 441 product performance-related events with an underlying reported etiology related to pump function. This includes 435 events with a pump etiology and 6 events with both a pump and other etiology (including device and non-device etiologies). Of these, 361 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 27.9% (1,354/4,845). 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 441 pump events, 44.7 % (197/441) were assigned as device related by the physician, not returned to Medtronic RPA (see Figure 3.3).

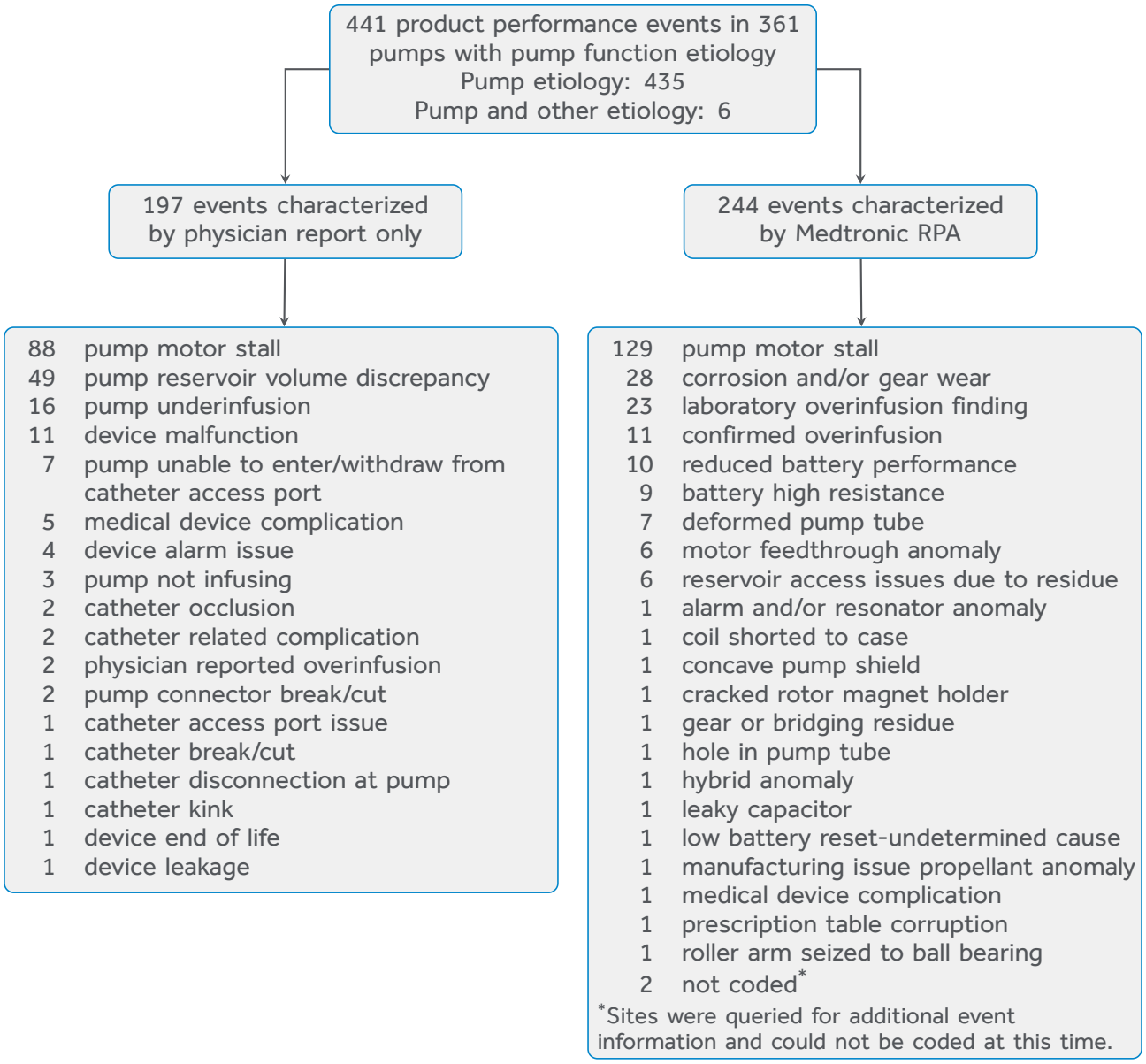


Figure 3.3: Distribution of Pump Function Etiology Product Performance Events

Overinfusion

Medtronic executed a field action in March 2014 informing healthcare professionals of overinfusion associated with the SynchroMed II Infusion System. In September 2016, an updated customer letter (https://www.medtronic.com/content/dam/medtronic-com/professional/documents/product-advisories/tdd/hcp_overinfusion_letter.pdf) was provided which stated an overinfusion occurrence rate for registry patients. This rate was based on pumps which had both laboratory overinfusion through returned product analysis and an in-vivo complaint of either clinical overinfusion symptoms or lower than expected residual volume. This definition was used because environmental factors during shipping may impact

the results of returned product testing. As of October 31, 2018, there were 5 pumps in the registry that met this definition as stated in the customer letter. The 5 pumps with overinfusion provided 95% confidence that the occurrence rate is less than 0.0011 (0.11%). The use of non-indicated drug formulations (such as admixtures, compounded drugs and unapproved drug concentrations) increases the likelihood for overinfusion. Medtronic continues to monitor pump performance relative to overinfusion.

Table 3.9: Overinfusion Rate

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

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

The pump product performance-related events by model, pre-SynchroMed II enhancements and SynchroMed II enhancements are summarized in Table 3.10 to Table 3.14. For specific pump details by serial number, please visit http://synchromed2enhancements.medtronic.com.

Table 3.10: Event Summary Table: SynchroMed II 20 mL

Pump Event	**N**
RPA Determination	**46**
Pump Motor Stall	21
Battery High Resistance	6
Corrosion And/Or Gear Wear	4
Laboratory Overinfusion Finding	3
Motor Feedthrough Anomaly	3
Reduced Battery Performance	2
Other[a]	7
Physician's Determination	**52**
Pump Motor Stall	22
Pump Reservoir Volume Discrepancy	10
Device Malfunction	4
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Device Alarm Issue	3
Medical Device Complication	3
Other[a]	6
Total	**98**

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

Table 3.11: Event Summary Table: SynchroMed II 40 mL

Pump Event	N
RPA Determination	**139**
Pump Motor Stall	86
Laboratory Overinfusion Finding	18
Reduced Battery Performance	7
Corrosion And/Or Gear Wear	6
Deformed Pump Tube	5
Confirmed Overinfusion	4
Reservoir Access Issues Due To Residue	3
Battery High Resistance	2
Motor Feedthrough Anomaly	2
Other[a]	6
Physician's Determination	**90**
Pump Motor Stall	36
Pump Reservoir Volume Discrepancy	27
Pump Underinfusion	8
Device Malfunction	5
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Pump Not Infusing	2
Other[a]	9
Total	**229**

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

Table 3.12: Event Summary Table: SynchroMed II Pre-enhancements

Pump Event	Total
RPA Determination	**185**
Pump Motor Stall	107
Laboratory Overinfusion Finding	21
Corrosion And/Or Gear Wear	10
Reduced Battery Performance	9
Battery High Resistance	8
Deformed Pump Tube	6
Confirmed Overinfusion	5
Motor Feedthrough Anomaly	5
Reservoir Access Issues Due To Residue	4
Other[a]	10
Physician's Determination	**131**
Pump Motor Stall	54
Pump Reservoir Volume Discrepancy	33
Device Malfunction	8
Pump Underinfusion	8
Pump Unable To Enter/Withdraw From Catheter Access Port	7
Device Alarm Issue	4
Medical Device Complication	4
Pump Not Infusing	3
Catheter Occlusion	2
Physician Reported Overinfusion	2
Pump Connector Break/Cut	2
Other[a]	4
Total	**316**

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

Table 3.13: Event Summary Table: SynchroMed II GW3/FT Enhancements

Pump Event	Total
RPA Determination	**0**
Physician's Determination	**9**
Pump Motor Stall[a]	3
Pump Reservoir Volume Discrepancy	3
Catheter Access Port Issue	1
Catheter Disconnection At Pump	1
Device Malfunction	1
Total	**9**

[a] All 3 stalls were reported as temporary and recovered without sequelae. 1 pump was a suspected physician magnet stop, 1 pump recovered within 1 hour, and 1 pump recovered within 26 hours. Sites were queried for additional event information.

Table 3.14: Event Summary Table: SynchroMed II GW3/FT/DLC Enhancements

Pump Event	Total
RPA Determination	**0**
Physician's Determination	**2**
Pump Motor Stall[a]	1
Pump Reservoir Volume Discrepancy[b]	1
Total	**2**

[a] Stall was reported as temporary and recovered without sequelae. Suspected physician magnet stop. Site was queried for additional event information.

[b] No interventions performed.

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:

- 361 had follow up time cut-off due to product performance-related events.
- 7,551 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.

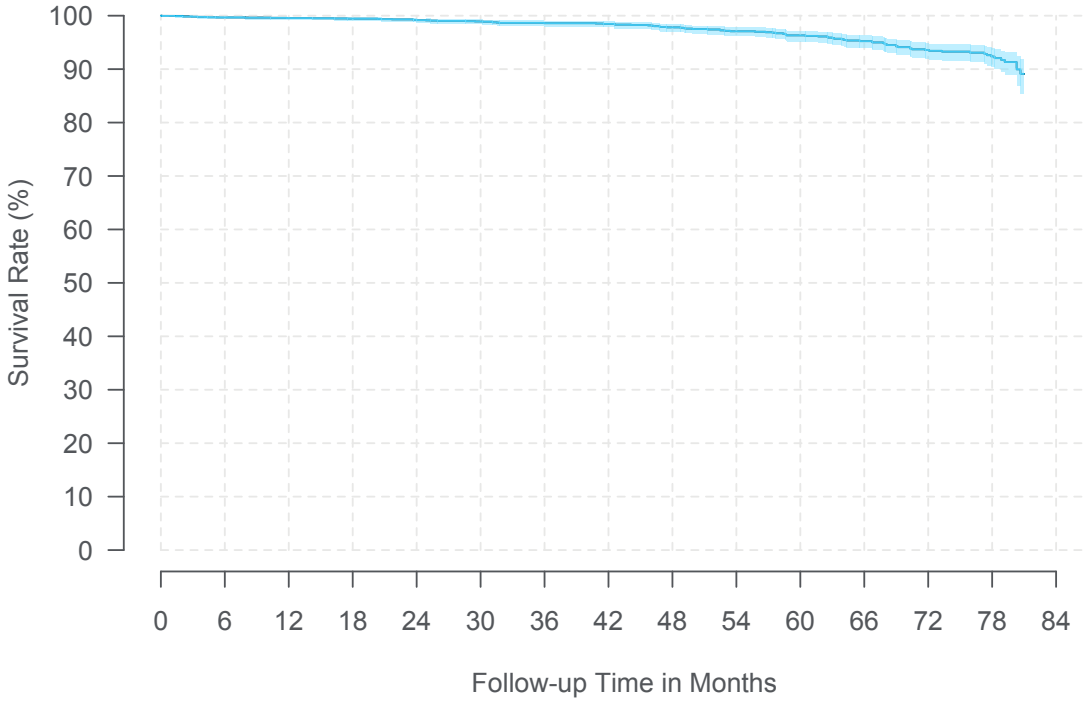
- 2,466 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

3.3.3 Pump Survival

The following figures and tables represent SynchroMed II pump survival and 95% confidence intervals. 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 past reports.

Model SynchroMed II 20 mL

Model/Name	SynchroMed II 20 mL
FDA Approval Date	September 2003
Pumps Enrolled	3,628
Pumps Currently Active in Study	1,117
Device Events	98
Cumulative Months of Follow-up	128,633



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (99.2%, 99.7%)	99.2% (98.8%, 99.5%)	98.6% (98.0%, 99.0%)	97.8% (97.0%, 98.4%)	96.3% (95.2%, 97.2%)
Sample Size	2,560	2,124	1,668	1,286	942

Time Interval	6 Years	At 81 Months			
Survival (95% CI)	93.6% (91.9%, 94.9%)	89.1% (85.4%, 91.9%)			
Sample Size	651	80			

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

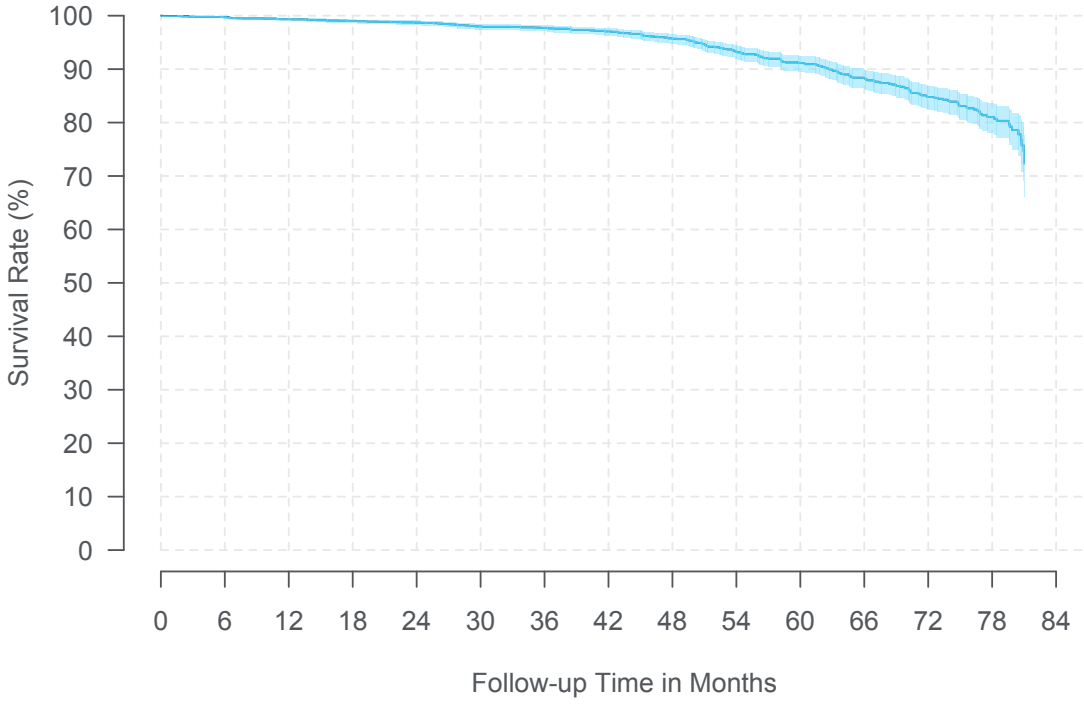
[a] Dependent on flow rate

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

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

Model SynchroMed II 40 mL

Model/Name	SynchroMed II 40 mL
FDA Approval Date	September 2003
Pumps Enrolled	5,563
Pumps Currently Active in Study	1,380
Device Events	229
Cumulative Months of Follow-up	152,127



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.3% (99.0%, 99.6%)	98.7% (98.3%, 99.0%)	97.7% (97.1%, 98.2%)	95.7% (94.7%, 96.5%)	91.1% (89.5%, 92.5%)
Sample Size	3,310	2,576	1,901	1,286	865

Time Interval	6 Years	At 81 Months			
Survival (95% CI)	84.8% (82.4%, 86.8%)	72.3% (66.1%, 77.7%)			
Sample Size	531	62			

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

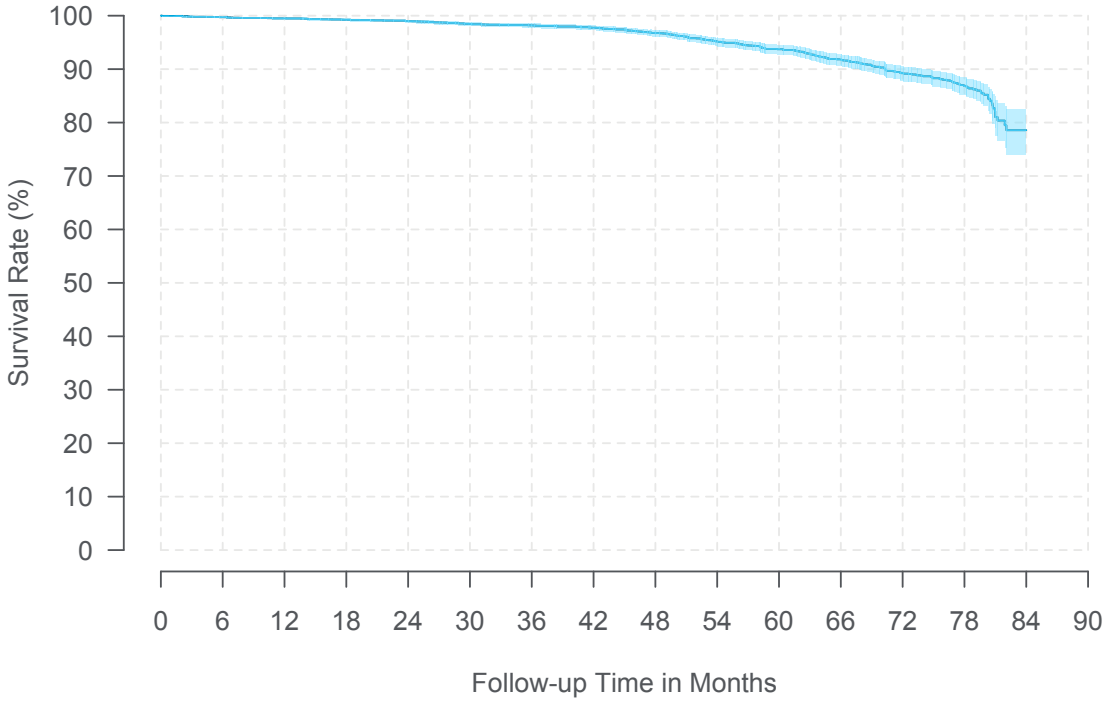
[a] Dependent on flow rate

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

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

SynchroMed II 20mL and 40mL: Pre-enhancements

Model/Name	Pre-enhancements
FDA Approval Date	September 2003
Pumps Enrolled	7,591
Pumps Currently Active in Study	1,237
Device Events	316
Cumulative Months of Follow-up	265,163

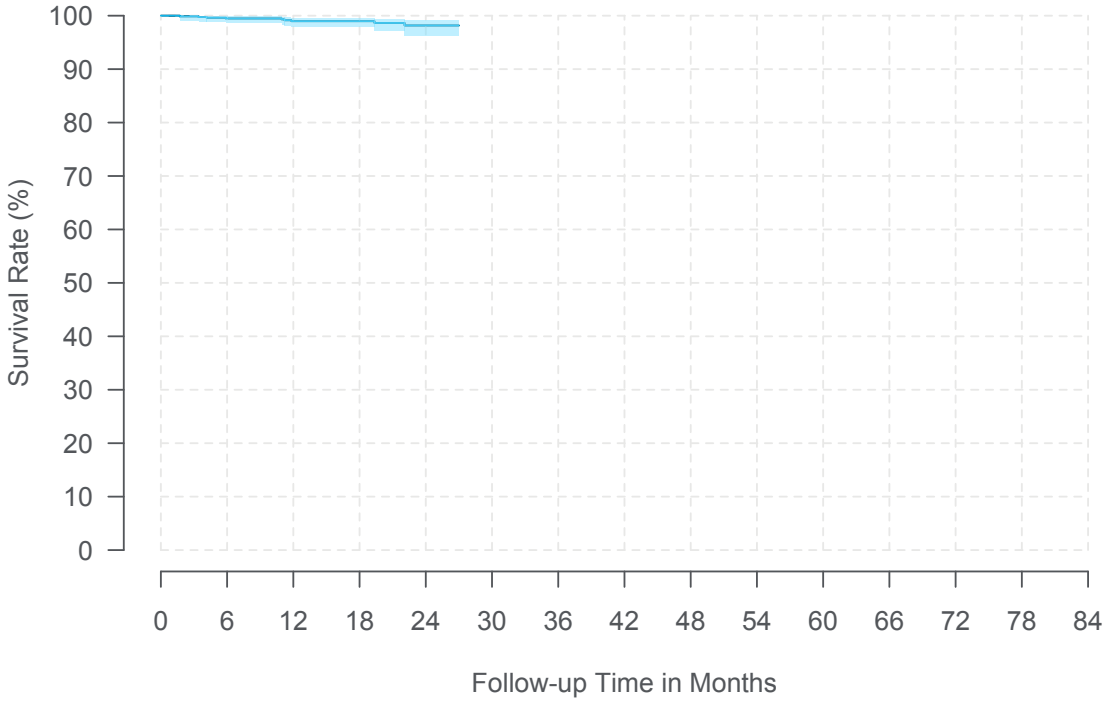


Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (99.3%, 99.7%)	99.0% (98.7%, 99.2%)	98.2% (97.7%, 98.5%)	96.7% (96.1%, 97.3%)	93.7% (92.8%, 94.6%)
Sample Size	5,288	4,555	3,568	2,571	1,807

Time Interval	6 Years	7 Years			
Survival (95% CI)	89.2% (87.8%, 90.5%)	78.6% (74.0%, 82.4%)			
Sample Size	1,182	29			

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

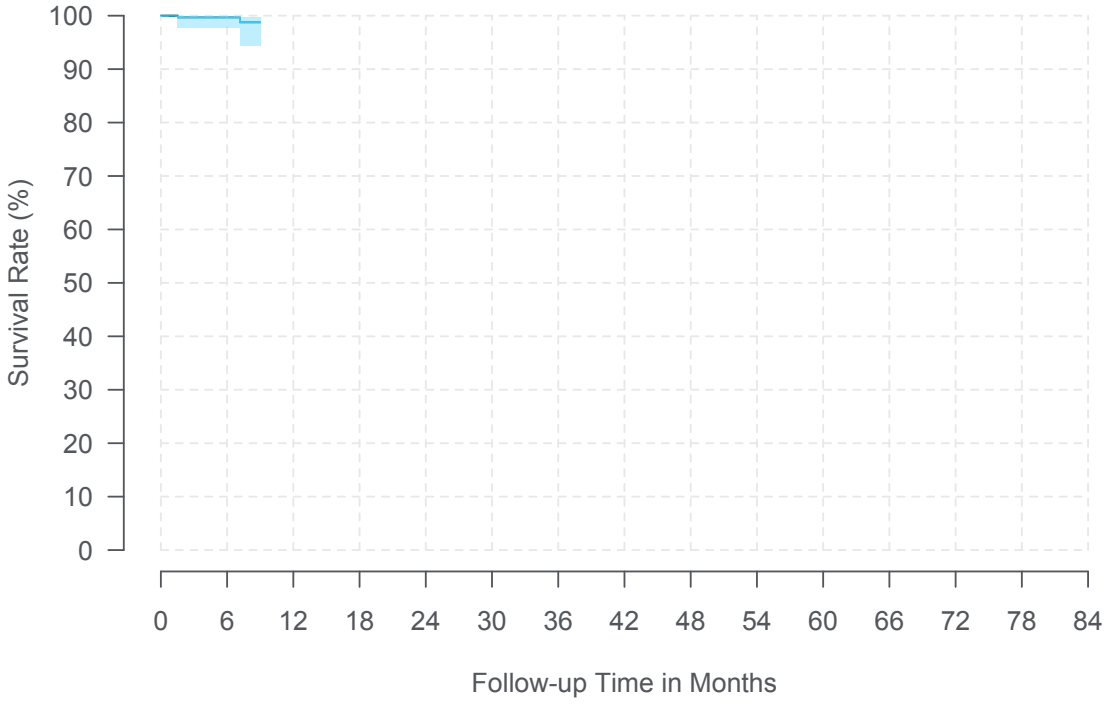
Model/Name	GW3/FT enhancements
FDA Approval Date	September 2015 (GW3)/November 2015 (FT)
Pumps Enrolled	892
Pumps Currently Active in Study	623
Device Events	9
Cumulative Months of Follow-up	13,322



Time Interval	1 Year	2 Years	At 27 Months
Survival	99.0%	98.2%	98.2%
(95% CI)	(97.8%, 99.5%)	(96.2%, 99.1%)	(96.2%, 99.1%)
Sample Size	565	143	66

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

Model/Name	GW3/FT/DLC enhancements
FDA Approval Date	April 2017 (DLC)
Pumps Enrolled	683
Pumps Currently Active in Study	622
Device Events	2
Cumulative Months of Follow-up	2,024



Time Interval	6 Months	9 Months
Survival	99.7%	98.8%
(95% CI)	(97.8%, 100%)	(94.3%, 99.7%)
Sample Size	146	61

3.3.4 Pump Survival Summary

Table 3.15: Targeted Drug Delivery Pump Characteristics

Model/Name	FDA Approval Date	Pumps Enrolled	Pumps Active	Device Events	Cumulative Follow-up Months
SynchroMed II 20 mL	September 2003	3,628	1,117	98	128,633
SynchroMed II 40 mL	September 2003	5,563	1,380	229	152,127
SynchroMed II Pre-enhancements	September 2003	7,591	1,237	316	265,163
SynchroMed II GW3/FT enhancements	September 2015 (GW3) November 2015 (FT)	892	623	9	13,322
SynchroMed II GW3/FT/DLC enhancements	April 2017 (DLC)	683	622	2	2,024

Table 3.16: Targeted Drug Delivery Pump Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
SynchroMed II 20 mL	99.6% (99.2%, 99.7%)	99.2% (98.8%, 99.5%)	98.6% (98.0%, 99.0%)	97.8% (97.0%, 98.4%)	96.3% (95.2%, 97.2%)
SynchroMed II 40 mL	99.3% (99.0%, 99.6%)	98.7% (98.3%, 99.0%)	97.7% (97.1%, 98.2%)	95.7% (94.7%, 96.5%)	91.1% (89.5%, 92.5%)
SynchroMed II Pre-enhancements	99.5% (99.3%, 99.7%)	99.0% (98.7%, 99.2%)	98.2% (97.7%, 98.5%)	96.7% (96.1%, 97.3%)	93.7% (92.8%, 94.6%)
SynchroMed II GW3/FT enhancements	99.0% (97.8%, 99.5%)	98.2% (96.2%, 99.1%)			
SynchroMed II GW3/FT/DLC enhancements					

Model Name	6 Years	7 Years			
SynchroMed II 20 mL	93.6% (91.9%, 94.9%)				
SynchroMed II 40 mL	84.8% (82.4%, 86.8%)				
SynchroMed II Pre-enhancements	89.2% (87.8%, 90.5%)	78.6% (74.0%, 82.4%)			
SynchroMed II GW3/FT enhancements					
SynchroMed II GW3/FT/DLC 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®, and Gablofen® are the only FDA approved

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

In this registry, patient status updates were obtained every 6 months, until discontinuation of therapy, or until the patient was lost to follow-up. Medications within the pump were recorded at each 6-month follow-up. 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, 2018, 7,576 patients (55.9% female, mean/SD age 54/17.6years) have enrolled in the registry and have been implanted with 9,191 SynchroMed II pumps. At least one drug record was available for 8,808 pumps; if no drug records were available (n=383 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) or Prialt® (preservative-free ziconotide sterile solution) these pumps were considered On-Label. For this analysis, if only the generic chemical classification, such as morphine or ziconotide, was entered then the assumption was that the drug is On-Label.
  - For pumps used for spasticity patients, if the drug record has only one drug, and it is either Lioresal® (bacoflen injection) or Gablofen® (bacoflen injection), that drug record was considered On-Label. Note: The classification was based on the name of the drug only, not the reported concentration of the drug. For this analysis, if only the generic chemical classification, such as baclofen, was entered then the assumption was that the drug is On-Label.
  - Pumps with an On-Label drug history and currently containing preservative free water or preservative free saline, or if previously contained preservative free water/saline and currently containing On-Label drug were considered On-Label.
- **Off-Label:** Any drugs not within the approved indications specified above are considered Off-Label. Additionally, any drug record with more than one drug at a time in the pump (admixture) was considered Off-Label.

- If a pump had any known exposure to Off-Label drugs (i.e., the Off-Label data have been collected in the registry), that pump was considered Off-Label, regardless of the amount of exposure time.
- If a pump is filled with a medication that was reported as compounded, that pump was considered Off-Label.

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

3.4.2 Data Analysis

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

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

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

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

3.4.3 Results

A total of 2,759 (31.3%) SynchroMed II pumps were classified as On-Label where there was no evidence of Off-Label drug/admixture exposure. A total of 6,049 (68.7 %) pumps were classified as Off-Label where there was evidence of pump exposure to an Off-Label drug/admixture. There were a total of 327 reported SynchroMed II pump product performance events during the study observation period. In addition to the 327 pump failures, there were 14 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 5.6-6.8 years) with no associated physician or patient complaint.

Three of the 327 pump failure events occurred in pumps with no drug records available. Of the remaining 324 SynchroMed II pump failures, 165 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 3.7% (324/8,808) with a median follow-up of 26.05 months.

For the 165 pump failures due to motor stall, 79 of the events were associated with the patient presenting clinical signs or symptoms of possible drug withdrawal or increasing pain or spasticity. The other 86 events had no patient reported signs or symptoms associated with the event, but had a physician report of a motor stall occurrence. There were no issues reported when pumps were replaced and/or re-started, such as drug overdose. None of the pump failures resulted in a patient death.

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

Primary Indication[a]	On-Label N=2,759	Off-Label N=6,049
Non-malignant Pain	864 (16.6%)	4,329 (83.4%)
Malignant Pain	41 (3.0%)	1,346 (97.0%)
Spasticity	1,853 (89.6%)	216 (10.4%)
Multiple/Unknown	1 (0.6%)[b]	158 (99.4%)

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

[b] Pump contains water/saline.

Total Study Population

A total of 2,759 SynchroMed II pumps were classified as On-Label for all therapies, where there was no evidence of Off-Label drug/admixture exposure. A total of 6,049 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 3.4 and Figure 3.5 respectively.

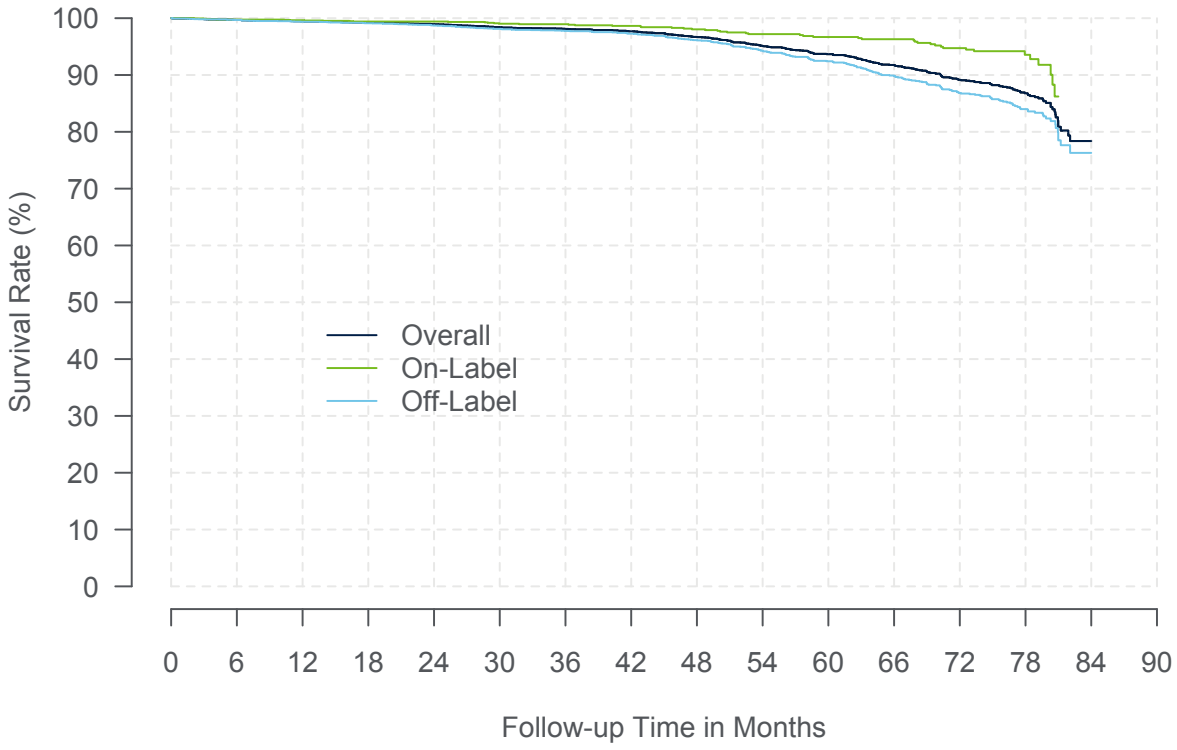


Figure 3.4: SynchroMed II Cumulative Survival (All Therapies)

Table 3.18: Survival Summary Table: All Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 81 Mos	7 Yrs
Overall	Survival	99.5%	98.9%	98.1%	96.7%	93.7%	89.2%	80.9%	78.4%
	Sample Size	5,774	4,643	3,535	2,544	1,795	1,176	140	28
On-Label	Survival	99.6%	99.4%	98.9%	98.0%	96.7%	94.7%	86.2%	
	Sample Size	1,799	1,420	1,048	747	535	370	35	
Off-Label	Survival	99.4%	98.7%	97.7%	96.1%	92.4%	86.8%	78.5%	76.3%
	Sample Size	3,975	3,223	2,487	1,797	1,260	806	105	20

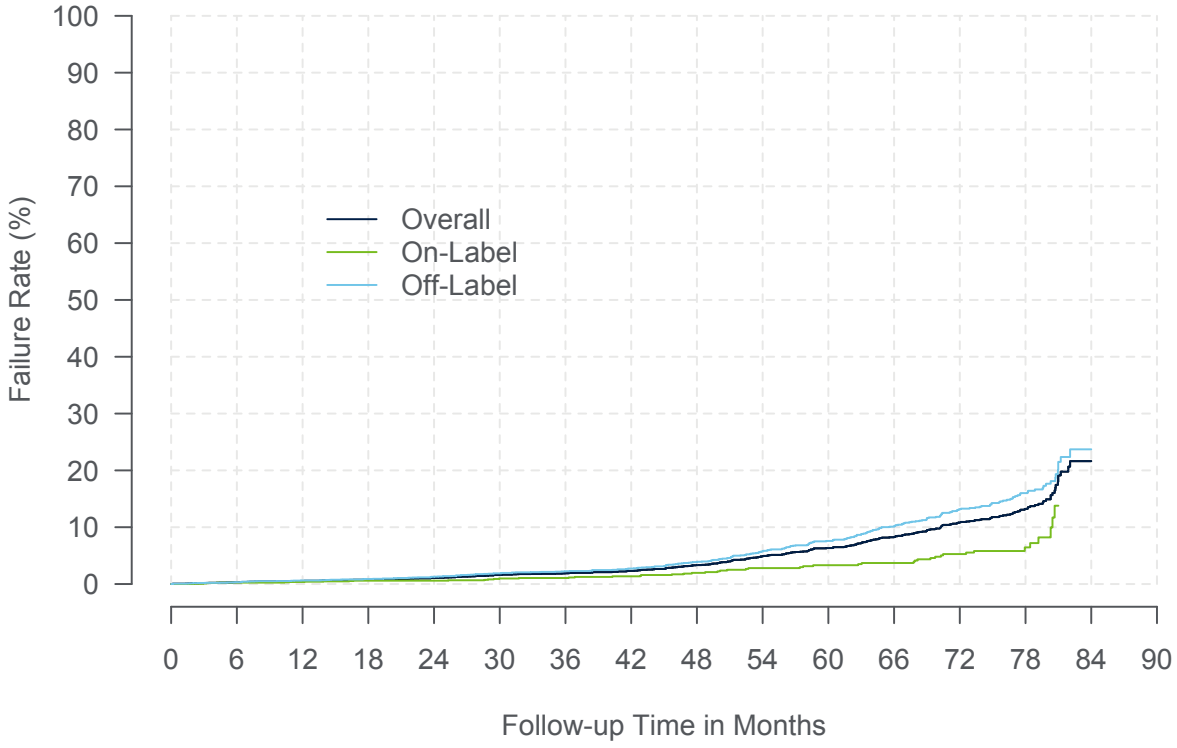


Figure 3.5: SynchroMed II Cumulative Failure (All Therapies)

Table 3.19: Failure Summary Table: All Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 81 Mos	7 Yrs
Overall	Failure	0.5%	1.1%	1.9%	3.3%	6.3%	10.8%	19.1%	21.6%
	Sample Size	5,774	4,643	3,535	2,544	1,795	1,176	140	28
On-Label	Failure	0.4%	0.6%	1.1%	2.0%	3.3%	5.3%	13.8%	
	Sample Size	1,799	1,420	1,048	747	535	370	35	
Off-Label	Failure	0.6%	1.3%	2.3%	3.9%	7.6%	13.2%	21.5%	23.7%
	Sample Size	3,975	3,223	2,487	1,797	1,260	806	105	20

Pain Study Population

A total of 905 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 5,675 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 3.6 and Figure 3.7 respectively.

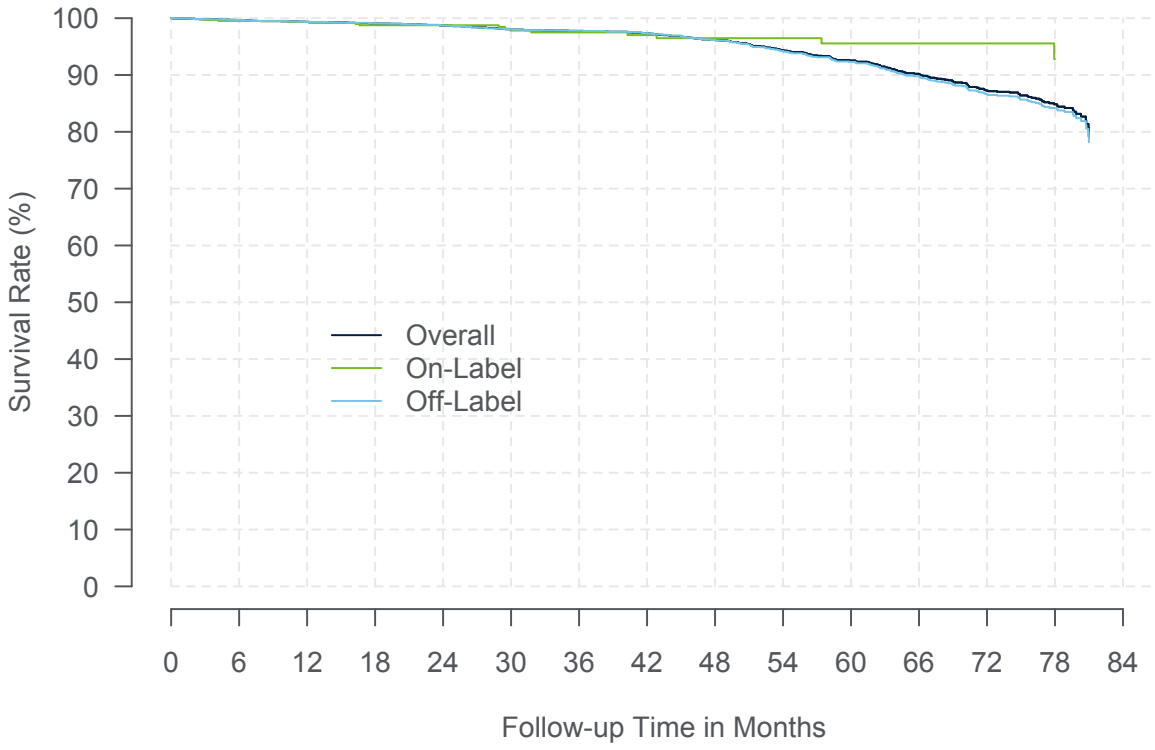


Figure 3.6: SynchroMed II Cumulative Survival (Pain Therapies)

Table 3.20: Survival Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Survival	99.3%	98.7%	97.8%	96.1%	92.5%	87.3%	84.8%	79.1%
	Sample Size	4,257	3,396	2,570	1,819	1,271	816	427	101
On-Label	Survival	99.3%	98.8%	97.5%	96.5%	95.6%	95.6%	92.8%	
	Sample Size	549	384	246	149	99	65	31	
Off-Label	Survival	99.4%	98.7%	97.8%	96.1%	92.3%	86.6%	84.2%	78.2%
	Sample Size	3,708	3,012	2,324	1,670	1,172	751	396	94

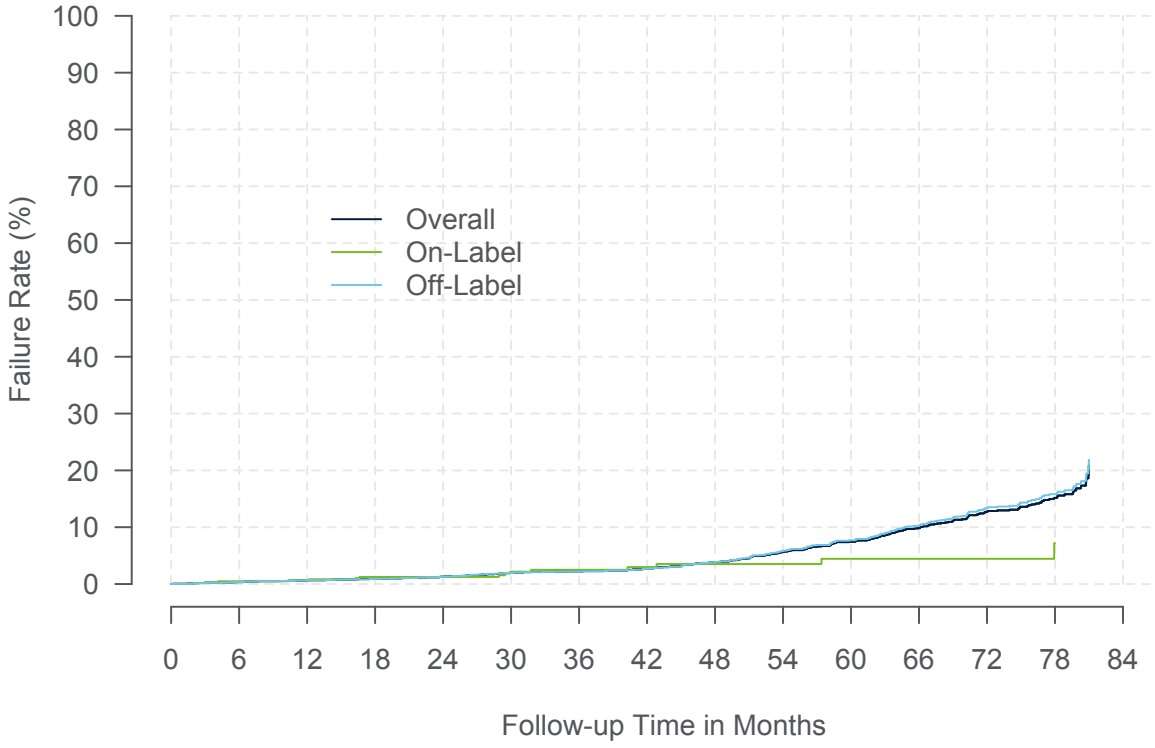


Figure 3.7: SynchroMed II Cumulative Failure (Pain Therapies)

Table 3.21: Failure Summary Table: Pain Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Failure	0.7%	1.3%	2.2%	3.9%	7.5%	12.7%	15.2%	20.9%
	Sample Size	4,257	3,396	2,570	1,819	1,271	816	427	101
On-Label	Failure	0.7%	1.2%	2.5%	3.5%	4.4%	4.4%	7.2%	
	Sample Size	549	384	246	149	99	65	31	
Off-Label	Failure	0.6%	1.3%	2.2%	3.9%	7.7%	13.4%	15.8%	21.8%
	Sample Size	3,708	3,012	2,324	1,670	1,172	751	396	94

Spasticity Study Population

A total of 1,853 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 216 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 3.8 and Figure 3.9 respectively.

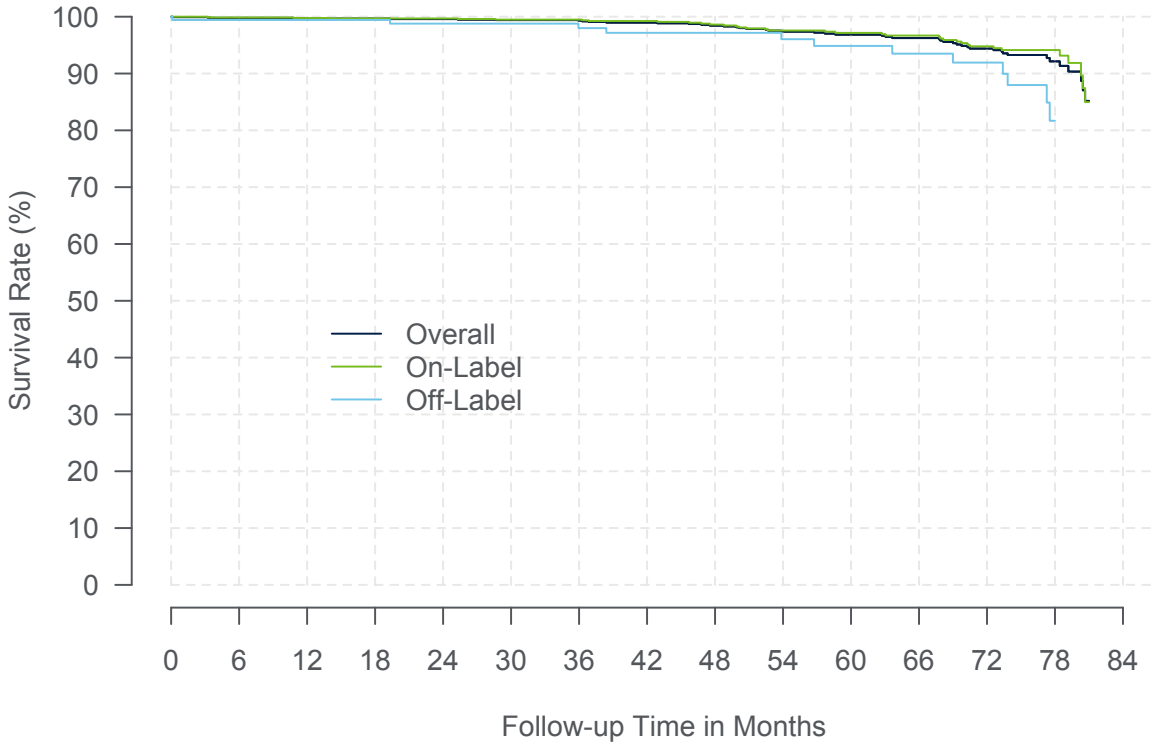


Figure 3.8: SynchroMed II Cumulative Survival (Spasticity Therapies)

Table 3.22: Survival Summary Table: Spasticity Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Survival	99.7%	99.6%	99.3%	98.4%	96.8%	94.4%	92.1%	85.2%
	Sample Size	1,418	1,182	924	695	511	356	131	38
On-Label	Survival	99.8%	99.7%	99.5%	98.6%	97.2%	94.8%	94.1%	85.0%
	Sample Size	1,250	1,036	802	598	436	305	109	28
Off-Label	Survival	99.4%	98.8%	98.0%	97.2%	94.9%	91.9%	81.7%	
	Sample Size	168	146	122	97	75	51	22	

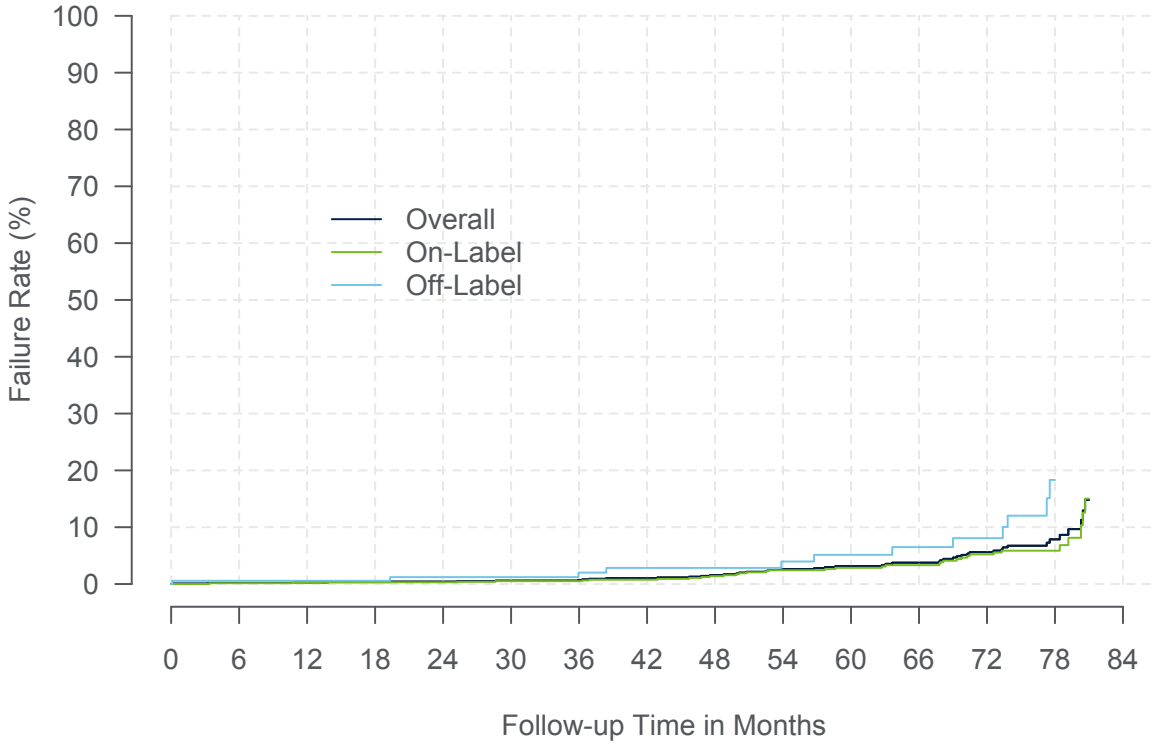


Figure 3.9: SynchroMed II Cumulative Failure (Spasticity Therapies)

Table 3.23: Failure Summary Table: Spasticity Therapies

Category	Time Interval	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	at 78 Mos	at 81 Mos
Overall	Failure	0.3%	0.4%	0.7%	1.6%	3.2%	5.6%	7.9%	14.8%
	Sample Size	1,418	1,182	924	695	511	356	131	38
On-Label	Failure	0.2%	0.3%	0.5%	1.4%	2.8%	5.2%	5.9%	15.0%
	Sample Size	1,250	1,036	802	598	436	305	109	28
Off-Label	Failure	0.6%	1.2%	2.0%	2.8%	5.1%	8.1%	18.3%	
	Sample Size	168	146	122	97	75	51	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 2.2 (95% confidence interval [1.649, 2.986]) times greater risk of pump failure compared to On-Label medication exposure for the entire pump population. The rate of pump failure accelerates in the Off-Label group after 48 months of follow-up. At 81 months of follow-up the survival from

pump failure for On-Label pumps was 86.2% compared to a survival of 78.5% for Off-Label pumps.

- The data represent the reported registry experience with a median follow-up time of 26.1 months. The longer-term data are based on a lower number of pumps and are subject to change as more follow-up data are obtained via the registry. Survival curve truncation or plateaus do not imply that the implanted devices will not be adversely impacted beyond the time points of the current data.
- The On-Label pump group was comprised of 67.2% of pumps with spasticity as the indication (1,853 vs. 905: Spasticity versus Pain pumps respectively). While the Off-Label group consisted of 93.8% of pumps with pain indications (5,675 vs. 216: 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 6-month 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, 2018, there were 9,519 catheters followed in the registry. The total number of catheters was not equal to the total number of pumps (n=10,378) 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 system (DART). The aggregate prospective follow-up time for all catheters was 309,770 months (25,814 years). Table 3.24 provides the number and percentage of catheters by model.

Table 3.24: Targeted Drug Delivery Catheter Counts by Model

Model Name	N (%)
Currently Manufactured[a]	**2,242 (23.6%)**
8780 (US & OUS)	1,094 (11.5%)
8781 (US & OUS)	884 (9.3%)
8731SC (OUS)	264 (2.8%)
Revised Catheters	**1,678 (17.6%)**
Revised Not As Designed[b]	698 (7.3%)
Grafted Not As Designed[c]	472 (5.0%)
Ascenda Revised As Designed[d]	256 (2.7%)
Revised As Designed[e]	252 (2.7%)
No Longer Manufactured	**5,310 (55.8%)**
8709	2,879 (30.3%)
8709SC	1,081 (11.4%)
8711	650 (6.8%)
8731	515 (5.4%)
8703W	185 (1.9%)
Other/Unspecified	**289 (3.0%)**
Total	**9,519 (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] 8780 or 8781 Ascenda catheters repaired with the 8782 or 8784 revision kit.

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

3.5.1 Catheter Events

There were 1,350 product performance-related events with an underlying reported etiology related to catheter function. This includes 1,340 events with a catheter etiology and 10 events with both a catheter and other etiology (including device and non-device etiologies). The majority of the events were catheter occlusion (n=350), catheter dislodgement (n=321), catheter break/cut (n=221), or catheter kink (n=185). Of the 1,350 events, 1,159 were the initial product performance event that affected catheter survival estimates.

The catheter product performance-related events are summarized by model in Table 3.25 to Table 3.35.

Table 3.25: Event Summary Table: 8709

Catheter Event	N
Catheter Dislodgement	94
Catheter Occlusion	79
Catheter Break/Cut	77
Catheter Kink	30
Catheter Disconnection At Pump	20
Catheter Leakage	13
Catheter Related Complication	13
Pump Connector Break/Cut	10
Medical Device Complication	2
Pump Unable To Enter/Withdraw From Catheter Access Port	2
Other[a]	9
Total	**349**

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

Table 3.26: Event Summary Table: 8709SC

Catheter Event	N
Catheter Dislodgement	35
Catheter Occlusion	33
Catheter Break/Cut	32
Catheter Related Complication	9
Catheter Leakage	8
Catheter Kink	6
Catheter Disconnection At Pump	4
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Catheter Damage	2
Medical Device Complication	2
Other[a]	5
Total	**139**

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

Table 3.27: Event Summary Table: 8711

Catheter Event	N
Catheter Occlusion	28
Catheter Break/Cut	19
Catheter Related Complication	14
Catheter Dislodgement	13
Catheter Kink	7
Catheter Leakage	3
Pump Unable To Enter/Withdraw From Catheter Access Port	3
Catheter Disconnection At Pump	2
Other[a]	4
Total	**93**

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

Table 3.28: Event Summary Table: 8731

Catheter Event	N
Catheter Occlusion	23
Catheter Dislodgement	19
Catheter Kink	4
Catheter Related Complication	4
Catheter Break/Cut	2
Catheter Disconnection At Pump	2
Other[a]	3
Total	**57**

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

Table 3.29: Event Summary Table: 8731SC

Catheter Event	N
Catheter Occlusion	10
Catheter Dislodgement	7
Catheter Kink	4
Catheter Related Complication	3
Pump Unable To Enter/Withdraw From Catheter Access Port	2
Other[a]	2
Total	**28**

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

Table 3.30: Event Summary Table: 8780

Catheter Event	N
Catheter Occlusion	29
Catheter Dislodgement	16
Catheter Kink	14
Catheter Break/Cut	7
Catheter Leakage	3
Catheter Disconnection At Pump	2
Catheter Related Complication	2
Other[a]	1
Total	**74**

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

Table 3.31: Event Summary Table: 8781

Catheter Event	N
Catheter Kink	41
Catheter Dislodgement	25
Catheter Occlusion	14
Catheter Break/Cut	5
Catheter Related Complication	4
Catheter Disconnection At Pump	3
Catheter Leakage	3
Other[a]	2
Total	**97**

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

Table 3.32: Event Summary Table: Ascenda Revised As Designed

Catheter Event	N
Catheter Occlusion	6
Catheter Dislodgement	5
Catheter Kink	4
Other[a]	5
Total	**20**

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

Table 3.33: Event Summary Table: Grafted Not As Designed

Catheter Event	N
Catheter Dislodgement	26
Catheter Occlusion	26
Catheter Break/Cut	11
Catheter Kink	7
Catheter Related Complication	7
Catheter Leakage	5
Pump Unable To Enter/Withdraw From Catheter Access Port	4
Other[a]	5
Total	**91**

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

Table 3.34: Event Summary Table: Revised As Designed

Catheter Event	N
Catheter Occlusion	14
Catheter Dislodgement	10
Catheter Kink	4
Catheter Related Complication	3
Catheter Break/Cut	2
Other[a]	3
Total	**36**

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

Table 3.35: Event Summary Table: Revised Not As Designed

Catheter Event	N
Catheter Occlusion	42
Catheter Dislodgement	24
Catheter Break/Cut	16
Catheter Kink	14
Catheter Leakage	6
Catheter Related Complication	6
Pump Unable To Enter/Withdraw From Catheter Access Port	5
Catheter Disconnection At Pump	4
Other[a]	7
Total	**124**

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

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:

- 1,159 had follow-up time cut-off due to product performance-related events.
- 6,038 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.
- 2,322 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.

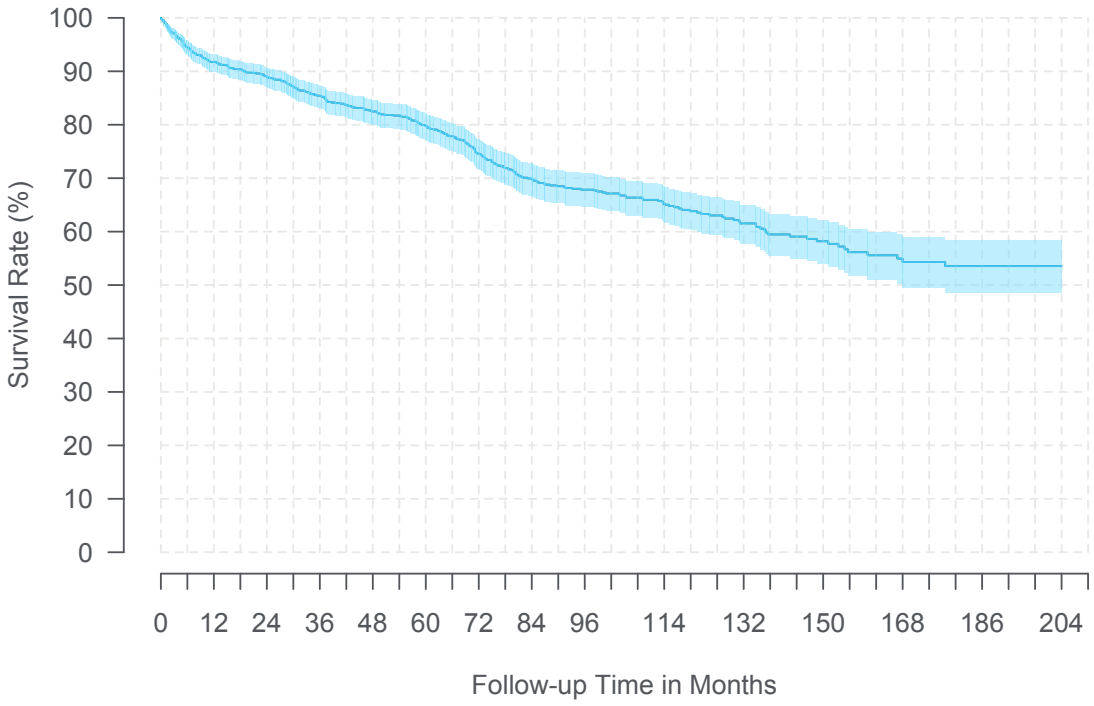
3.5.2 Catheter Survival

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.

Model 8709

Model/Name	8709/InDura
FDA Approval Date	May 1998
Catheters Enrolled	2,879
Catheters Currently Active in Study	199
Device Events	349
Cumulative Months of Follow-up	92,522



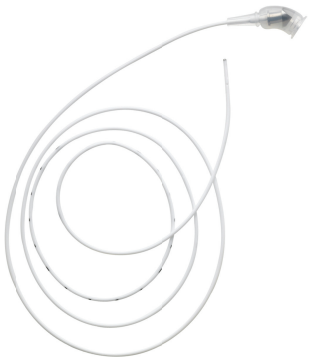
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.8% (90.0%, 93.2%)	89.0% (87.0%, 90.7%)	85.4% (83.2%, 87.4%)	82.5% (80.1%, 84.6%)	79.8% (77.2%, 82.2%)
Sample Size	979	926	865	771	660

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	74.6% (71.7%, 77.3%)	69.9% (66.8%, 72.8%)	67.8% (64.6%, 70.8%)	66.4% (63.0%, 69.5%)	63.8% (60.3%, 67.1%)
Sample Size	565	492	403	314	252

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	61.5% (57.8%, 65.1%)	59.1% (55.0%, 62.9%)	56.1% (51.6%, 60.4%)	54.3% (49.5%, 58.9%)	53.5% (48.5%, 58.3%)
Sample Size	202	145	104	84	64

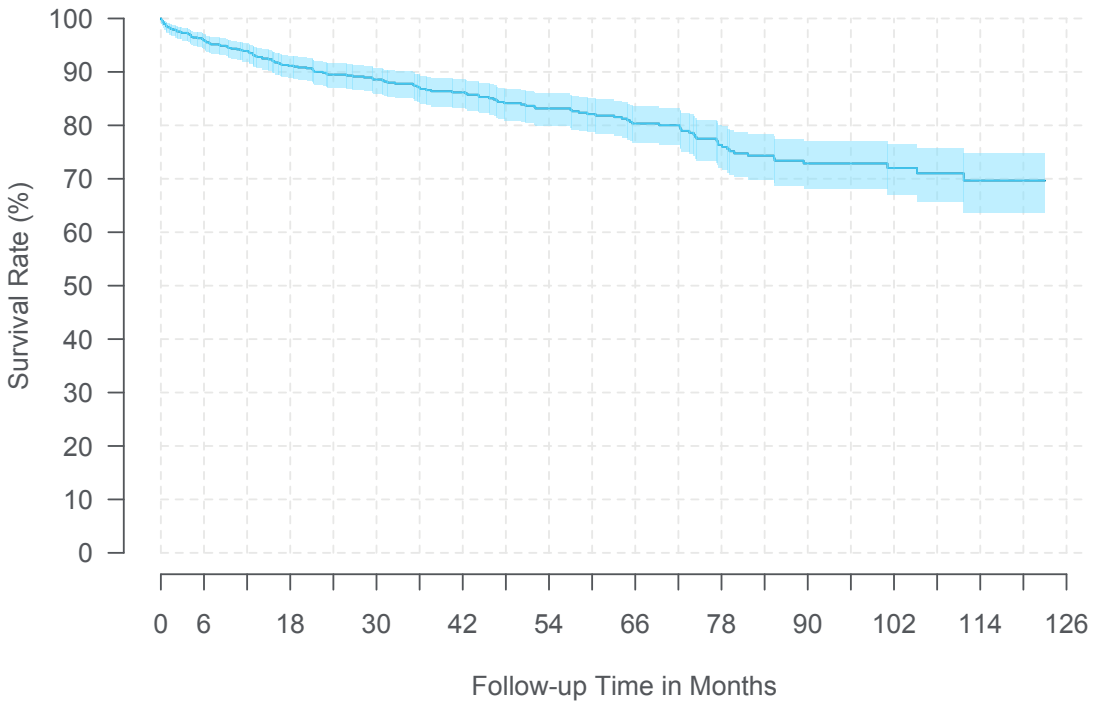
Time Interval	16 Years	17 Years			
Survival (95% CI)	53.5% (48.5%, 58.3%)	53.5% (48.5%, 58.3%)			
Sample Size	44	23			

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



Model 8709SC

Model/Name	8709SC/InDura 1P
FDA Approval Date	March 2006
Catheters Enrolled	1,081
Catheters Currently Active in Study	238
Device Events	139
Cumulative Months of Follow-up	39,966

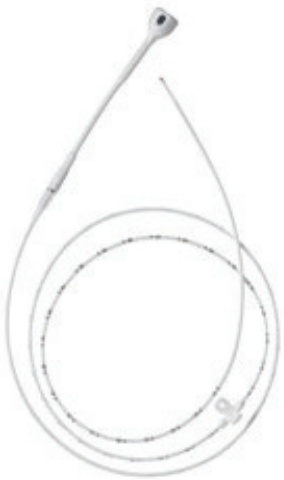


Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.9% (92.0%, 95.4%)	89.5% (87.0%, 91.5%)	87.0% (84.2%, 89.3%)	84.1% (81.0%, 86.8%)	82.1% (78.7%, 85.0%)
Sample Size	664	515	433	359	297

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	80.0% (76.3%, 83.2%)	74.3% (69.8%, 78.3%)	72.9% (68.1%, 77.0%)	71.0% (65.6%, 75.7%)	69.7% (63.7%, 74.9%)
Sample Size	231	165	105	62	24

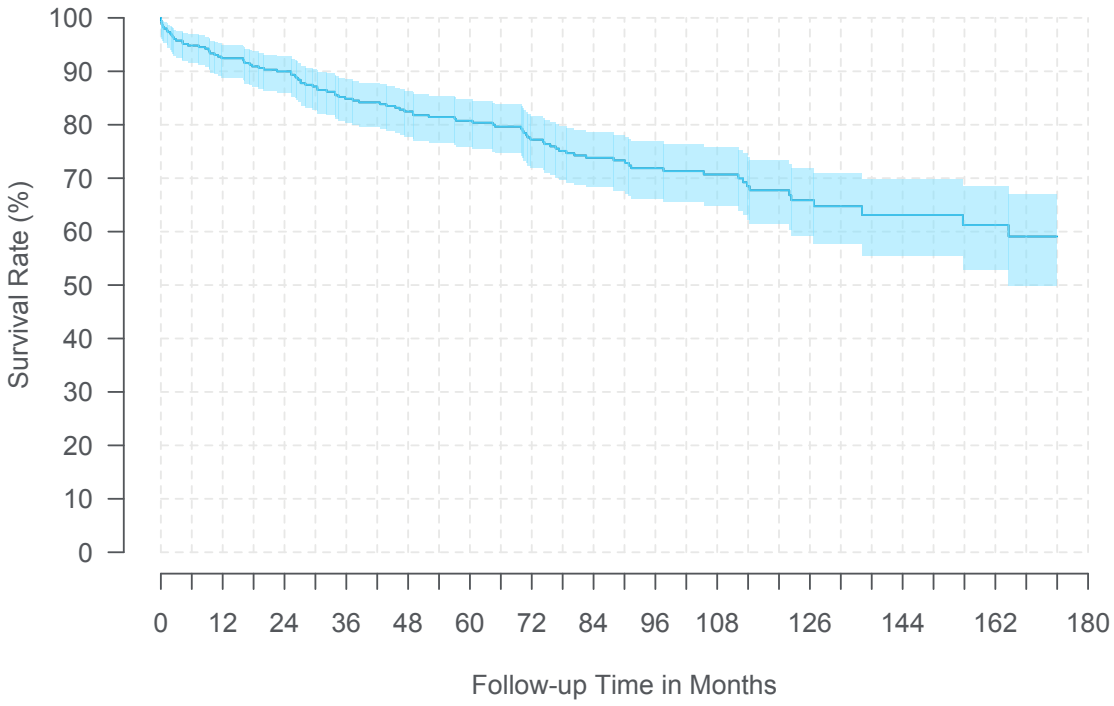
Time Interval	At 123 Months				
Survival (95% CI)	69.7% (63.7%, 74.9%)				
Sample Size	20				

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



Mode 8711

Model/Name	8711/InDura
FDA Approval Date	October 1999
Catheters Enrolled	650
Catheters Currently Active in Study	119
Device Events	93
Cumulative Months of Follow-up	28,560



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

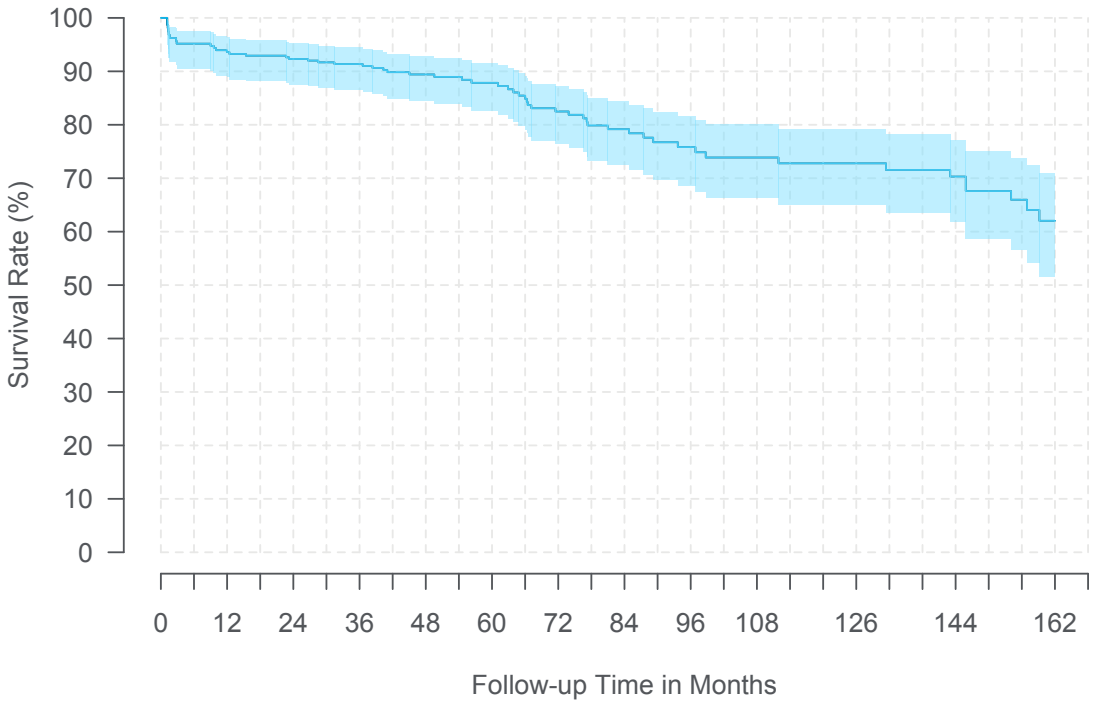
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	77.2% (72.0%, 81.6%)	73.8% (68.3%, 78.6%)	71.9% (66.1%, 76.8%)	70.7% (64.8%, 75.8%)	67.7% (61.3%, 73.3%)
Sample Size	187	166	132	105	77

Time Interval	11 Years	12 Years	13 Years	14 Years	At 174 Months
Survival (95% CI)	64.8% (57.7%, 70.9%)	63.1% (55.5%, 69.8%)	61.2% (52.9%, 68.6%)	59.1% (49.9%, 67.1%)	59.1% (49.9%, 67.1%)
Sample Size	43	36	32	26	23

Specification: 711	
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

Model 8731

Model/Name	8731
FDA Approval Date	October 2002
Catheters Enrolled	515
Catheters Currently Active in Study	59
Device Events	57
Cumulative Months of Follow-up	22,466



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.6% (88.9%, 96.4%)	92.3% (87.6%, 95.3%)	91.4% (86.6%, 94.5%)	89.4% (84.5%, 92.9%)	87.8% (82.6%, 91.6%)
Sample Size	262	306	253	196	149

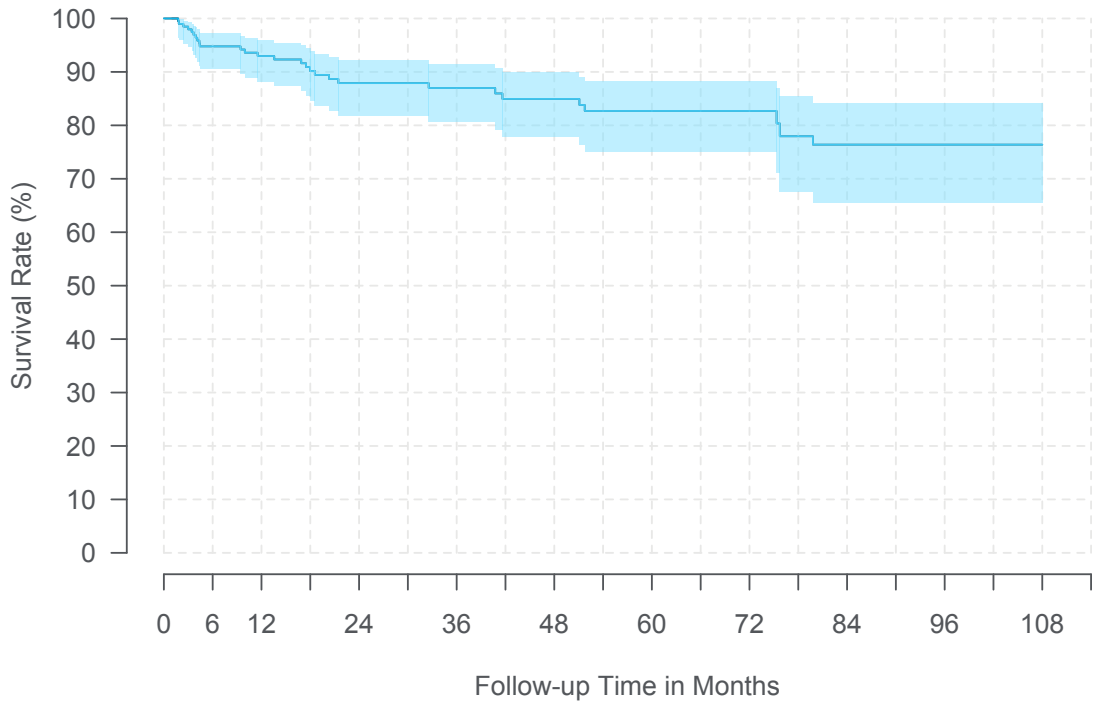
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	82.5% (76.4%, 87.2%)	79.2% (72.6%, 84.4%)	75.8% (68.6%, 81.6%)	73.9% (66.3%, 80.0%)	72.8% (65.0%, 79.2%)
Sample Size	134	105	80	68	63

Time Interval	11 Years	12 Years	13 Years	At 162 Months	
Survival (95% CI)	71.5% (63.4%, 78.2%)	70.3% (61.9%, 77.2%)	66.0% (56.6%, 73.8%)	62.0% (51.6%, 70.9%)	
Sample Size	58	54	35	26	

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

Model 8731SC

Model/Name	8731SC
FDA Approval Date	March 2006
Catheters Enrolled	264
Catheters Currently Active in Study	95
Device Events	28
Cumulative Months of Follow-up	9,154



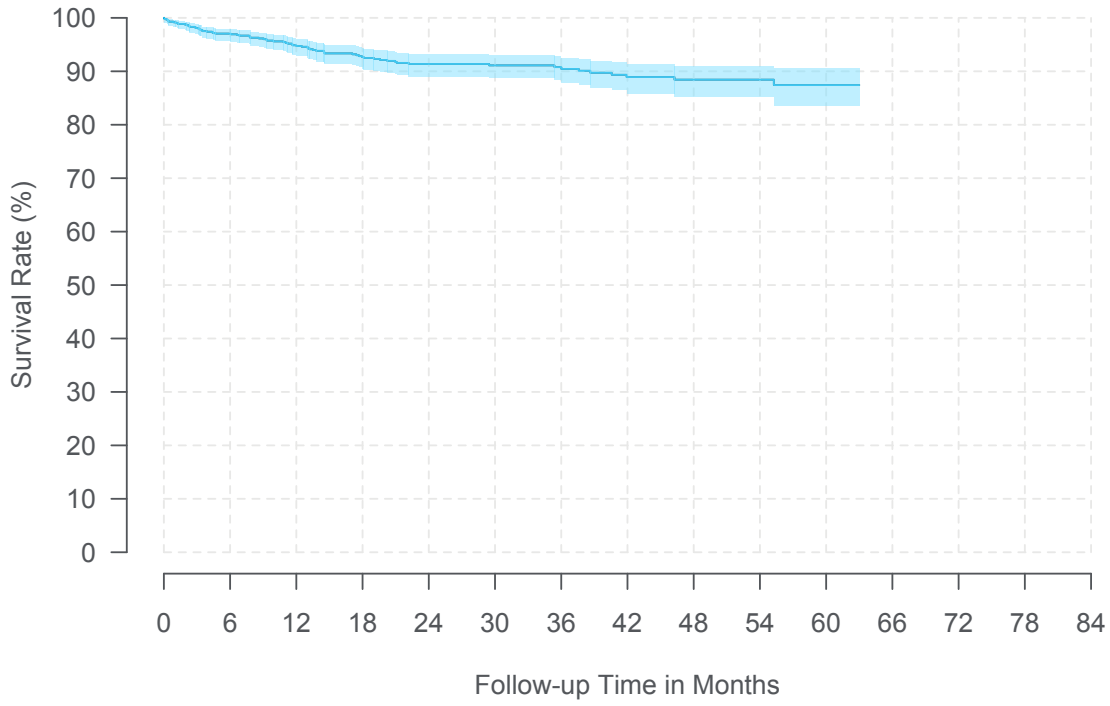
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	93.0% (88.2%, 95.9%)	87.9% (81.8%, 92.1%)	87.0% (80.6%, 91.4%)	84.9% (77.9%, 89.9%)	82.7% (75.0%, 88.2%)
Sample Size	147	107	92	77	63

Time Interval	6 Years	7 Years	8 Years	9 Years	
Survival (95% CI)	82.7% (75.0%, 88.2%)	76.4% (65.6%, 84.2%)	76.4% (65.6%, 84.2%)	76.4% (65.6%, 84.2%)	
Sample Size	40	50	33	20	

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

Model 8780

Model/Name	8780/Ascenda
FDA Approval Date	May 2012
Catheters Enrolled	1,094
Catheters Currently Active in Study	688
Device Events	74
Cumulative Months of Follow-up	24,878



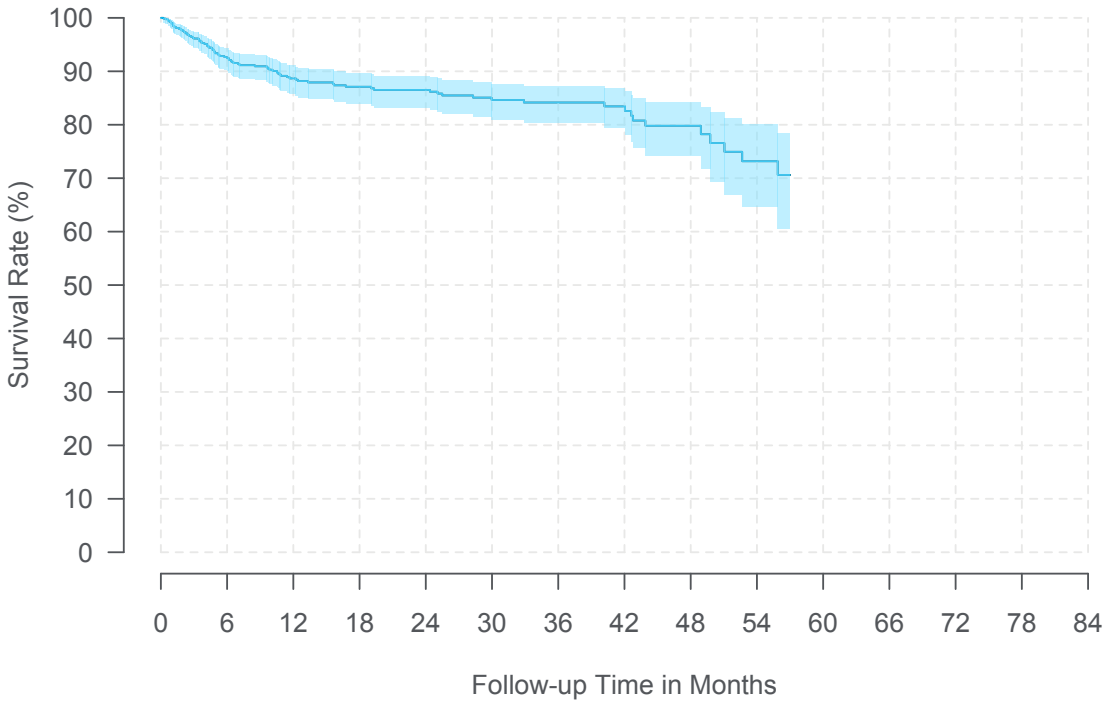
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	94.7% (93.0%, 96.1%)	91.4% (89.1%, 93.2%)	90.8% (88.3%, 92.8%)	88.4% (85.2%, 91.0%)	87.4% (83.5%, 90.5%)
Sample Size	647	432	267	164	48

Time Interval	At 63 Months
Survival (95% CI)	87.4% (83.5%, 90.5%)
Sample Size	33

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

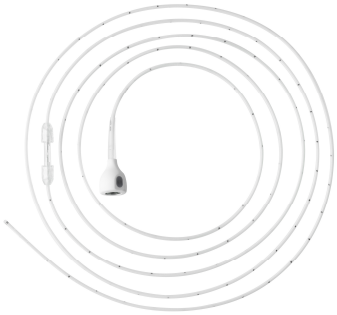
Model 8781

Model/Name	8781/Ascenda
FDA Approval Date	May 2012
Catheters Enrolled	884
Catheters Currently Active in Study	394
Device Events	97
Cumulative Months of Follow-up	15,247



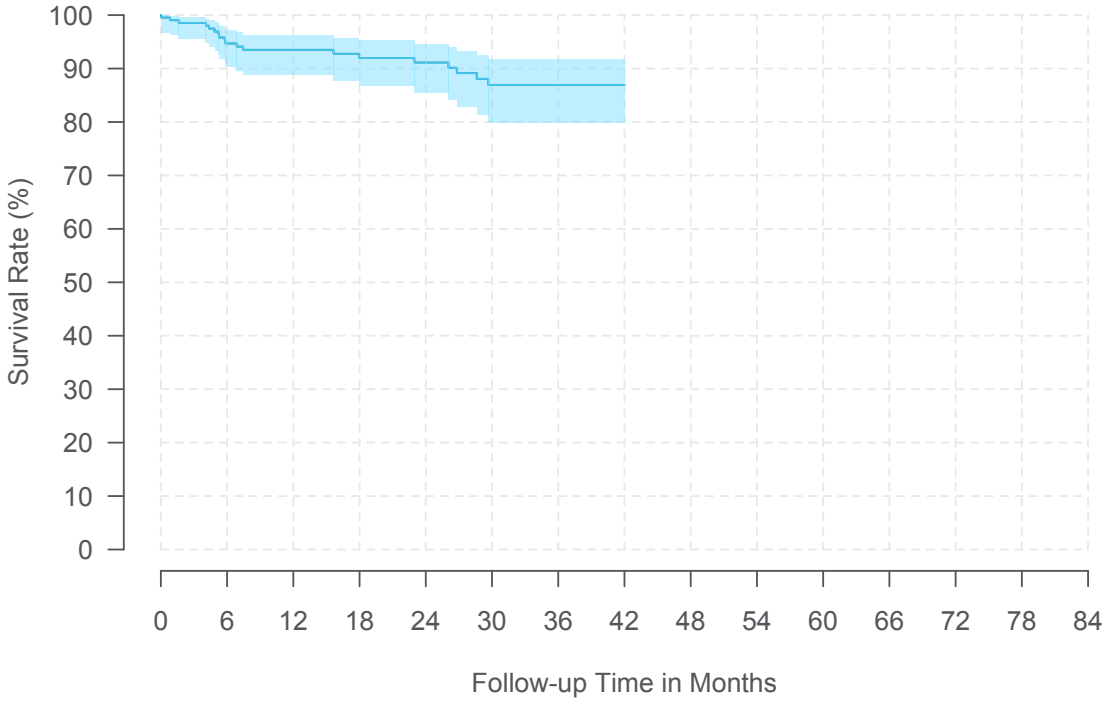
Time Interval	1 Year	2 Years	3 Years	4 Years	At 57 Months
Survival (95% CI)	88.7% (85.7%, 91.0%)	86.5% (83.2%, 89.2%)	84.2% (80.4%, 87.3%)	79.8% (74.3%, 84.3%)	70.6% (60.6%, 78.5%)
Sample Size	359	258	151	53	25

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



Ascenda Revised As Designed

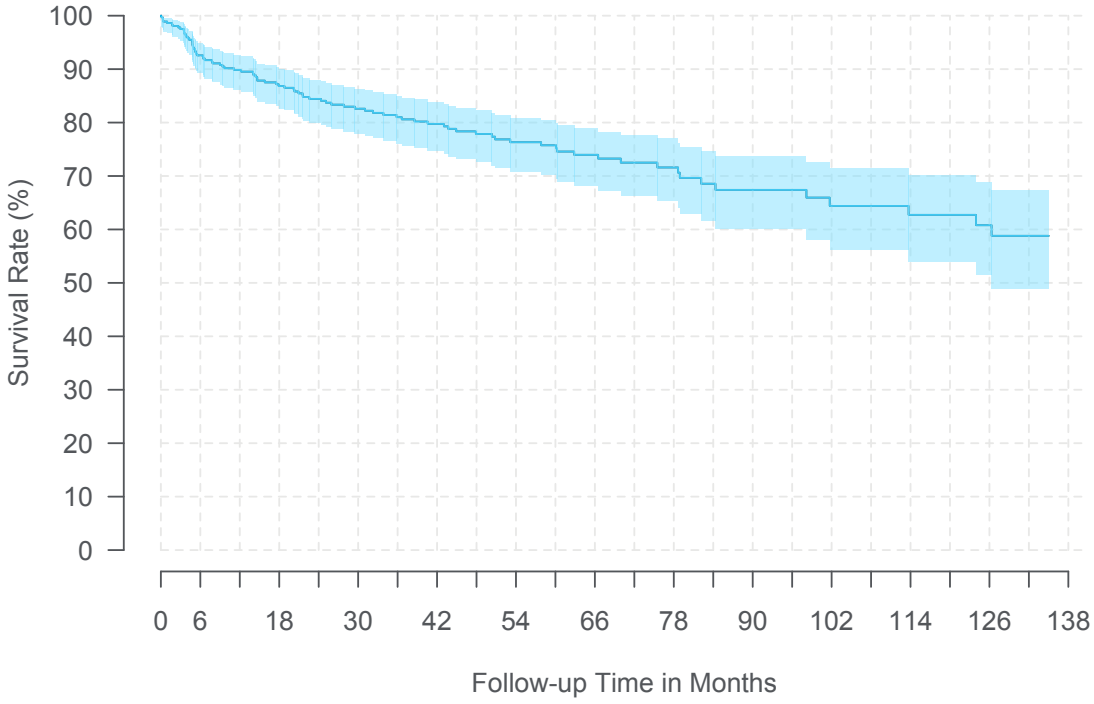
Model/Name	Ascenda Revised As Designed
FDA Approval Date	May 2012
Catheters Enrolled	256
Catheters Currently Active in Study	126
Device Events	20
Cumulative Months of Follow-up	4,863



Time Interval	1 Year	2 Years	3 Years	At 42 Months
Survival (95% CI)	93.5% (88.8%, 96.3%)	91.1% (85.6%, 94.6%)	86.9% (79.8%, 91.7%)	86.9% (79.8%, 91.7%)
Sample Size	136	99	56	30

Grafted Not As Designed

Model/Name	Grafted Not As Designed
FDA Approval Date	NA
Catheters Enrolled	472
Catheters Currently Active in Study	147
Device Events	91
Cumulative Months of Follow-up	19,390



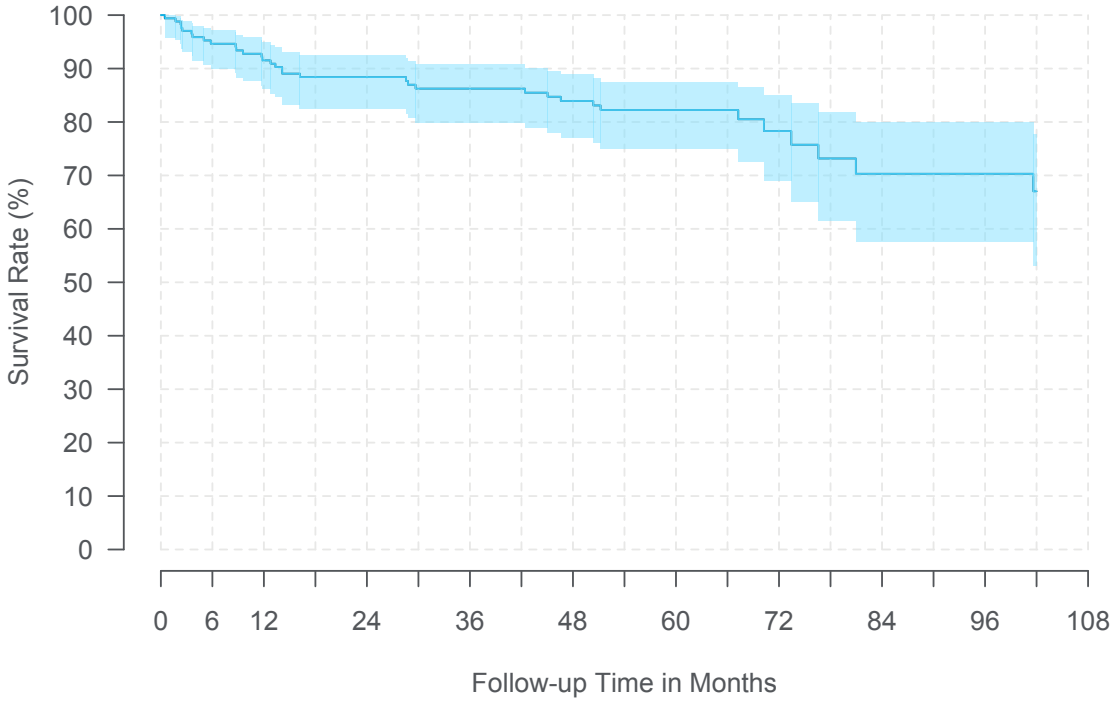
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	89.8% (86.1%, 92.6%)	84.4% (80.0%, 88.0%)	81.0% (76.2%, 85.0%)	77.9% (72.6%, 82.2%)	75.8% (70.2%, 80.4%)
Sample Size	282	235	199	159	128

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	72.5% (66.4%, 77.7%)	68.6% (61.5%, 74.6%)	67.4% (60.1%, 73.7%)	64.4% (56.2%, 71.5%)	62.7% (54.0%, 70.2%)
Sample Size	86	59	46	41	34

Time Interval	11 Years	At 135 Months			
Survival (95% CI)	58.8% (48.9%, 67.4%)	58.8% (48.9%, 67.4%)			
Sample Size	23	21			

Revised As Designed

Model/Name	Revised As Designed
FDA Approval Date	October 2002
Catheters Enrolled	252
Catheters Currently Active in Study	86
Device Events	36
Cumulative Months of Follow-up	9,567

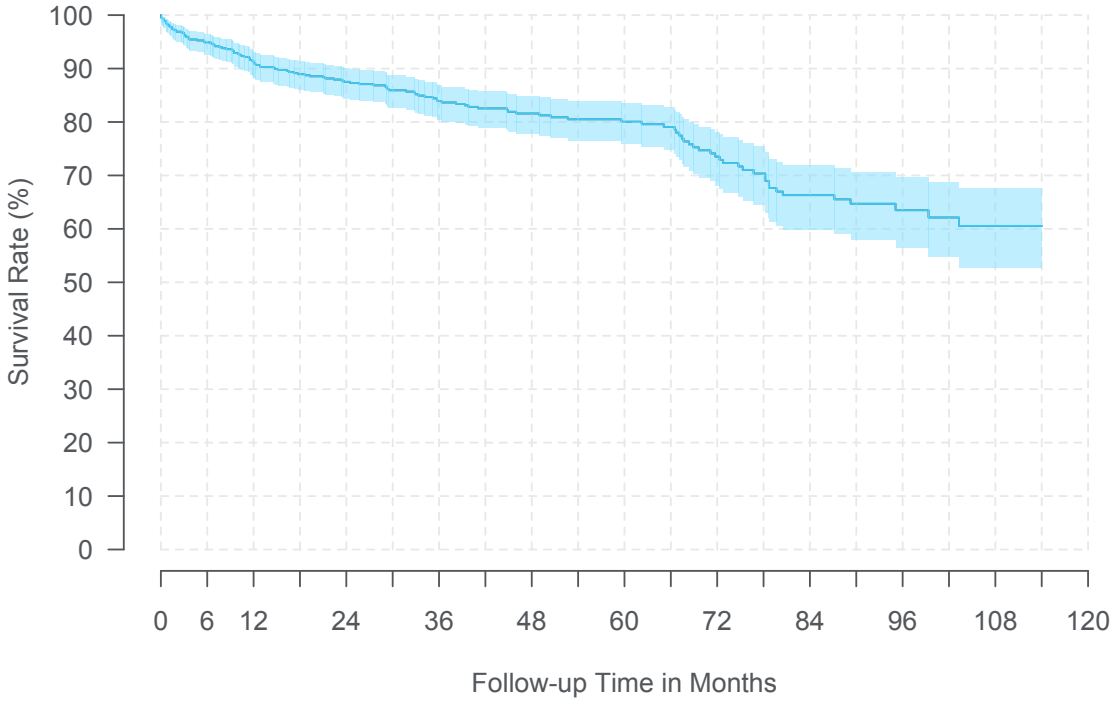


Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.5% (86.1%, 94.9%)	88.4% (82.4%, 92.4%)	86.2% (79.8%, 90.7%)	83.9% (77.1%, 88.9%)	82.2% (75.1%, 87.5%)
Sample Size	149	129	116	102	73

Time Interval	6 Years	7 Years	8 Years	At 102 Months	
Survival (95% CI)	78.3% (69.0%, 85.1%)	70.3% (57.5%, 79.9%)	70.3% (57.5%, 79.9%)	67.0% (53.0%, 77.7%)	
Sample Size	32	22	21	20	

Revised Not As Designed

Model/Name	Revised Not As Designed
FDA Approval Date	NA
Catheters Enrolled	698
Catheters Currently Active in Study	193
Device Events	124
Cumulative Months of Follow-up	27,867



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.0% (88.3%, 93.2%)	87.5% (84.4%, 90.0%)	83.9% (80.4%, 86.9%)	81.6% (77.8%, 84.8%)	80.1% (76.0%, 83.5%)
Sample Size	488	412	322	244	179

Time Interval	6 Years	7 Years	8 Years	9 Years	At 114 Months
Survival (95% CI)	73.5% (68.2%, 78.1%)	66.3% (59.9%, 72.0%)	63.5% (56.5%, 69.7%)	60.6% (52.7%, 67.5%)	60.6% (52.7%, 67.5%)
Sample Size	122	92	50	28	23

3.5.3 Catheter Survival Summary

Table 3.36: Targeted Drug Delivery Catheter Characteristics

Model Name	FDA Approval Date	Catheters Enrolled	Catheters Active	Device Events	Cumulative Follow-up Months
8709	May 1998	2,879	199	349	92,522
8709SC	March 2006	1,081	238	139	39,966
8711	October 1999	650	119	93	28,560
8731	October 2002	515	59	57	22,466
8731SC	March 2006	264	95	28	9,154
8780	May 2012	1,094	688	74	24,878
8781	May 2012	884	394	97	15,247
Ascenda Revised As Designed	May 2012	256	126	20	4,863
Grafted Not As Designed	NA	472	147	91	19,390
Revised As Designed	October 2002	252	86	36	9,567
Revised Not As Designed	NA	698	193	124	27,867

Table 3.37: Targeted Drug Delivery Catheter Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
8709	91.8% (90.0%, 93.2%)	89.0% (87.0%, 90.7%)	85.4% (83.2%, 87.4%)	82.5% (80.1%, 84.6%)	79.8% (77.2%, 82.2%)
8709SC	93.9% (92.0%, 95.4%)	89.5% (87.0%, 91.5%)	87.0% (84.2%, 89.3%)	84.1% (81.0%, 86.8%)	82.1% (78.7%, 85.0%)
8711	92.4% (88.8%, 94.9%)	90.0% (86.0%, 92.9%)	84.9% (80.4%, 88.4%)	82.5% (77.7%, 86.3%)	80.7% (75.8%, 84.7%)
8731	93.6% (88.9%, 96.4%)	92.3% (87.6%, 95.3%)	91.4% (86.6%, 94.5%)	89.4% (84.5%, 92.9%)	87.8% (82.6%, 91.6%)
8731SC	93.0% (88.2%, 95.9%)	87.9% (81.8%, 92.1%)	87.0% (80.6%, 91.4%)	84.9% (77.9%, 89.9%)	82.7% (75.0%, 88.2%)
8780	94.7% (93.0%, 96.1%)	91.4% (89.1%, 93.2%)	90.8% (88.3%, 92.8%)	88.4% (85.2%, 91.0%)	87.4% (83.5%, 90.5%)
8781	88.7% (85.7%, 91.0%)	86.5% (83.2%, 89.2%)	84.2% (80.4%, 87.3%)	79.8% (74.3%, 84.3%)	
Ascenda Revised As Designed	93.5% (88.8%, 96.3%)	91.1% (85.6%, 94.6%)	86.9% (79.8%, 91.7%)		
Grafted Not As Designed	89.8% (86.1%, 92.6%)	84.4% (80.0%, 88.0%)	81.0% (76.2%, 85.0%)	77.9% (72.6%, 82.2%)	75.8% (70.2%, 80.4%)
Revised As Designed	91.5% (86.1%, 94.9%)	88.4% (82.4%, 92.4%)	86.2% (79.8%, 90.7%)	83.9% (77.1%, 88.9%)	82.2% (75.1%, 87.5%)
Revised Not As Designed	91.0% (88.3%, 93.2%)	87.5% (84.4%, 90.0%)	83.9% (80.4%, 86.9%)	81.6% (77.8%, 84.8%)	80.1% (76.0%, 83.5%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
8709	74.6% (71.7%, 77.3%)	69.9% (66.8%, 72.8%)	67.8% (64.6%, 70.8%)	66.4% (63.0%, 69.5%)	63.8% (60.3%, 67.1%)
8709SC	80.0% (76.3%, 83.2%)	74.3% (69.8%, 78.3%)	72.9% (68.1%, 77.0%)	71.0% (65.6%, 75.7%)	69.7% (63.7%, 74.9%)
8711	77.2% (72.0%, 81.6%)	73.8% (68.3%, 78.6%)	71.9% (66.1%, 76.8%)	70.7% (64.8%, 75.8%)	67.7% (61.3%, 73.3%)
8731	82.5% (76.4%, 87.2%)	79.2% (72.6%, 84.4%)	75.8% (68.6%, 81.6%)	73.9% (66.3%, 80.0%)	72.8% (65.0%, 79.2%)
8731SC	82.7% (75.0%, 88.2%)	76.4% (65.6%, 84.2%)	76.4% (65.6%, 84.2%)	76.4% (65.6%, 84.2%)	
8780					
8781					
Ascenda Revised As Designed					
Grafted Not As Designed	72.5% (66.4%, 77.7%)	68.6% (61.5%, 74.6%)	67.4% (60.1%, 73.7%)	64.4% (56.2%, 71.5%)	62.7% (54.0%, 70.2%)
Revised As Designed	78.3% (69.0%, 85.1%)	70.3% (57.5%, 79.9%)	70.3% (57.5%, 79.9%)		
Revised Not As Designed	73.5% (68.2%, 78.1%)	66.3% (59.9%, 72.0%)	63.5% (56.5%, 69.7%)	60.6% (52.7%, 67.5%)	

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
8709	61.5% (57.8%, 65.1%)	59.1% (55.0%, 62.9%)	56.1% (51.6%, 60.4%)	54.3% (49.5%, 58.9%)	53.5% (48.5%, 58.3%)
8709SC					
8711	64.8% (57.7%, 70.9%)	63.1% (55.5%, 69.8%)	61.2% (52.9%, 68.6%)	59.1% (49.9%, 67.1%)	
8731	71.5% (63.4%, 78.2%)	70.3% (61.9%, 77.2%)	66.0% (56.6%, 73.8%)		
8731SC					
8780					
8781					
Ascenda Revised As Designed					
Grafted Not As Designed	58.8% (48.9%, 67.4%)				
Revised As Designed					
Revised Not As Designed					

Model Name	16 Years	17 Years			
8709	53.5% (48.5%, 58.3%)	53.5% (48.5%, 58.3%)			
8709SC					
8711					
8731					
8731SC					
8780					
8781					
Ascenda Revised As Designed					
Grafted Not As Designed					
Revised As Designed					
Revised Not As Designed					

4 Spinal Cord Stimulation Systems

4.1 Study Participants

4.1.1 Centers

In this section, 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, 2018. Eighty-two centers in North America, Europe and South America, have enrolled and contributed patients to the spinal cord stimulation systems section of this report.

4.1.2 Patients

Of the 5,287 spinal cord stimulation patients enrolled, 45.4% were implanted for the treatment of failed back pain, 43.4% were implanted for the treatment of other primary indications, 10.6% were implanted for the treatment of CRPS, and 0.7% were implanted for indications that were not specified in the database (see Figure 4.1 and Table 4.1).

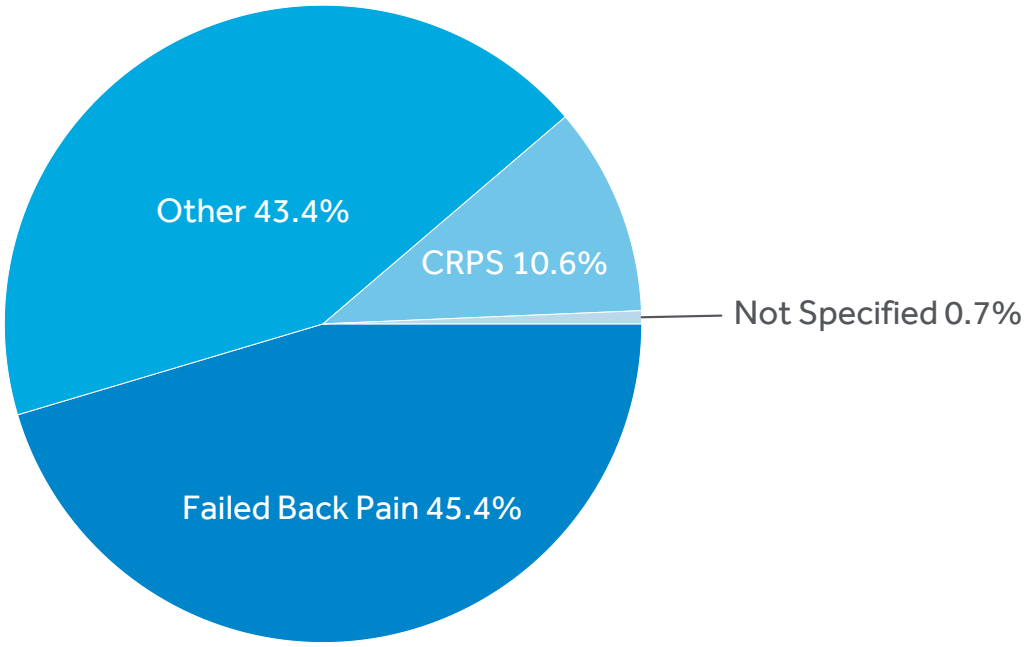


Figure 4.1: Spinal Cord Stimulation Primary Treatment Indications

Table 4.1: Spinal Cord Stimulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Failed Back Pain	**2,400 (45.39%)**
Post Laminectomy Pain	862 (16.30%)
Failed Back Surgery Syndrome (FBSS)	795 (15.04%)
Combination back and leg pain	623 (11.78%)
Multiple Back Operations	86 (1.63%)
Arachnoiditis	22 (0.42%)
Unsuccessful Disc Surgery	12 (0.23%)
Other Primary Indication	**2,292 (43.35%)**
Other chronic pain	823 (15.57%)
Radicular Pain Syndrome	705 (13.33%)
Degenerative Disc Disease	226 (4.27%)
Cervical pain	64 (1.21%)
Traumatic nerve injury	39 (0.74%)
Diabetic neuropathy	32 (0.61%)
Post Herpetic Neuralgia	17 (0.32%)
Chronic cluster headache	16 (0.30%)
Facial pain	7 (0.13%)
Angina	6 (0.11%)
Epidural Fibrosis	4 (0.08%)
Post herniorrhaphy pain	3 (0.06%)
Other Secondary Indication	350 (6.62%)
CRPS	**560 (10.59%)**
CRPS I	435 (8.23%)
CRPS II	125 (2.36%)
Not Specified	**35 (0.66%)**
Total Patients	**5,287 (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).

4.2 Event Summary

There were 1,382 product performance events reported between June 2004 and October 31, 2018, in patients with spinal cord stimulation systems. These events represent 34.9% of the total reported events (1,382/3,959), occured in 661 of the 5,287 (12.5%) total patients enrolled,

and are presented graphically within this report (e.g. events per patient years as well as survival curves). In addition, there were 2,571 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=6).

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 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 176 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. 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.

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 (%)[b]
RPA Determination	**3**	**0.03**	**3 (0.06%)**
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%)
Physician's Determination	**1,379**	**12.83**	**659 (12.46%)**
Lead Migration/Dislodgement	620	5.77	330 (6.24%)
High Impedance	363	3.38	163 (3.08%)
Lead Fracture	79	0.73	53 (1.00%)
Neurostimulator Unable To Recharge[d]	66	0.61	62 (1.17%)
Device Malfunction[e]	54	0.50	51 (0.96%)
Device Stimulation Issue[f]	49	0.46	28 (0.53%)
Low Impedance	43	0.40	18 (0.34%)
Device Breakage[g]	18	0.17	18 (0.34%)
Extension Fracture	17	0.16	11 (0.21%)
Medical Device Complication[h]	14	0.13	9 (0.17%)
Device Lead Damage	7	0.07	5 (0.09%)
Extension Migration	7	0.07	5 (0.09%)
Antenna Cable Breakage	5	0.05	5 (0.09%)
Device Connection Issue	5	0.05	3 (0.06%)
Device Difficult To Use	5	0.05	4 (0.08%)
Device Telemetry Issue	5	0.05	5 (0.09%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%)[b]
Device Failure[i]	4	0.04	3 (0.06%)
Device Electrical Impedance Issue	3	0.03	3 (0.06%)
Neurostimulator Migration	3	0.03	3 (0.06%)
Therapeutic Product Ineffective	3	0.03	2 (0.04%)
Device Battery Issue	2	0.02	2 (0.04%)
Device Loosening	2	0.02	2 (0.04%)
Inadequate Lead Connection	2	0.02	1 (0.02%)
Device Kink	1	0.01	1 (0.02%)
Lead Insulation Failure	1	0.01	1 (0.02%)
Medical Device Site Warmth	1	0.01	1 (0.02%)
Total	**1,382**	**12.85**	**661 (12.50%)**

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

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

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

[d] There were a total of 3,403 patients that used rechargeable SCS neurostimulators in the registry. A total of 1.4% (62/3,403) of patients with a rechargeable SCS neurostimulator experienced a neurostimulator unable to recharge product performance event.

[e] Device malfunction includes 12 recharging malfunctions, 8 malfunctioning programmer, 5 stimulator turning off and on, 4 suspected dysfunction, 5 antenna malfunctions, 3 neurostimulator malfunctions, 2 contacts not working, 2 inability to turn neurostimulator on, 3 events for non-functional lead electrodes, 2 device shut off, 1 programmer reporting error message, 1 issue with INS clock, 1 stimulator error message, 1 SCS stopped abruptly, 1 extension stuck in neurostimulator, 1 patient reported warming of neurostimulator during MRI, 1 generator reporting inconsistent time usage, and 1 recharging cable malfunction.

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

[g] Device breakage includes 6 broken charger belts, 5 broken charger, 3 broken patient programmers, 1 broken recharger cord, 1 frayed cord to charger antenna, 1 broken recharger strap, and 1 frayed wire to charger.

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

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

A total of 1,089 (78.8%) of the 1,382 product performance events were related to the lead, 84 (6.1%) were related to "other component", 61 (4.4%) were related to the neurostimulator, 49

(3.5%) were related to "multiple etiologies" (which includes events where at least one device and one non-device etiology was indicated), 38 (2.7%) were related to recharging process, 36 (2.6%) were related to the extension, 10 (0.7%) were related to programming/stimulation, 6 (0.4%) were related to incisional site/device tract, 5 (0.4%) were related to surgery/anesthesia, 3 (0.2%) were related to "other etiology", and 1 (0.1%) was related to MRI. Relatedness is determined by the physician.

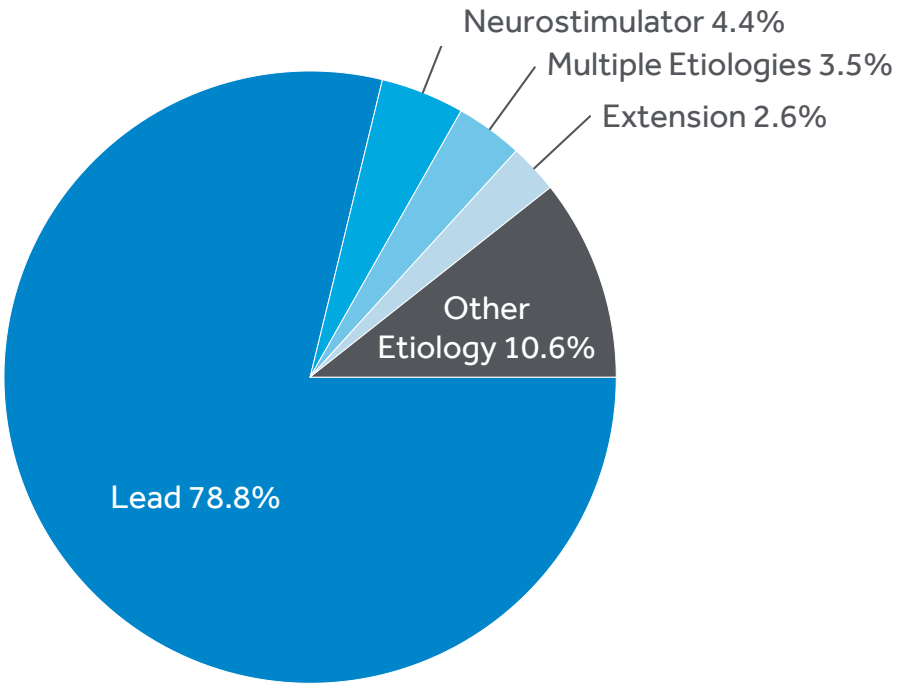


Figure 4.2: Spinal Cord Stimulation System Product Performance Events by Relatedness

Table 4.3 and Table 4.4 describe the interventions taken for reported impedance events. In 20.4% and 11.6% of the high and low impedance events, the action taken was a surgical intervention. However, impedance could be used as a diagnostic measurement and may not result in any intervention or clinical impact. The majority of events required no intervention or device reprogramming only (78.0% for high impedance and 88.3% for low impedance). All events are reflected in lead survival curves.

Table 4.3: Spinal Cord Stimulation System High Impedance Event by Last Intervention

Intervention	N (%) of High Impedance Events
Reprogramming	181 (49.9%)
No Action Taken	102 (28.1%)
Surgical Intervention	74 (20.4%)
Therapy Suspended	6 (1.7%)
Total High Impedance Events	**363 (100%)**

Table 4.4: Spinal Cord Stimulation System Low Impedance Event by Last Intervention

Intervention	N (%) of Low Impedance Events
Reprogramming	25 (58.1%)
No Action Taken	13 (30.2%)
Surgical Intervention	5 (11.6%)
Total Low Impedance Events	**43 (100%)**

4.2.2 Non-Product Performance Events

Adverse events and device events that were not related to a product performance event are categorized in Table 4.5 by event group term. These events do not include deaths (see Section 4.2.3) or normal battery depletions. As explained in the Methodology section of this report, this registry's event reporting has evolved over time. Therefore, the event counts are strictly the sum of the events collected up to the October 31, 2018 data cut-off. **All 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 System Non-Product Performance Events

Non-Product Performance Events	Event Counts
Device issues	**740**
Device Stimulation Issue	341
Neurostimulator Unable To Recharge	216
Device Battery Issue	48
Neurostimulator Migration	48
Neurostimulator Inversion	25
Device Malfunction	23
No Anomaly Found By RPA	8
Device Inappropriate Shock Delivery	7
Device Extrusion	6
Other[f]	18

...continued

Non-Product Performance Events	Event Counts
Therapeutic and nontherapeutic effects (excluding toxicity)	**582**
Therapeutic Product Ineffective	333
Therapeutic Response Decreased	155
Therapy Non-Responder	56
Inadequate Analgesia	33
Other[f]	5
Complications associated with device	**419**
Medical Device Site Pain	260
Medical Device Discomfort	37
Medical Device Site Extravasation	25
Medical Device Site Erythema	21
Medical Device Site Erosion	13
Medical Device Site Burn	7
Medical Device Site Irritation	7
Medical Device Site Swelling	7
Medical Device Complication	5
Medical Device Site Haematoma	5
Medical Device Site Inflammation	5
Other[f]	27
Infections - pathogen unspecified	**165**
Medical Device Site Infection	109
Wound Infection	36
Infection	14
Other[f]	6
General system disorders NEC	**148**
Pain	129
No Anomaly Found By RPA	11
Other[f]	8
Musculoskeletal and connective tissue disorders NEC	**117**
Back Pain	44
Pain In Extremity	43
Musculoskeletal Pain	16
Musculoskeletal Chest Pain	8
Other[f]	6
Neurological disorders NEC	**90**
Paraesthesia	50
Sensory Disturbance	9
Cerebrospinal Fluid Leakage	7
Burning Sensation	6
Hypoaesthesia	6
Other[f]	12

...continued

Non-Product Performance Events	Event Counts
Medication errors and other product use errors and issues	**86**
Device Difficult To Use	63
Device Use Error	17
Other[f]	6
Procedural related injuries and complications NEC	**65**
Wound Dehiscence	15
Medical Device Site Erythema	13
Seroma	7
Suture Related Complication	6
Other[f]	24
Muscle disorders	**20**
Muscle Spasms	14
Other[f]	6
Headaches	**18**
Headache	16
Other[f]	2
Injuries NEC	**16**
Wound Secretion	7
Other[f]	9
Epidermal and dermal conditions	**15**
Other[f]	15
Spinal cord and nerve root disorders	**14**
Radiculopathy	11
Other[f]	3
Tissue disorders NEC	**11**
Impaired Healing	11
Bacterial infectious disorders	**10**
Other[f]	10
Gastrointestinal signs and symptoms	**9**
Other[f]	9
Anxiety disorders and symptoms	**8**
Other[f]	8
Allergic conditions	**7**
Hypersensitivity	6
Other[f]	1
Joint disorders	**7**
Arthralgia	6
Other[f]	1
Other[f]	**24**
Total	**2,571**

[a] Event reported by the physician with an etiology that was either not device related or had no associated device event.

[b] Neurostimulator unable to recharge includes events with patients which were unable to recharge due to an issue not related to the device.

[c] Device battery issues includes events reported as battery discharge or depletion not due to a device malfunction.

[d] Device malfunction includes events reported as device issues due to patient use or other non-device defect etiology.

[e] For products that are returned with a suspected device issue, and RPA establishes a root cause or finds no anomaly, results reported herein reflect the finding from Returned Product Analysis (RPA).

[f] Composed of event codes with fewer than 5 events each.

4.2.3 Patient Deaths

There were 176 deaths reported for patients with spinal cord stimulation systems, none of which were reported as a direct result of a product performance event.

Since 2004, a total of 40 (22.7%) deaths have been reported in this patient registry study based upon patients receiving therapy for other chronic pain, 30 (17.0%) for radicular pain syndrome, 25 (14.2%) for post laminectomy pain, 23 (13.1%) for failed back surgery syndrome (FBSS), 14 (8.0%) for combination back and leg pain, 12 (6.8%) for CRPS I, 7 (4.0%) for degenerative disc disease, 7 (4.0%) for multiple back operations, 2 (1.1%) for CRPS II, 2 (1.1%) for diabetic neuropathy, 2 (1.1%) for post herpetic neuralgia, 1 (0.6%) for cervical pain, 1 (0.6%) for traumatic nerve injury, and 10 (5.7%) for other indications (see Table 4.6). The percentage is based upon the total patient death events and not based upon the rate of occurrence. As mentioned previously, **all tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 4.6: Spinal Cord Stimulation System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Other Chronic Pain	40 (22.7%)
Radicular Pain Syndrome	30 (17.0%)
Post Laminectomy Pain	25 (14.2%)
Failed Back Surgery Syndrome (FBSS)	23 (13.1%)
Combination Back and Leg Pain	14 (8.0%)
CRPS I	12 (6.8%)
Degenerative Disc Disease	7 (4.0%)
Multiple Back Operations	7 (4.0%)
CRPS II	2 (1.1%)
Diabetic Neuropathy	2 (1.1%)
Post Herpetic Neuralgia	2 (1.1%)
Cervical Pain	1 (0.6%)
Traumatic Nerve Injury	1 (0.6%)
Other	10 (5.7%)
Total	**176 (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, 2018, there were 5,763 neurostimulators followed in the registry. The difference between the total number of patients (n=5,287) versus neurostimulators is is due to the fact that some patients were subsequently re-implanted. The aggregate prospective follow-up time for all spinal cord neurostimulators was 125,172 months (10,431 years). Table 4.7 provides the number and percentage of neurostimulators by model.

Table 4.7: Spinal Cord Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**4,035 (70.0%)**
RestoreSensor SureScan MRI (97714)	1,360 (23.6%)
PrimeAdvanced (37702)	668 (11.6%)
PrimeAdvanced SureScan MRI (97702)	650 (11.3%)
RestoreSensor (37714)	379 (6.6%)
RestoreAdvanced (37713)	357 (6.2%)
Intellis with AdaptiveStim (97715)	317 (5.5%)
RestoreAdvanced SureScan MRI (97713)	116 (2.0%)
Itrel 4 (37703)	102 (1.8%)
RestoreUltra SureScan MRI (97712)	86 (1.5%)
No longer manufactured	**1,718 (29.8%)**
RestoreULTRA (37712)	581 (10.1%)
Synergy (7427)	461 (8.0%)
Restore (37711)	447 (7.8%)
Itrel 3 (7425)	96 (1.7%)
RestorePrime (37701)	56 (1.0%)
Synergy Versitrel (7427V)	53 (0.9%)
SynergyPlus (7479)	16 (0.3%)
SynergyCompact (7479B)	8 (0.1%)
Other/Unspecified	**10 (0.2%)**
Total	**5,763 (100%)**

4.3.1 Neurostimulator Events

There were 71 product performance-related events with an underlying reported etiology related to spinal cord neurostimulator function. This includes 61 events with a neurostimulator etiology and 10 events with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 66 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 22.5% (336/1,493). 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 71 spinal cord neurostimulator events, 95.8 % (68/71) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 4.8). Three of the 71 spinal cord stimulator events were confirmed by Medtronic RPA as broken bond wire, grommet loose, or medical device complication, and 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.

Table 4.8: Spinal Cord Stimulation Neurostimulator Product Performance Events by Determination

Product Performance Events	N (%)
RPA Determination	**3 (4.2%)**
Broken Bond Wire	1 (1.4%)
Grommet Loose	1 (1.4%)
Medical Device Complication	1 (1.4%)
Physician's Determination	**68 (95.8%)**
Neurostimulator Unable To Recharge	19 (26.8%)
High Impedance	18 (25.4%)
Device Malfunction	15 (21.1%)
Lead Migration/Dislodgement	4 (5.6%)
Device Stimulation Issue	2 (2.8%)
Low Impedance	2 (2.8%)
Medical Device Complication	2 (2.8%)
Device Battery Issue	1 (1.4%)
Device Difficult To Use	1 (1.4%)
Device Telemetry Issue	1 (1.4%)
Extension Migration	1 (1.4%)
Medical Device Site Warmth	1 (1.4%)
Neurostimulator Migration	1 (1.4%)
Total	**71 (100%)**

The neurostimulator product performance-related events are summarized by model in Table 4.9 to Table 4.21. Other/unspecified models and models without events are not shown.

Table 4.9: Event Summary Table: Intellis with AdaptiveStim (model 97715)

Neurostimulator Event	N
High impedance	1
Total	**1**

Table 4.10: Event Summary Table: Itrel 4 (model 37703)

Neurostimulator Event	N
Device malfunction	1
High impedance	1
Total	**2**

Table 4.11: Event Summary Table: PrimeAdvanced (model 37702)

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

Table 4.12: Event Summary Table: PrimeAdvanced SureScan MRI (model 97702)

Neurostimulator Event	N
High impedance	3
Device battery issue	1
Lead migration/dislodgement	1
Neurostimulator unable to recharge	1
Total	**6**

Table 4.13: Event Summary Table: Restore (model 37711)

Neurostimulator Event	N
Neurostimulator unable to recharge	4
Device malfunction	1
Total	**5**

Table 4.14: Event Summary Table: RestoreAdvanced (model 37713)

Neurostimulator Event	N
Medical device complication	1
Total	**1**

Table 4.15: Event Summary Table: RestoreAdvanced SureScan MRI (model 97713)

Neurostimulator Event	N
Device malfunction	1
Total	**1**

Table 4.16: Event Summary Table: RestoreSensor (model 37714)

Neurostimulator Event	N
Neurostimulator unable to recharge	2
Device difficult to use	1
Device malfunction	1
Total	**4**

Table 4.17: Event Summary Table: RestoreSensor SureScan MRI (model 97714)

Neurostimulator Event	N
Device malfunction	7
Neurostimulator unable to recharge	7
High impedance	4
Lead migration/dislodgement	3
Device telemetry issue	1
Grommet loose	1
Low impedance	1
Medical device site warmth	1
Neurostimulator migration	1
Total	**26**

Table 4.18: Event Summary Table: RestoreULTRA (model 37712)

Neurostimulator Event	N
Neurostimulator unable to recharge	5
Device malfunction	2
Medical device complication	1
Total	**8**

Table 4.19: Event Summary Table: RestoreUltra SureScan MRI (model 97712)

Neurostimulator Event	N
Extension migration	1
Total	**1**

Table 4.20: Event Summary Table: Synergy (model 7427)

Neurostimulator Event	N
Broken bond wire	1
Device stimulation issue	1
Total	**2**

Table 4.21: Event Summary Table: Synergy Versitrel (model 7427V)

Neurostimulator Event	N
High impedance	2
Total	**2**

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:

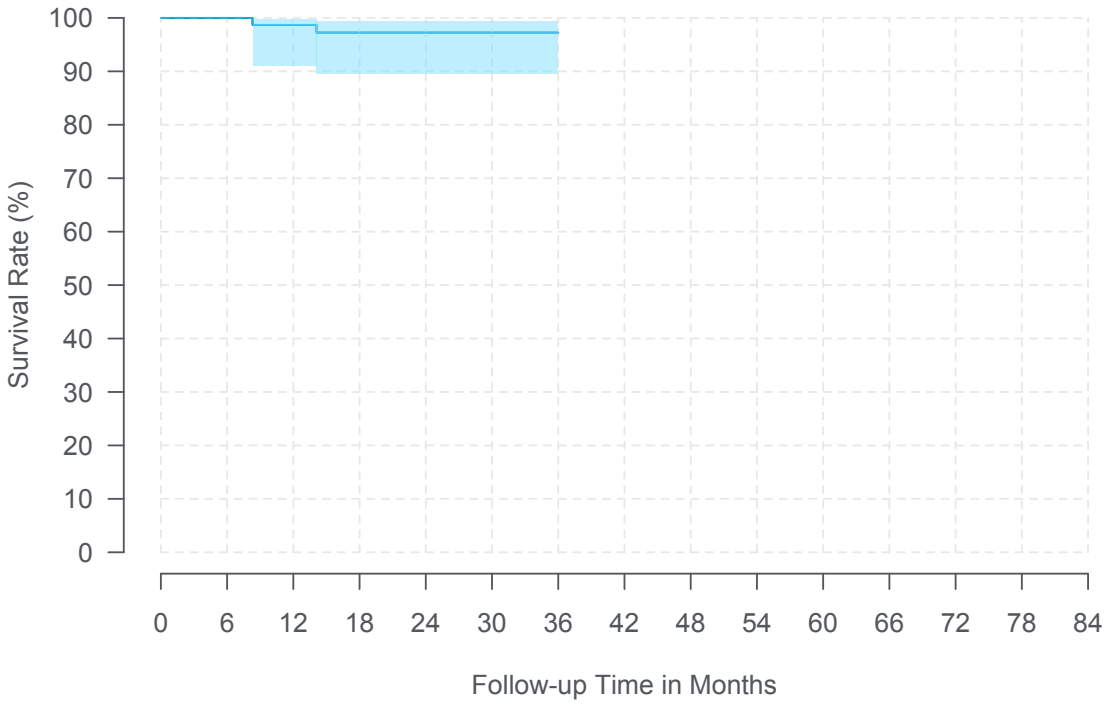
- 66 had follow-up time cut-off due to product performance-related events.
- 3,930 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 1,767 were free 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 Survival

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. The survival of Intellis (model 97715) is not shown due to insufficient follow-up data.

Model Itrel 4

Model Name	Itrel 4 (model 37703)
FDA Approval Date	May 2012
Neurostimulators Enrolled	102
Neurostimulators Currently Active in Study	67
Device Events	2
Cumulative Months of Follow-up	2,123

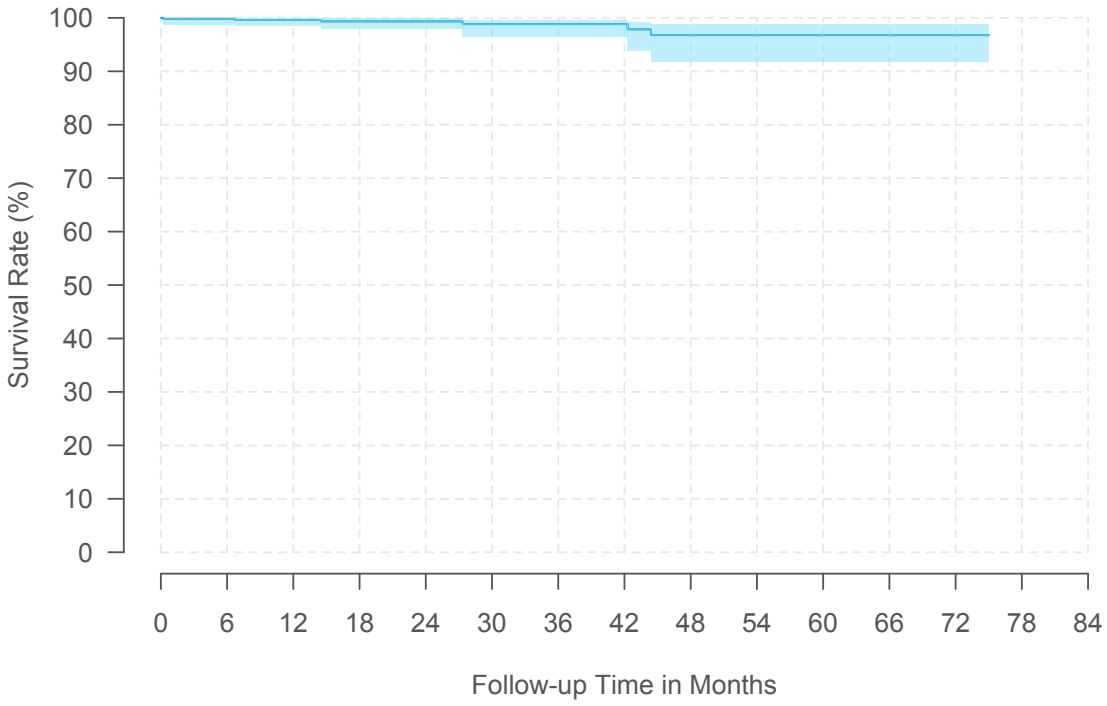


Time Interval	1 Year	2 Years	3 Years
Survival	98.7%	97.3%	97.3%
(95% CI)	(91.1%, 99.8%)	(89.4%, 99.3%)	(89.4%, 99.3%)
Sample Size	72	45	20

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

Model PrimeAdvanced

Model Name	PrimeAdvanced (model 37702)
FDA Approval Date	July 2006
Neurostimulators Enrolled	668
Neurostimulators Currently Active in Study	46
Device Events	7
Cumulative Months of Follow-up	14,440



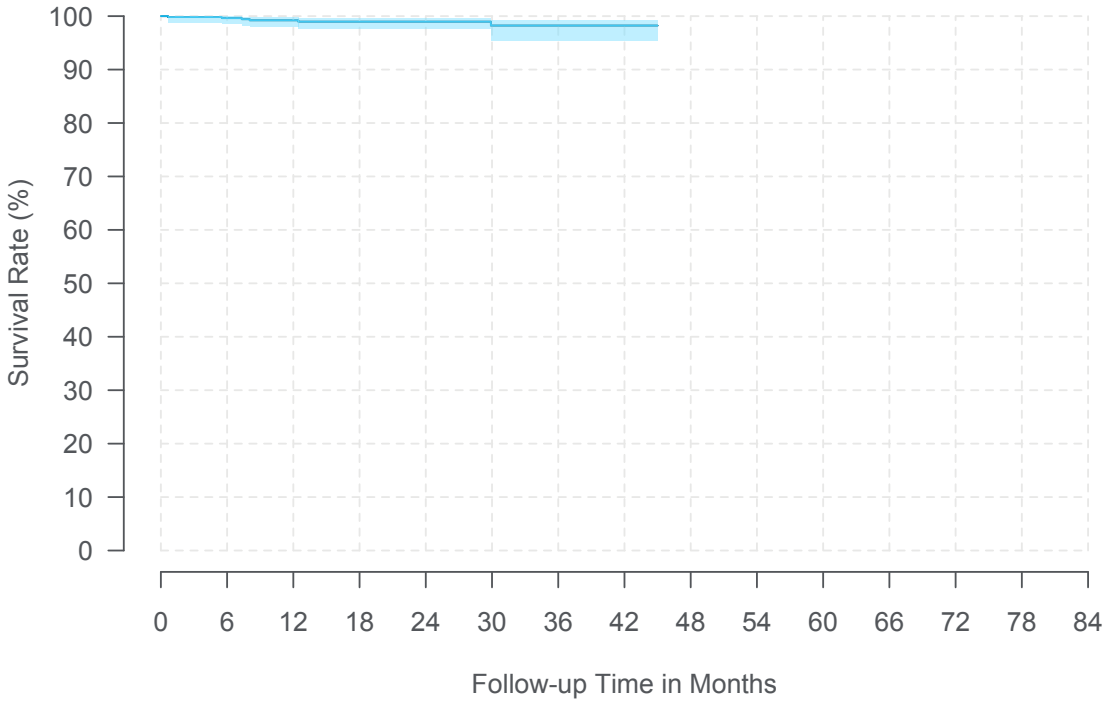
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.6% (98.5%, 99.9%)	99.3% (97.9%, 99.8%)	98.8% (96.6%, 99.6%)	96.8% (91.7%, 98.8%)	96.8% (91.7%, 98.8%)
Sample Size	390	235	133	77	45

Time Interval	6 Years	At 75 Months			
Survival (95% CI)	96.8% (91.7%, 98.8%)	96.8% (91.7%, 98.8%)			
Sample Size	24	21			

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

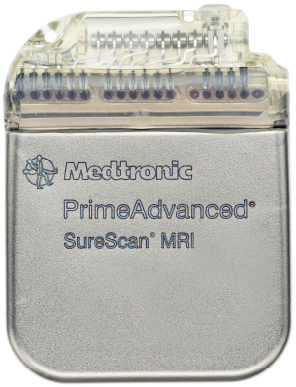
Model PrimeAdvanced SureScan MRI

Model Name	PrimeAdvanced SureScan MRI (model 97702)
FDA Approval Date	March 2013
Neurostimulators Enrolled	650
Neurostimulators Currently Active in Study	382
Device Events	6
Cumulative Months of Follow-up	11,899



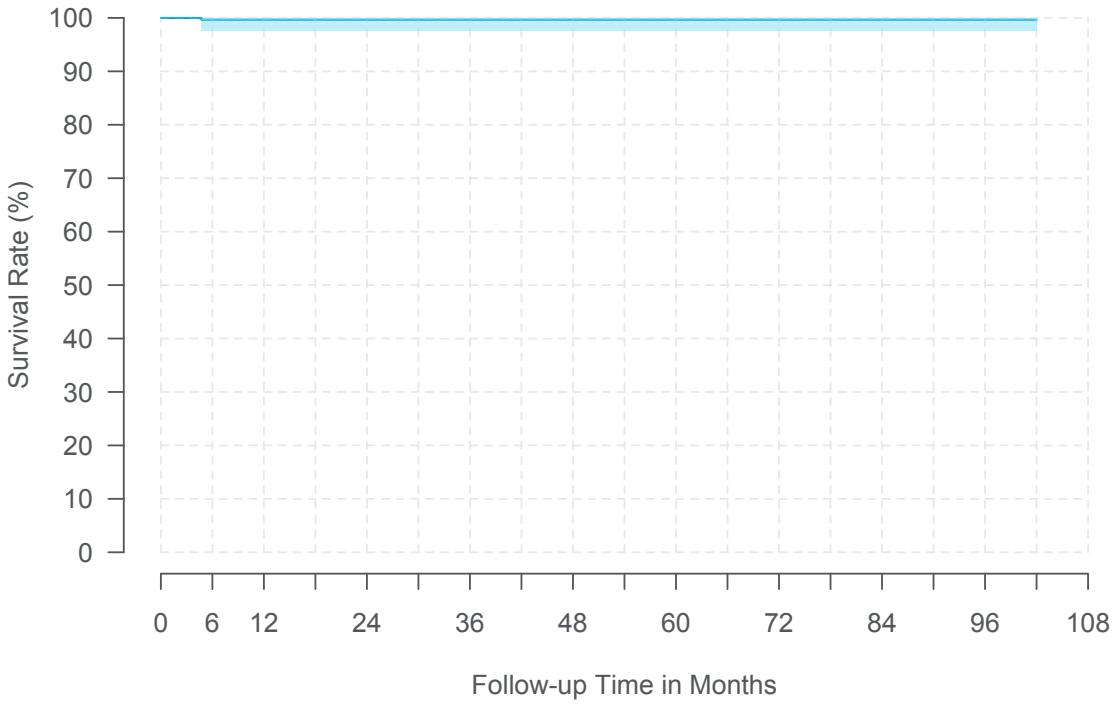
Time Interval	1 Year	2 Years	3 Years	At 45 Months
Survival (95% CI)	99.2% (97.9%, 99.7%)	99.0% (97.5%, 99.6%)	98.2% (95.4%, 99.3%)	98.2% (95.4%, 99.3%)
Sample Size	403	208	84	27

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



Model RestoreAdvanced

Model Name	RestoreAdvanced (model 37713)
FDA Approval Date	July 2006
Neurostimulators Enrolled	357
Neurostimulators Currently Active in Study	20
Device Events	1
Cumulative Months of Follow-up	11,087



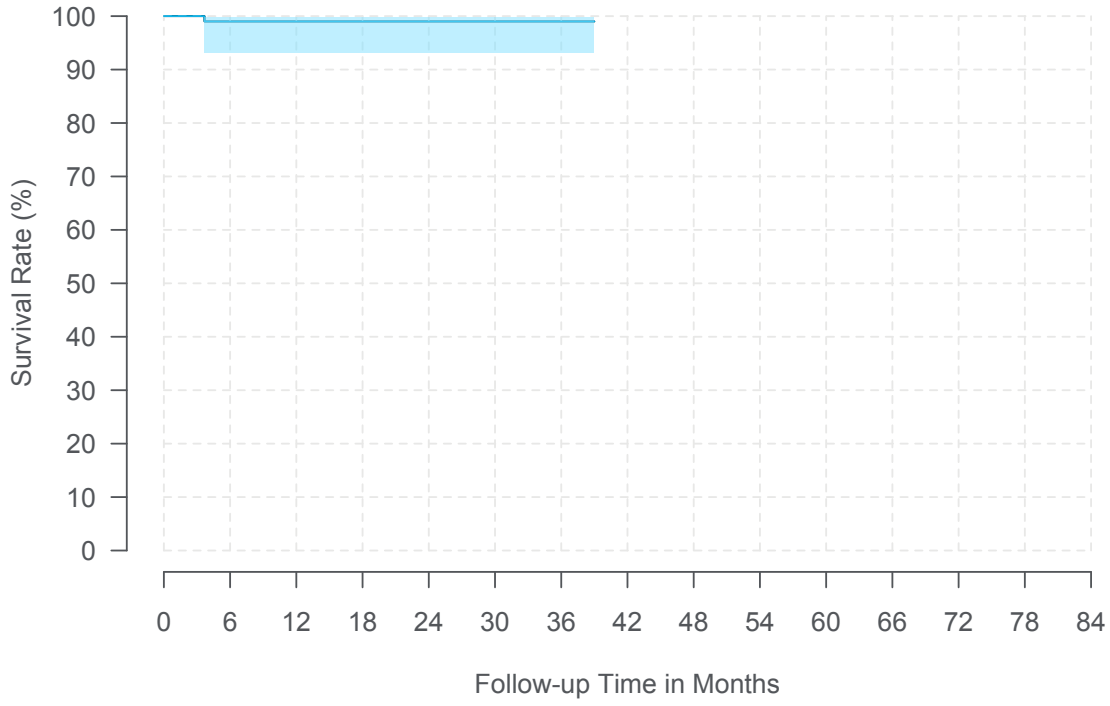
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)
Sample Size	238	169	114	82	61

Time Interval	6 Years	7 Years	8 Years	At 102 Months	
Survival (95% CI)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	
Sample Size	45	31	26	21	

Specification: RestoreAdvanced	
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

Model RestoreAdvanced SureScan MRI

Model Name	RestoreAdvanced SureScan MRI (model 97713)
FDA Approval Date	March 2013
Neurostimulators Enrolled	116
Neurostimulators Currently Active in Study	59
Device Events	1
Cumulative Months of Follow-up	2,710

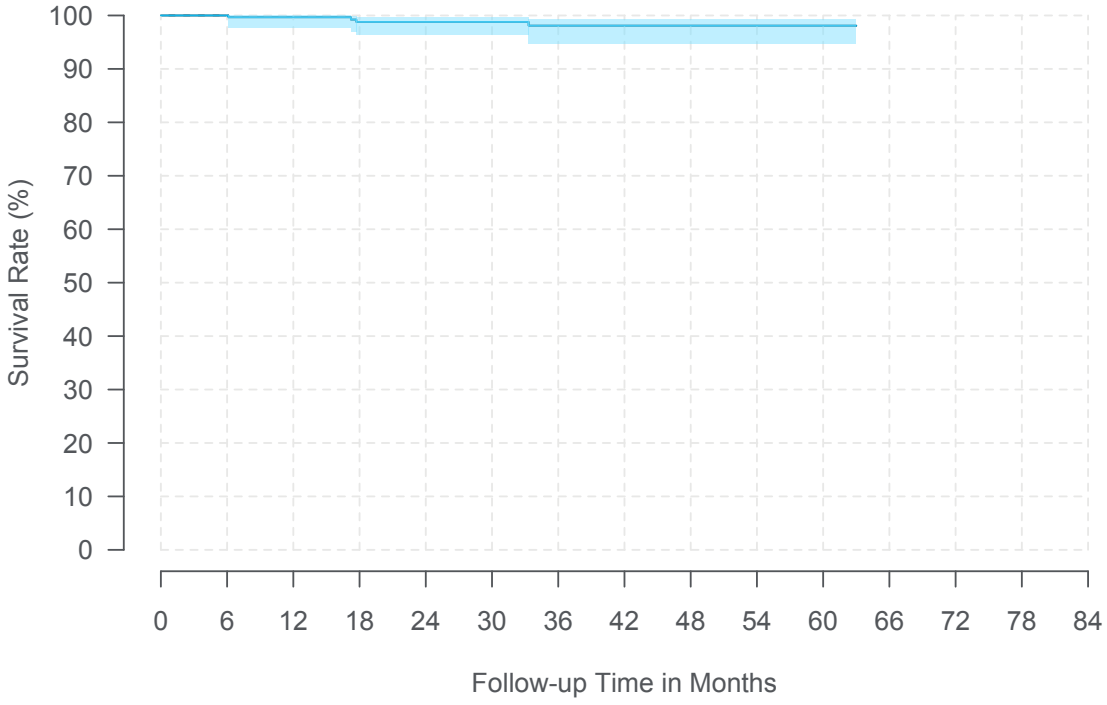


Time Interval	1 Year	2 Years	3 Years	At 39 Months
Survival (95% CI)	99.0% (93.1%, 99.9%)	99.0% (93.1%, 99.9%)	99.0% (93.1%, 99.9%)	99.0% (93.1%, 99.9%)
Sample Size	79	56	31	25

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

Model RestoreSensor

Model Name	RestoreSensor (model 37714)
FDA Approval Date	November 2011
Neurostimulators Enrolled	379
Neurostimulators Currently Active in Study	83
Device Events	4
Cumulative Months of Follow-up	10,281



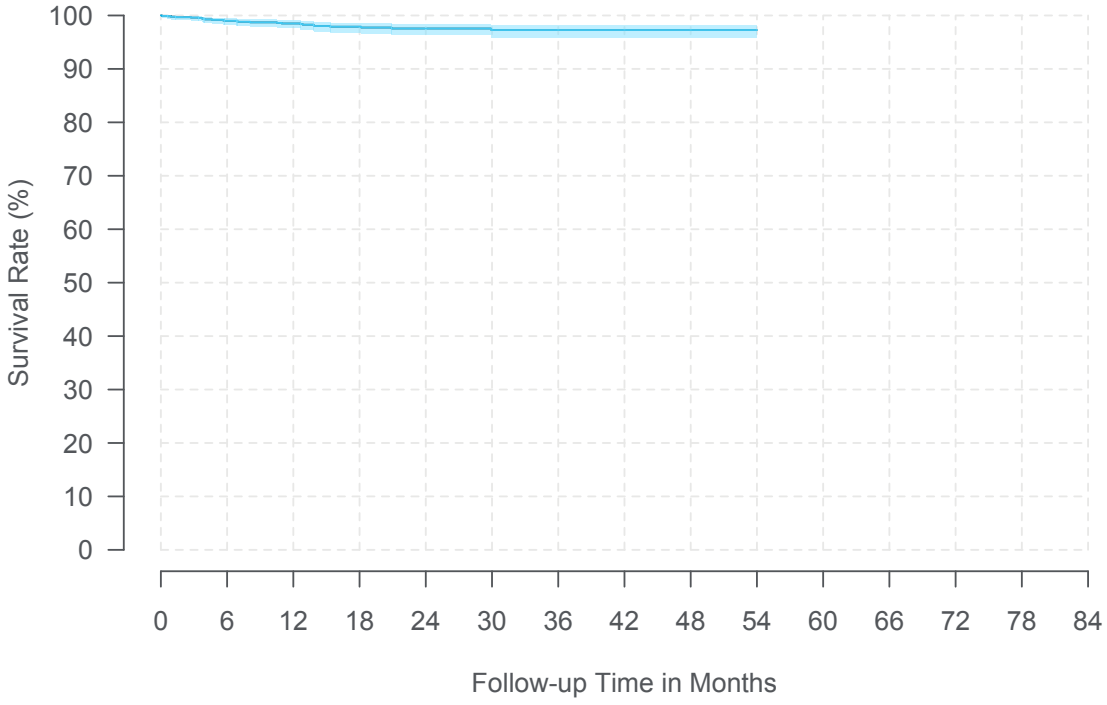
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.7% (97.7%, 100%)	98.8% (96.3%, 99.6%)	98.1% (94.8%, 99.3%)	98.1% (94.8%, 99.3%)	98.1% (94.8%, 99.3%)
Sample Size	259	184	127	78	30

Time Interval	At 63 Months
Survival (95% CI)	98.1% (94.8%, 99.3%)
Sample Size	20

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

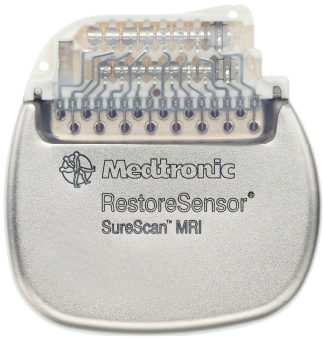
Model RestoreSensor SureScan MRI

Model Name	RestoreSensor SureScan MRI (model 97714)
FDA Approval Date	March 2013
Neurostimulators Enrolled	1,360
Neurostimulators Currently Active in Study	750
Device Events	26
Cumulative Months of Follow-up	27,345



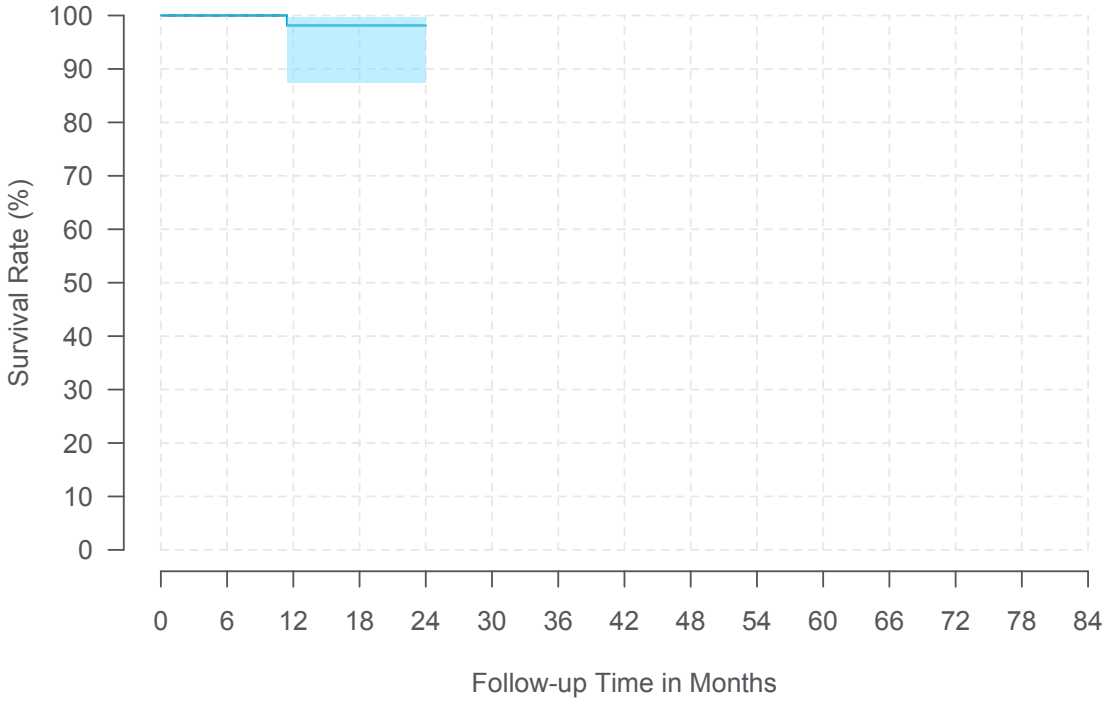
Time Interval	1 Year	2 Years	3 Years	4 Years	At 54 Months
Survival (95% CI)	98.5% (97.6%, 99.1%)	97.6% (96.3%, 98.4%)	97.3% (95.9%, 98.2%)	97.3% (95.9%, 98.2%)	97.3% (95.9%, 98.2%)
Sample Size	881	471	229	69	28

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



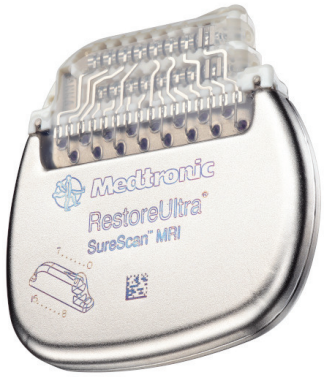
Model RestoreUltra SureScan MRI

Model Name	RestoreUltra SureScan MRI (model 97712)
FDA Approval Date	March 2013
Neurostimulators Enrolled	86
Neurostimulators Currently Active in Study	48
Device Events	1
Cumulative Months of Follow-up	1,384



Time Interval	1 Year	2 Years
Survival	98.1%	98.1%
(95% CI)	(87.5%, 99.7%)	(87.5%, 99.7%)
Sample Size	51	22

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



4.3.3 Neurostimulator Survival Summary

Table 4.22: Spinal Cord Stimulation Primary Cell Neurostimulator Characteristics

Model Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Cumulative Follow-up Months
Itrel 4 (model 37703)	May 2012	102	67	2	2,123
PrimeAdvanced (model 37702)	July 2006	668	46	7	14,440
PrimeAdvanced SureScan MRI (model 97702)	March 2013	650	382	6	11,899

Table 4.23: Spinal Cord Stimulation Primary Cell Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Itrel 4 (model 37703)	98.7% (91.1%, 99.8%)	97.3% (89.4%, 99.3%)	97.3% (89.4%, 99.3%)		
PrimeAdvanced (model 37702)	99.6% (98.5%, 99.9%)	99.3% (97.9%, 99.8%)	98.8% (96.6%, 99.6%)	96.8% (91.7%, 98.8%)	96.8% (91.7%, 98.8%)
PrimeAdvanced SureScan MRI (model 97702)	99.2% (97.9%, 99.7%)	99.0% (97.5%, 99.6%)	98.2% (95.4%, 99.3%)		

Model Name	6 Years				
Itrel 4 (model 37703)					
PrimeAdvanced (model 37702)	96.8% (91.7%, 98.8%)				
PrimeAdvanced SureScan MRI (model 97702)					

Table 4.24: Spinal Cord Stimulation Rechargeable Neurostimulator Characteristics

Model Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Cumulative Follow-up Months
RestoreAdvanced (model 37713)	July 2006	357	20	1	11,087
RestoreAdvanced SureScan MRI (model 97713)	March 2013	116	59	1	2,710
RestoreSensor (model 37714)	November 2011	379	83	4	10,281
RestoreSensor SureScan MRI (model 97714)	March 2013	1,360	750	26	27,345
RestoreUltra SureScan MRI (model 97712)	March 2013	86	48	1	1,384

Table 4.25: Spinal Cord Stimulation Rechargeable Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
RestoreAdvanced (model 37713)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)
RestoreAdvanced SureScan MRI (model 97713)	99.0% (93.1%, 99.9%)	99.0% (93.1%, 99.9%)	99.0% (93.1%, 99.9%)		
RestoreSensor (model 37714)	99.7% (97.7%, 100%)	98.8% (96.3%, 99.6%)	98.1% (94.8%, 99.3%)	98.1% (94.8%, 99.3%)	98.1% (94.8%, 99.3%)
RestoreSensor SureScan MRI (model 97714)	98.5% (97.6%, 99.1%)	97.6% (96.3%, 98.4%)	97.3% (95.9%, 98.2%)	97.3% (95.9%, 98.2%)	
RestoreUltra SureScan MRI (model 97712)	98.1% (87.5%, 99.7%)	98.1% (87.5%, 99.7%)			

Model Name	6 Years	7 Years	8 Years		
RestoreAdvanced (model 37713)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)	99.7% (97.6%, 100%)		
RestoreAdvanced SureScan MRI (model 97713)					
RestoreSensor (model 37714)					
RestoreSensor SureScan MRI (model 97714)					
RestoreUltra SureScan MRI (model 97712)					

4.4 Leads

From June 2004 to the report cut-off date of October 31, 2018, there were 9,443 leads followed in the registry. The difference between the total number of leads (n=9,443) versus the number of neurostimulators (n=5,763) 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 232,973 months (19,414 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 4.26 provides the number and percentage of leads by model.

Table 4.26: Spinal Cord Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**8,529 (90.3%)**
Vectris SureScan MRI 1x8 Compact (977A2)	3,192 (33.8%)
1x8 Compact (3778)	2,161 (22.9%)
Pisces Standard (3487A)	986 (10.4%)
1x8 Standard (3777)	836 (8.9%)
Pisces Plus (3888)	446 (4.7%)
Specify 5-6-5 (39565)	286 (3.0%)
Pisces Compact (3887)	196 (2.1%)
1x8 SC (3776)	186 (2.0%)
Vectris SureScan MRI 1x8 Subcompact (977A1)	130 (1.4%)
Specify SureScan MRI 5-6-5 (977C1)	41 (0.4%)
Specify 2x8 (39286)	32 (0.3%)
Specify SureScan MRI 2x8 (977C2)	22 (0.2%)
AnkerStim Lead (Approved in Europe): 09100	15 (0.2%)
No longer manufactured	**680 (7.2%)**
Specify (3998)	156 (1.7%)
Pisces Z Standard (3890)	143 (1.5%)
Pisces Z Compact (3891)	130 (1.4%)
Resume TL (3986A)	108 (1.1%)
2x4 Hinged Specify (3999)	54 (0.6%)
Resume II (3587A)	53 (0.6%)
Pisces Z Plus (3892)	25 (0.3%)
On-Point (3987A)	9 (0.1%)
SymMix (3982A)	2 (0.0%)
Other/Unspecified	**234 (2.5%)**
Total	**9,443 (100%)**

Percutaneous leads composed over eighty-nine percent (89.3%) of leads in the registry (8,431/9,443), including 35.2% (3,322/9,443) in the Vectris SureScan lead family, 33.7% (3,183/9,443) in the Pisces-Octad lead family, 17.2% (1,628/9,443) in the Pisces-Quad lead

family, and 3.2% (298/9,443) in the Pisces-Quad Z lead family. Over eight percent (8.1%) of leads (763/9,443) were surgical leads. A small percent (2.6%) of leads (249/9,443) were designated as "Other" or were unspecified in the database.

4.4.1 Lead Events

There were 1,115 product performance-related events with an underlying reported etiology related to lead function. This includes 1,089 events with a lead etiology and 26 events with both a lead and other etiology (including device and non-device etiologies). Of these, 965 were the initial product performance event that affected lead survival estimates; the majority were lead migration/dislodgements (n=600), high impedance (n=315), lead fracture (n=75), device stimulation issue (n=45) and low impedance (n=38). There were 879 events in the 8,431 (10.4%) percutaneous leads, 52 events in the 763 (6.8%) surgical leads, and 33 events occurred in a lead with an unknown/other model number.

The lead product performance-related events are summarized by model in Table 4.27 to Table 4.45. Other/unspecified models and models without events are not shown.

Table 4.27: Event Summary Table: 1x8 Compact (model 3778)

Lead Event	N
Lead migration/dislodgement	207
High impedance	39
Lead fracture	19
Device stimulation issue	6
Medical device complication	4
Device malfunction	2
Low impedance	1
Total	**278**

Table 4.28: Event Summary Table: 1x8 SC (model 3776)

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

Table 4.29: Event Summary Table: 1x8 Standard (model 3777)

Lead Event	N
Lead migration/dislodgement	43
High impedance	15
Device stimulation issue	7
Device lead damage	2
Lead fracture	2
Low impedance	2
Total	**71**

Table 4.30: Event Summary Table: 2x4 Hinged Specify (model 3999)

Lead Event	N
Lead migration/dislodgement	2
High impedance	1
Total	**3**

Table 4.31: Event Summary Table: Pisces Compact (model 3887)

Lead Event	N
Lead migration/dislodgement	14
Lead fracture	8
High impedance	4
Device stimulation issue	2
Device lead damage	1
Total	**29**

Table 4.32: Event Summary Table: Pisces Plus (model 3888)

Lead Event	N
Lead migration/dislodgement	28
High impedance	11
Device stimulation issue	2
Lead fracture	1
Total	**42**

Table 4.33: Event Summary Table: Pisces Standard (model 3487A)

Lead Event	N
High impedance	88
Lead migration/dislodgement	56
Low impedance	25
Device stimulation issue	17
Lead fracture	10
Inadequate lead connection	2
Total	**198**

Table 4.34: Event Summary Table: Pisces Z Compact (model 3891)

Lead Event	N
Lead migration/dislodgement	18
Lead fracture	6
Device stimulation issue	4
Device lead damage	2
High impedance	2
Total	**32**

Table 4.35: Event Summary Table: Pisces Z Plus (model 3892)

Lead Event	N
High impedance	1
Lead fracture	1
Total	**2**

Table 4.36: Event Summary Table: Pisces Z Standard (model 3890)

Lead Event	N
Lead migration/dislodgement	4
High impedance	2
Lead fracture	2
Low impedance	2
Total	**10**

Table 4.37: Event Summary Table: Resume TL (model 3986A)

Lead Event	N
High impedance	10
Device connection issue	2
Device stimulation issue	2
Lead migration/dislodgement	2
Low impedance	2
Lead fracture	1
Total	**19**

Table 4.38: Event Summary Table: Resume II (model 3587A)

Lead Event	N
High impedance	3
Total	**3**

Table 4.39: Event Summary Table: Specify (model 3998)

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

Table 4.40: Event Summary Table: Specify 2x8 (model 39286)

Lead Event	N
High impedance	1
Total	**1**

Table 4.41: Event Summary Table: Specify 5-6-5 (model 39565)

Lead Event	N
Lead migration/dislodgement	10
High impedance	1
Lead fracture	1
Lead insulation failure	1
Total	**13**

Table 4.42: Event Summary Table: Specify SureScan MRI 2x8 (model 977C2)

Lead Event	N
Lead migration/dislodgement	1
Total	**1**

Table 4.43: Event Summary Table: Specify SureScan MRI 5-6-5 (model 977C1)

Lead Event	N
High impedance	1
Lead migration/dislodgement	1
Total	**2**

Table 4.44: Event Summary Table: Vectris SureScan MRI 1x8 Compact (model 977A2)

Lead Event	N
Lead migration/dislodgement	131
High impedance	41
Lead fracture	16
Low impedance	3
Device difficult to use	2
Device malfunction	1
Total	**194**

Table 4.45: Event Summary Table: Vectris SureScan MRI 1x8 Subcompact (model 977A1)

Lead Event	N
Lead migration/dislodgement	6
Lead fracture	2
High impedance	1
Total	**9**

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:

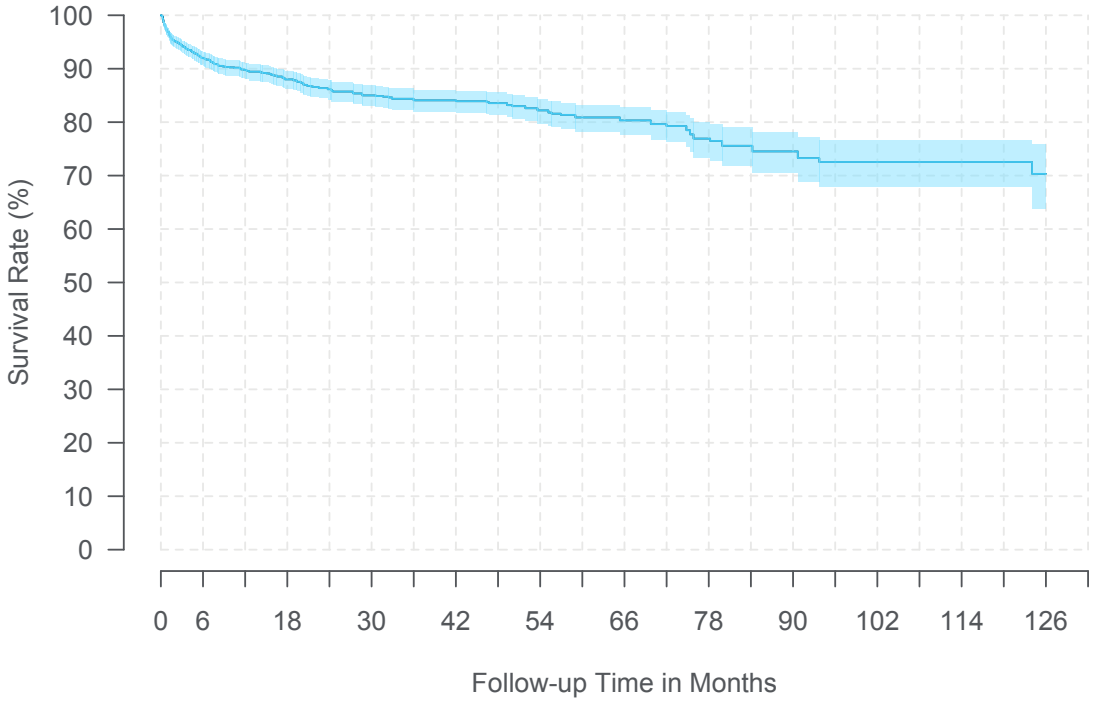
- 965 had follow-up time cut-off due to product performance-related events.
- 5,607 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,871 were free 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 Survival

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.

Model 1x8 Compact

Model Name	1x8 Compact (model 3778)
FDA Approval Date	April 2005
Leads Enrolled	2,161
Leads Currently Active in Study	267
Device Events	278
Cumulative Months of Follow-up	61,383



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	89.7% (88.2%, 91.1%)	86.2% (84.3%, 87.8%)	84.1% (82.0%, 86.0%)	83.6% (81.4%, 85.5%)	80.9% (78.3%, 83.2%)
Sample Size	1,203	794	591	448	335

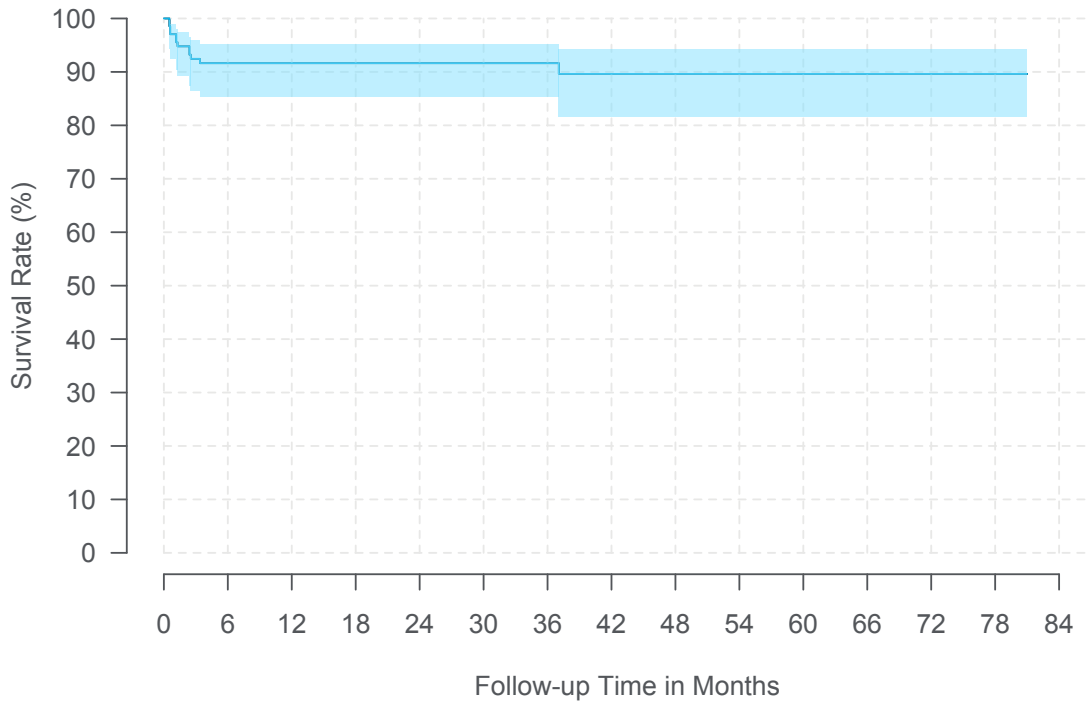
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	79.3% (76.3%, 81.9%)	75.6% (71.8%, 78.9%)	72.5% (68.0%, 76.6%)	72.5% (68.0%, 76.6%)	72.5% (68.0%, 76.6%)
Sample Size	218	144	98	70	41

Time Interval	At 126 Months
Survival (95% CI)	70.3% (63.8%, 75.9%)
Sample Size	24

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)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	4.0
Array Length (mm)	52.0

Model 1x8 SC

Model Name	1x8 SC (model 3776)
FDA Approval Date	November 2005
Leads Enrolled	186
Leads Currently Active in Study	29
Device Events	15
Cumulative Months of Follow-up	4,806



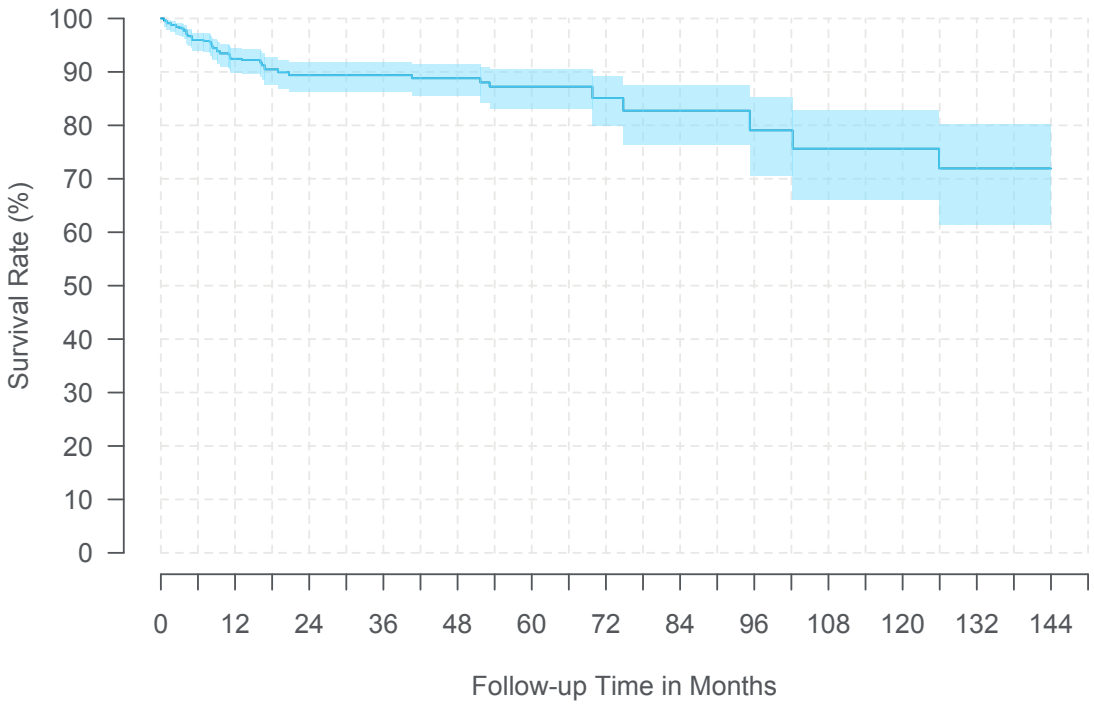
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.6% (85.4%, 95.3%)	91.6% (85.4%, 95.3%)	91.6% (85.4%, 95.3%)	89.6% (81.6%, 94.3%)	89.6% (81.6%, 94.3%)
Sample Size	84	62	47	34	23

Time Interval	At 69 Months
Survival (95% CI)	89.6% (81.6%, 94.3%)
Sample Size	20

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

Model 1x8 Standard

Model Name	1x8 Standard (model 3777)
FDA Approval Date	April 2005
Leads Enrolled	836
Leads Currently Active in Study	104
Device Events	71
Cumulative Months of Follow-up	21,419



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.4% (89.9%, 94.4%)	89.4% (86.3%, 91.8%)	89.4% (86.3%, 91.8%)	88.8% (85.5%, 91.4%)	87.2% (83.1%, 90.4%)
Sample Size	440	286	181	121	90

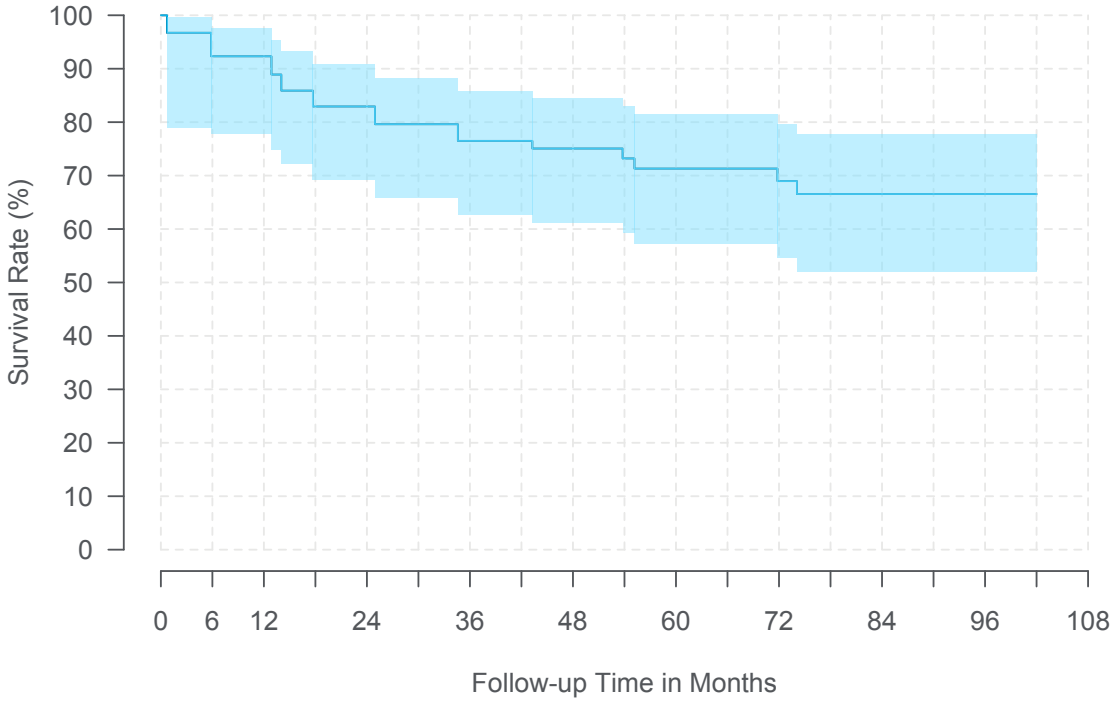
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	85.1% (79.8%, 89.1%)	82.7% (76.4%, 87.5%)	79.1% (70.7%, 85.3%)	75.6% (66.1%, 82.9%)	75.6% (66.1%, 82.9%)
Sample Size	75	53	42	53	51

Time Interval	11 Years	12 Years			
Survival (95% CI)	71.9% (61.3%, 80.1%)	71.9% (61.3%, 80.1%)			
Sample Size	30	20			

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)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	6.0
Array Length (mm)	66.0

Model Pisces Compact

Model Name	Pisces Compact (model 3887)
FDA Approval Date	January 1997
Leads Enrolled	196
Leads Currently Active in Study	50
Device Events	29
Cumulative Months of Follow-up	5,963



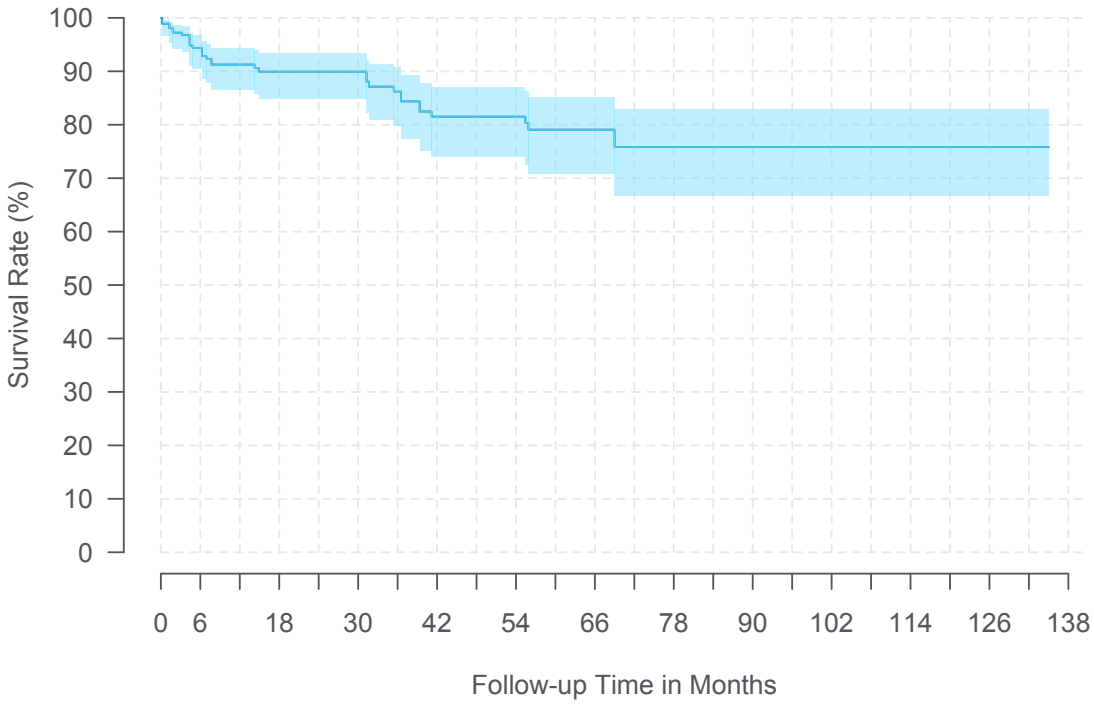
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	92.3% (77.7%, 97.5%)	82.9% (69.3%, 90.9%)	76.5% (62.7%, 85.7%)	75.1% (61.3%, 84.5%)	71.3% (57.3%, 81.4%)
Sample Size	51	52	49	43	37

Time Interval	6 Years	7 Years	At 93 Months		
Survival (95% CI)	69.0% (54.6%, 79.6%)	66.6% (51.9%, 77.7%)	66.6% (51.9%, 77.7%)		
Sample Size	29	22	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)	12.0
Inter-Electrode Spacing: Edge to Edge (mm)	4.0
Array Length (mm)	24.0

Model Pisces Plus

Model Name	Pisces Plus (model 3888)
FDA Approval Date	November 1992
Leads Enrolled	446
Leads Currently Active in Study	60
Device Events	42
Cumulative Months of Follow-up	10,009



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	91.3% (86.6%, 94.4%)	89.9% (84.9%, 93.4%)	86.2% (79.8%, 90.7%)	81.5% (74.0%, 87.0%)	79.1% (70.9%, 85.2%)
Sample Size	149	106	93	69	58

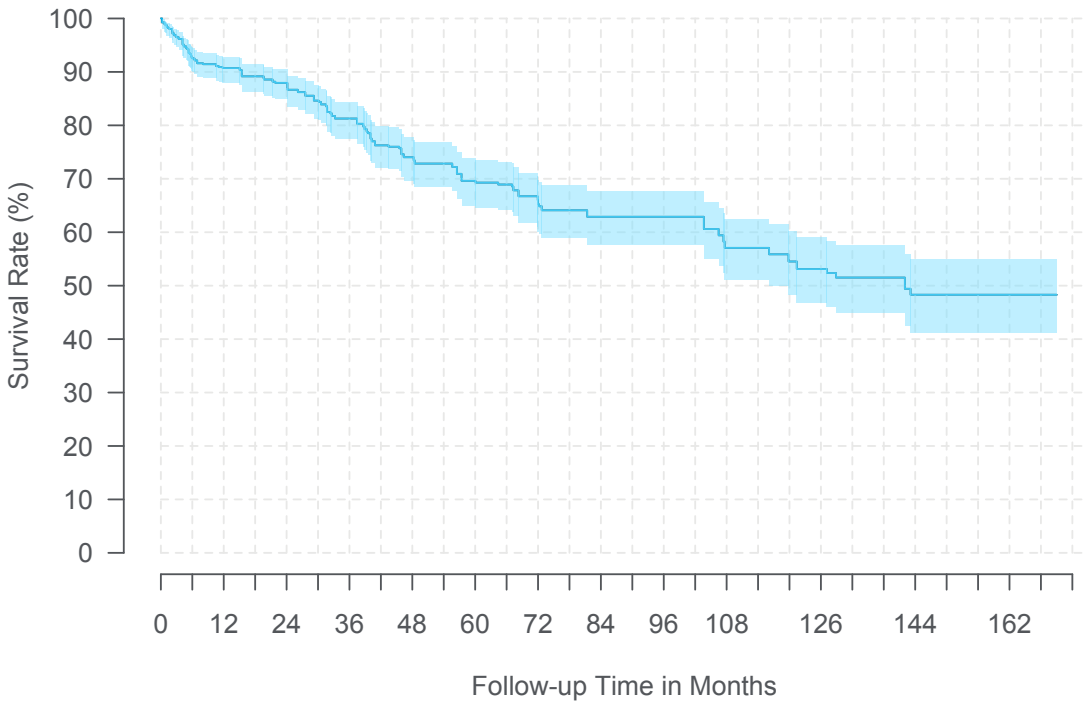
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)
Sample Size	42	33	30	28	25

Time Interval	At 126 Months				
Survival (95% CI)	75.8% (66.6%, 82.9%)				
Sample Size	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)	24.0
Inter-Electrode Spacing: Edge to Edge (mm)	12.0
Array Length (mm)	60.0

Model Pisces Standard

Model Name	Pisces Standard (model 3487A)
FDA Approval Date	May 1988
Leads Enrolled	986
Leads Currently Active in Study	99
Device Events	198
Cumulative Months of Follow-up	38,755



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	90.7% (88.0%, 92.8%)	87.9% (84.9%, 90.4%)	81.3% (77.6%, 84.4%)	74.0% (69.7%, 77.8%)	69.6% (65.0%, 73.8%)
Sample Size	498	408	336	252	207

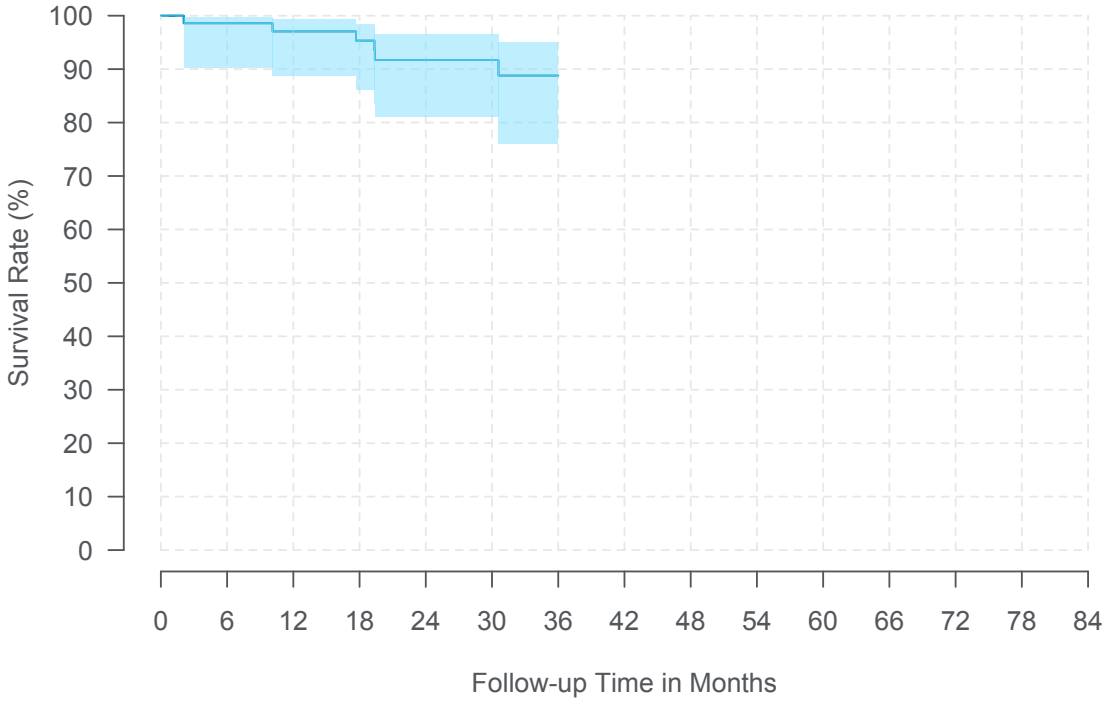
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	65.2% (60.2%, 69.8%)	62.9% (57.7%, 67.6%)	62.9% (57.7%, 67.6%)	57.1% (51.2%, 62.5%)	54.5% (48.4%, 60.2%)
Sample Size	173	147	116	97	80

Time Interval	11 Years	12 Years	13 Years	14 Years	At 171 Months
Survival (95% CI)	51.5% (45.0%, 57.6%)	48.3% (41.3%, 55.0%)	48.3% (41.3%, 55.0%)	48.3% (41.3%, 55.0%)	48.3% (41.3%, 55.0%)
Sample Size	57	43	26	21	20

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

Model Specify

Model Name	Specify (model 3998)
FDA Approval Date	February 1998
Leads Enrolled	156
Leads Currently Active in Study	24
Device Events	10
Cumulative Months of Follow-up	3,845

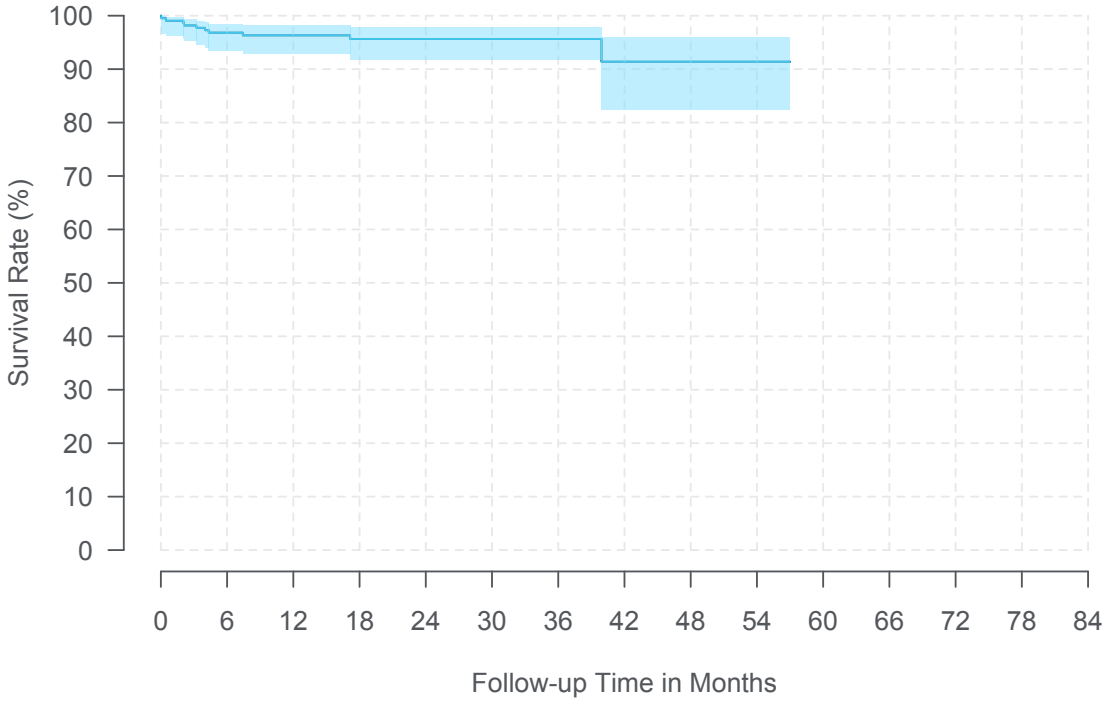


Time Interval	1 Year	2 Years	3 Years
Survival (95% CI)	97.1% (88.7%, 99.3%)	91.7% (81.1%, 96.5%)	88.8% (76.0%, 95.0%)
Sample Size	60	41	22

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

Model Specify 5-6-5

Model Name	Specify 5-6-5 (model 39565)
FDA Approval Date	June 2007
Leads Enrolled	286
Leads Currently Active in Study	53
Device Events	13
Cumulative Months of Follow-up	6,617

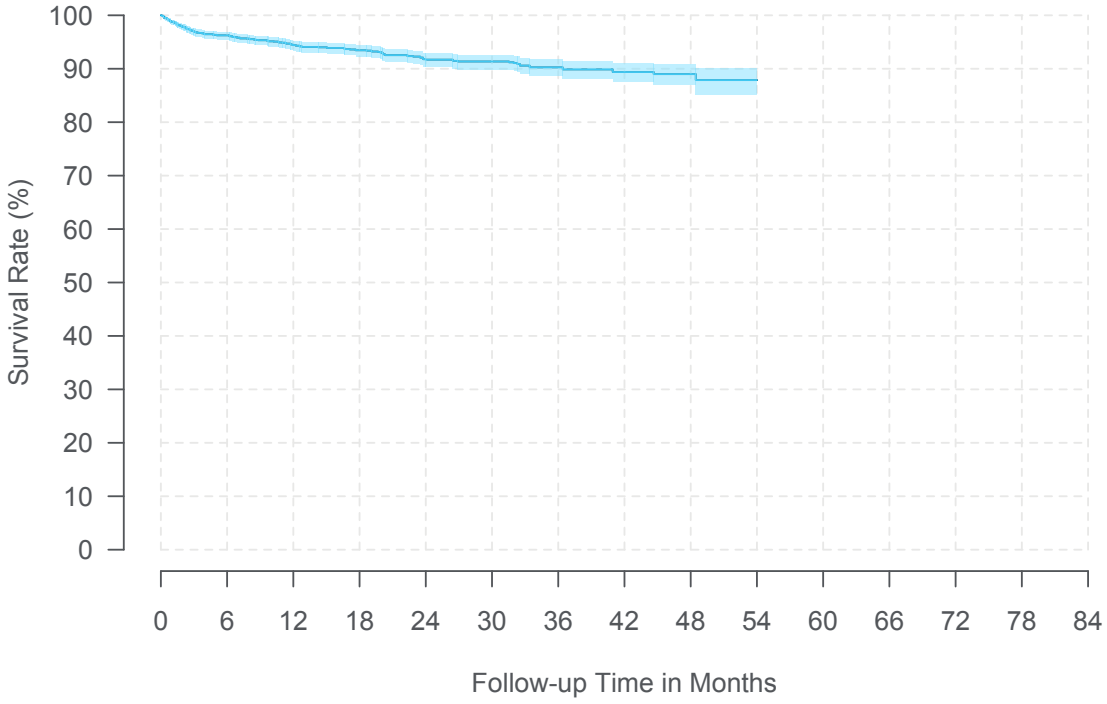


Time Interval	1 Year	2 Years	3 Years	4 Years	At 57 Months
Survival (95% CI)	96.3% (92.8%, 98.1%)	95.6% (91.7%, 97.7%)	95.6% (91.7%, 97.7%)	91.4% (82.3%, 95.9%)	91.4% (82.3%, 95.9%)
Sample Size	161	106	54	30	22

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)	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

Model Vectris SureScan MRI 1x8 Compact

Model Name	Vectris SureScan MRI 1x8 Compact (model 977A2)
FDA Approval Date	March 2013
Leads Enrolled	3,192
Leads Currently Active in Study	2,009
Device Events	194
Cumulative Months of Follow-up	56,468

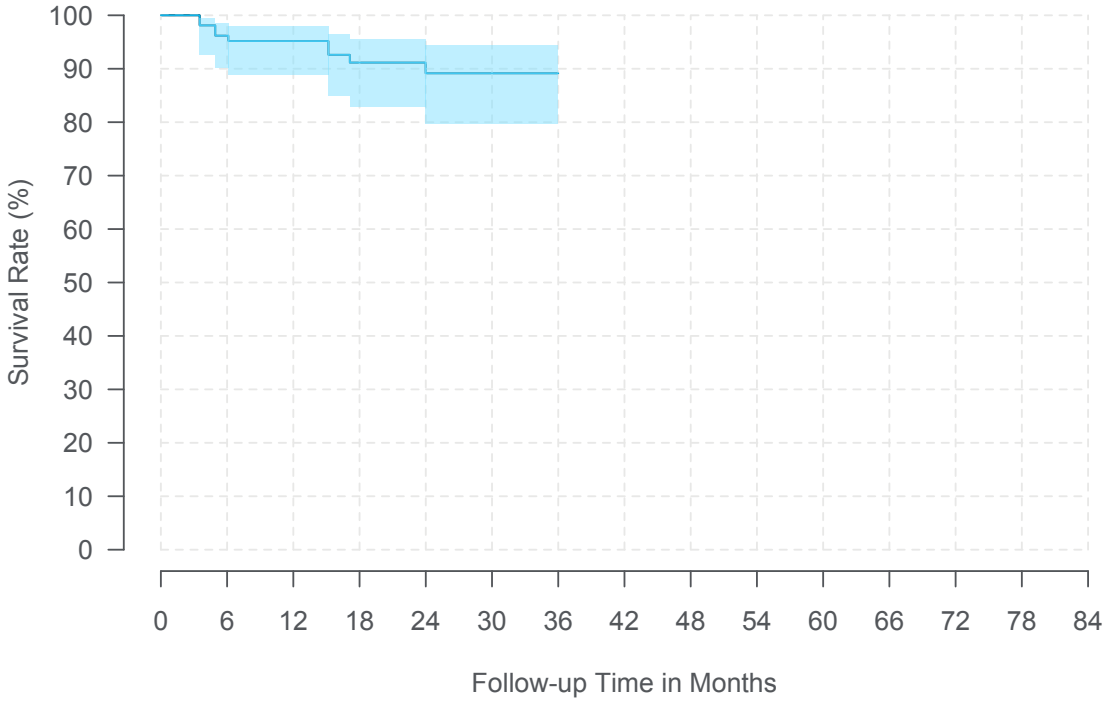


Time Interval	1 Year	2 Years	3 Years	4 Years	At 54 Months
Survival (95% CI)	94.4% (93.4%, 95.3%)	91.7% (90.3%, 92.9%)	90.3% (88.6%, 91.7%)	89.0% (86.9%, 90.8%)	87.9% (85.2%, 90.1%)
Sample Size	1,677	941	484	162	52

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

Model Vectris SureScan MRI 1x8 Subcompact

Model Name	Vectris SureScan MRI 1x8 Subcompact (model 977A1)
FDA Approval Date	March 2013
Leads Enrolled	130
Leads Currently Active in Study	54
Device Events	9
Cumulative Months of Follow-up	2,550



Time Interval	1 Year	2 Years	3 Years
Survival (95% CI)	95.2% (88.8%, 98.0%)	89.1% (79.6%, 94.4%)	89.1% (79.6%, 94.4%)
Sample Size	73	44	25

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

4.4.3 Lead Survival Summary

Table 4.46: Spinal Cord Stimulation Percutaneous Lead Characteristics

Model Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Cumulative Follow-up Months
1x8 Compact (model 3778)	April 2005	2,161	267	278	61,383
1x8 SC (model 3776)	November 2005	186	29	15	4,806
1x8 Standard (model 3777)	April 2005	836	104	71	21,419
Pisces Compact (model 3887)	January 1997	196	50	29	5,963
Pisces Plus (model 3888)	November 1992	446	60	42	10,009
Pisces Standard (model 3487A)	May 1988	986	99	198	38,755
Vectris SureScan MRI 1x8 Compact (model 977A2)	March 2013	3,192	2,009	194	56,468
Vectris SureScan MRI 1x8 Subcompact (model 977A1)	March 2013	130	54	9	2,550

Table 4.47: Spinal Cord Stimulation Percutaneous Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
1x8 Compact (model 3778)	89.7% (88.2%, 91.1%)	86.2% (84.3%, 87.8%)	84.1% (82.0%, 86.0%)	83.6% (81.4%, 85.5%)	80.9% (78.3%, 83.2%)
1x8 SC (model 3776)	91.6% (85.4%, 95.3%)	91.6% (85.4%, 95.3%)	91.6% (85.4%, 95.3%)	89.6% (81.6%, 94.3%)	89.6% (81.6%, 94.3%)
1x8 Standard (model 3777)	92.4% (89.9%, 94.4%)	89.4% (86.3%, 91.8%)	89.4% (86.3%, 91.8%)	88.8% (85.5%, 91.4%)	87.2% (83.1%, 90.4%)
Pisces Compact (model 3887)	92.3% (77.7%, 97.5%)	82.9% (69.3%, 90.9%)	76.5% (62.7%, 85.7%)	75.1% (61.3%, 84.5%)	71.3% (57.3%, 81.4%)
Pisces Plus (model 3888)	91.3% (86.6%, 94.4%)	89.9% (84.9%, 93.4%)	86.2% (79.8%, 90.7%)	81.5% (74.0%, 87.0%)	79.1% (70.9%, 85.2%)
Pisces Standard (model 3487A)	90.7% (88.0%, 92.8%)	87.9% (84.9%, 90.4%)	81.3% (77.6%, 84.4%)	74.0% (69.7%, 77.8%)	69.6% (65.0%, 73.8%)
Vectris SureScan MRI 1x8 Compact (model 977A2)	94.4% (93.4%, 95.3%)	91.7% (90.3%, 92.9%)	90.3% (88.6%, 91.7%)	89.0% (86.9%, 90.8%)	
Vectris SureScan MRI 1x8 Subcompact (model 977A1)	95.2% (88.8%, 98.0%)	89.1% (79.6%, 94.4%)	89.1% (79.6%, 94.4%)		

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
1x8 Compact (model 3778)	79.3% (76.3%, 81.9%)	75.6% (71.8%, 78.9%)	72.5% (68.0%, 76.6%)	72.5% (68.0%, 76.6%)	72.5% (68.0%, 76.6%)
1x8 SC (model 3776)					
1x8 Standard (model 3777)	85.1% (79.8%, 89.1%)	82.7% (76.4%, 87.5%)	79.1% (70.7%, 85.3%)	75.6% (66.1%, 82.9%)	75.6% (66.1%, 82.9%)
Pisces Compact (model 3887)	69.0% (54.6%, 79.6%)	66.6% (51.9%, 77.7%)			
Pisces Plus (model 3888)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)	75.8% (66.6%, 82.9%)
Pisces Standard (model 3487A)	65.2% (60.2%, 69.8%)	62.9% (57.7%, 67.6%)	62.9% (57.7%, 67.6%)	57.1% (51.2%, 62.5%)	54.5% (48.4%, 60.2%)
Vectris SureScan MRI 1x8 Compact (model 977A2)					
Vectris SureScan MRI 1x8 Subcompact (model 977A1)					

Model Name	11 Years	12 Years	13 Years	14 Years	
1x8 Compact (model 3778)					
1x8 SC (model 3776)					
1x8 Standard (model 3777)	71.9% (61.3%, 80.1%)	71.9% (61.3%, 80.1%)			
Pisces Compact (model 3887)					
Pisces Plus (model 3888)					
Pisces Standard (model 3487A)	51.5% (45.0%, 57.6%)	48.3% (41.3%, 55.0%)	48.3% (41.3%, 55.0%)	48.3% (41.3%, 55.0%)	
Vectris SureScan MRI 1x8 Compact (model 977A2)					
Vectris SureScan MRI 1x8 Subcompact (model 977A1)					

Table 4.48: Spinal Cord Stimulation Surgical Lead Characteristics

Model Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Cumulative Follow-up Months
Specify (model 3998)	February 1998	156	24	10	3,845
Specify 5-6-5 (model 39565)	June 2007	286	53	13	6,617

Table 4.49: Spinal Cord Stimulation Surgical Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Specify (model 3998)	97.1% (88.7%, 99.3%)	91.7% (81.1%, 96.5%)	88.8% (76.0%, 95.0%)		
Specify 5-6-5 (model 39565)	96.3% (92.8%, 98.1%)	95.6% (91.7%, 97.7%)	95.6% (91.7%, 97.7%)	91.4% (82.3%, 95.9%)	

4.5 Extensions

From June 2004 to the report cut-off date of October 31, 2018, there were 3,415 extensions followed in the registry. The difference between the total number of extensions (n=3,415) versus neurostimulators (n=5,763) were due to the fact that some systems did not use an extension. The aggregate prospective follow-up time for all extensions was 95,762 months (7,980 years). An extension is a set of thin wires with a protective coating that connects the neurostimulator to the lead. Table 4.50 provides the number and percentage of extensions by model.

Table 4.50: Spinal Cord Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**2,325 (68.1%)**
1x8 (37081)	1,453 (42.6%)
Bifurcated Stretch-Coil (37082)	632 (18.5%)
Single Stretch-Coil (37083)	240 (7.0%)
No longer manufactured	**1,076 (31.5%)**
Low Profile Quad (7489)	757 (22.2%)
Quadripolar in-line (7495)	276 (8.1%)
Synergy bifurcated 1x8 (7472)	25 (0.7%)
Quadripolar (7496)	9 (0.3%)
Synergy 1x8 (7471)	9 (0.3%)
Other/Unspecified	**14 (0.4%)**
Total	**3,415 (100%)**

4.5.1 Extension Events

There were 46 product performance-related events with an underlying reported etiology related to extension function. This includes 36 events with an extension etiology and 10 events with both an extension and other etiology (including device and non-device etiologies). Of these, 37 were the initial product performance event that affected extension survival estimates; the majority were extension fractures (n=17), and high impedance (n=17).

The extension product performance-related events are summarized by model in Table 4.51 to Table 4.55. Other/unspecified models and models without events are not shown.

Table 4.51: Event Summary Table: 1x8 Extension (model 37081)

Extension Event	N
High impedance	7
Extension fracture	6
Extension migration	2
Low impedance	1
Total	**16**

Table 4.52: Event Summary Table: Bifurcated Stretch-Coil Extension (model 37082)

Extension Event	N
Device connection issue	2
Extension fracture	2
Total	**4**

Table 4.53: Event Summary Table: Low Profile Quad Extension (model 7489)

Extension Event	N
Extension fracture	2
Extension migration	2
Medical device complication	1
Total	**5**

Table 4.54: Event Summary Table: Single Stretch-Coil Extension (model 37083)

Extension Event	N
Extension fracture	5
Device failure	1
Extension migration	1
Total	**7**

Table 4.55: Event Summary Table: Synergy bifurcated 1x8 extension (model 7472)

Extension Event	N
High impedance	4
Extension fracture	1
Total	**5**

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:

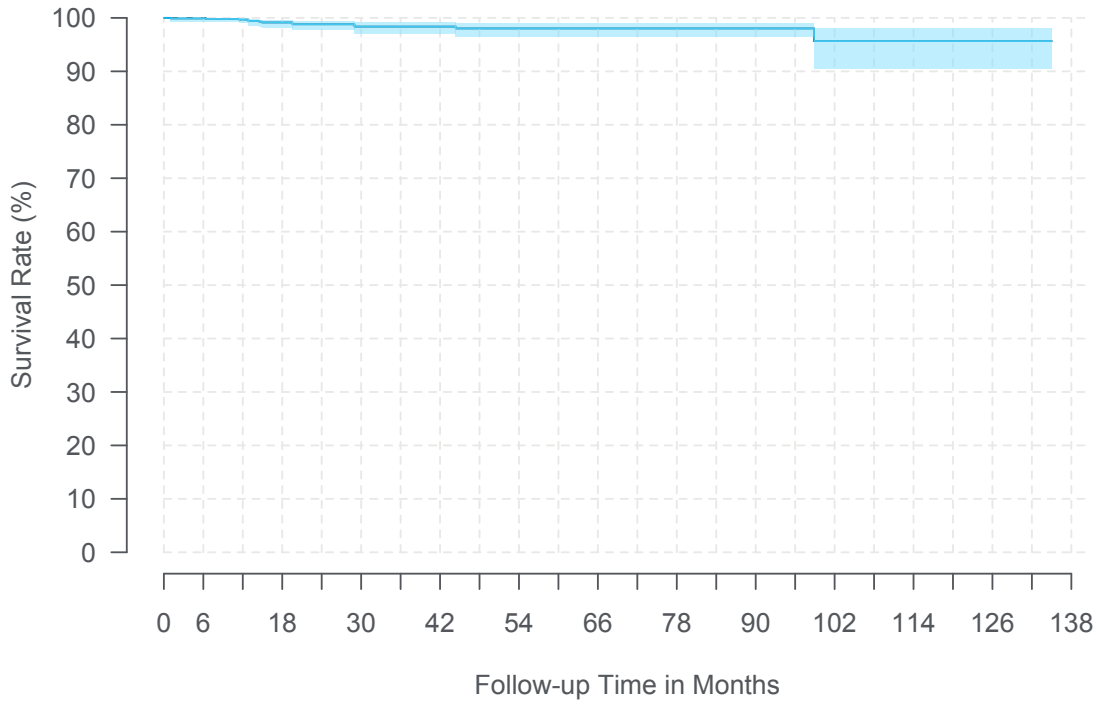
- 37 had follow-up time cut-off due to product performance-related events.
- 2,724 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 654 were free 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 Survival

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.

Model 1x8 Extension

Model Name	1x8 Extension (model 37081)
FDA Approval Date	April 2005
Extensions Enrolled	1,453
Extensions Currently Active in Study	398
Device Events	16
Cumulative Months of Follow-up	38,043



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.7% (99.0%, 99.9%)	98.8% (97.7%, 99.4%)	98.4% (97.0%, 99.1%)	98.0% (96.4%, 98.9%)	98.0% (96.4%, 98.9%)
Sample Size	801	498	331	262	206

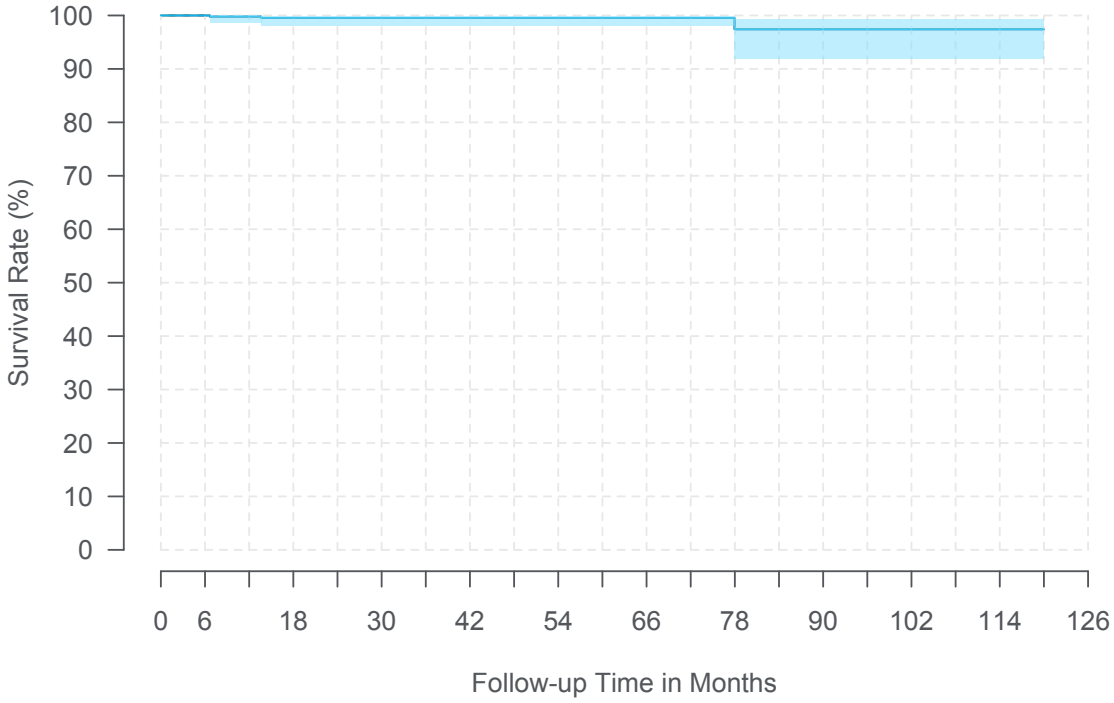
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	98.0% (96.4%, 98.9%)	98.0% (96.4%, 98.9%)	98.0% (96.4%, 98.9%)	95.7% (90.5%, 98.1%)	95.7% (90.5%, 98.1%)
Sample Size	160	118	90	64	49

Time Interval	11 Years	At 135 Months			
Survival (95% CI)	95.7% (90.5%, 98.1%)	95.7% (90.5%, 98.1%)			
Sample Size	25	21			

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

Model Bifurcated Stretch-Coil Extension

Model Name	Bifurcated Stretch-Coil Extension (model 37082)
FDA Approval Date	March 2006
Extensions Enrolled	632
Extensions Currently Active in Study	53
Device Events	4
Cumulative Months of Follow-up	21,192



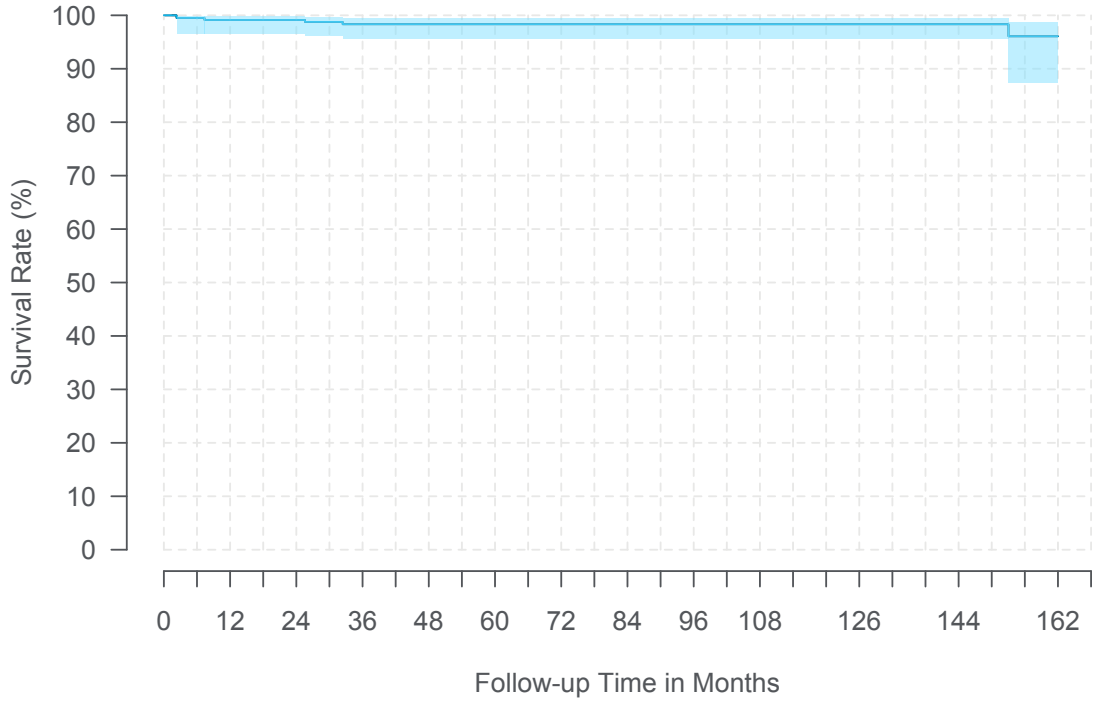
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.8% (98.5%, 100%)	99.5% (98.2%, 99.9%)	99.5% (98.2%, 99.9%)	99.5% (98.2%, 99.9%)	99.5% (98.2%, 99.9%)
Sample Size	423	297	208	153	122

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	99.5% (98.2%, 99.9%)	97.4% (91.9%, 99.2%)	97.4% (91.9%, 99.2%)	97.4% (91.9%, 99.2%)	97.4% (91.9%, 99.2%)
Sample Size	101	80	57	40	23

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

Model Low Profile Quad Extension

Model Name	Low Profile Quad Extension (model 7489)
FDA Approval Date	October 2002
Extensions Enrolled	757
Extensions Currently Active in Study	83
Device Events	5
Cumulative Months of Follow-up	19,726



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

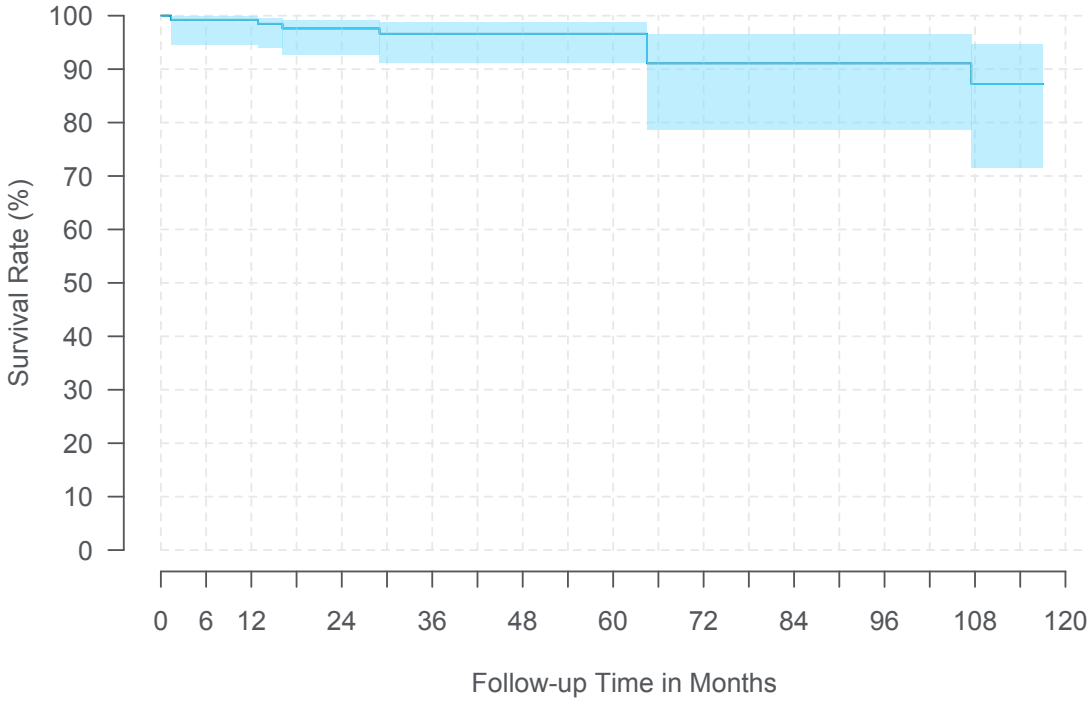
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)
Sample Size	83	68	66	64	65

Time Interval	11 Years	12 Years	13 Years	At 162 Months	
Survival (95% CI)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	96.1% (87.4%, 98.8%)	96.1% (87.4%, 98.8%)	
Sample Size	68	62	35	26	

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

Model Single Stretch-Coil Extension

Model Name	Single Stretch-Coil Extension (model 37083)
FDA Approval Date	September 2005
Extensions Enrolled	240
Extensions Currently Active in Study	51
Device Events	7
Cumulative Months of Follow-up	7,050



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.2% (94.6%, 99.9%)	97.6% (92.8%, 99.2%)	96.6% (91.1%, 98.7%)	96.6% (91.1%, 98.7%)	96.6% (91.1%, 98.7%)
Sample Size	134	112	68	52	34

Time Interval	6 Years	7 Years	8 Years	9 Years	At 117 Months
Survival (95% CI)	91.1% (78.6%, 96.4%)	91.1% (78.6%, 96.4%)	91.1% (78.6%, 96.4%)	87.2% (71.5%, 94.6%)	87.2% (71.5%, 94.6%)
Sample Size	29	30	26	22	20

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

4.5.3 Extension Survival Summary

Table 4.56: Spinal Cord Stimulation Extension Characteristics

Model Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Device Events	Cumulative Follow-up Months
1x8 Extension (model 37081)	April 2005	1,453	398	16	38,043
Bifurcated Stretch-Coil Extension (model 37082)	March 2006	632	53	4	21,192
Low Profile Quad Extension (model 7489)	October 2002	757	83	5	19,726
Single Stretch-Coil Extension (model 37083)	September 2005	240	51	7	7,050

Table 4.57: Spinal Cord Stimulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
1x8 Extension (model 37081)	99.7% (99.0%, 99.9%)	98.8% (97.7%, 99.4%)	98.4% (97.0%, 99.1%)	98.0% (96.4%, 98.9%)	98.0% (96.4%, 98.9%)
Bifurcated Stretch-Coil Extension (model 37082)	99.8% (98.5%, 100%)	99.5% (98.2%, 99.9%)	99.5% (98.2%, 99.9%)	99.5% (98.2%, 99.9%)	99.5% (98.2%, 99.9%)
Low Profile Quad Extension (model 7489)	99.1% (96.5%, 99.8%)	99.1% (96.5%, 99.8%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)
Single Stretch-Coil Extension (model 37083)	99.2% (94.6%, 99.9%)	97.6% (92.8%, 99.2%)	96.6% (91.1%, 98.7%)	96.6% (91.1%, 98.7%)	96.6% (91.1%, 98.7%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
1x8 Extension (model 37081)	98.0% (96.4%, 98.9%)	98.0% (96.4%, 98.9%)	98.0% (96.4%, 98.9%)	95.7% (90.5%, 98.1%)	95.7% (90.5%, 98.1%)
Bifurcated Stretch-Coil Extension (model 37082)	99.5% (98.2%, 99.9%)	97.4% (91.9%, 99.2%)	97.4% (91.9%, 99.2%)	97.4% (91.9%, 99.2%)	97.4% (91.9%, 99.2%)
Low Profile Quad Extension (model 7489)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)
Single Stretch-Coil Extension (model 37083)	91.1% (78.6%, 96.4%)	91.1% (78.6%, 96.4%)	91.1% (78.6%, 96.4%)	87.2% (71.5%, 94.6%)	

Model Name	11 Years	12 Years	13 Years		
1x8 Extension (model 37081)	95.7% (90.5%, 98.1%)				
Bifurcated Stretch-Coil Extension (model 37082)					
Low Profile Quad Extension (model 7489)	98.3% (95.6%, 99.4%)	98.3% (95.6%, 99.4%)	96.1% (87.4%, 98.8%)		
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, 2018. Thirty-eight centers in North America, Europe and South America, have enrolled and contributed patients to the deep brain stimulation systems section of this report.

5.1.2 Patients

Of the 2,537 deep brain stimulation patients enrolled, the primary indications for implant were as follows: 64.2% were implanted for the treatment of Parkinson's Disease, 22.9% were implanted for the treatment of essential tremor, 8.4% were implanted for the treatment of dystonia, 0.9% were implanted for the treatment of epilepsy, 0.9% were implanted for the treatment of obssesive compulsive disorder, 2.4% were implanted for the treatment of other indications, and 0.4% were implanted for indications that were not specified in the database at the time of data cut-off (see Figure 5.1 and Table 5.1).

As outlined in the PSR protocol, enrollment may be limited when the number of patients enrolled are sufficient to characterize product performance. As such an enrollment guide was implemented in the Fall of 2016, limiting future enrollment of Parkinson's disease patients. The enrollment guide was implemented using a staged approach across all sites. Therapy-naïve patients in other indications (e.g., essential tremor, dystonia) continue to be enrolled to generate evidence for those indications.

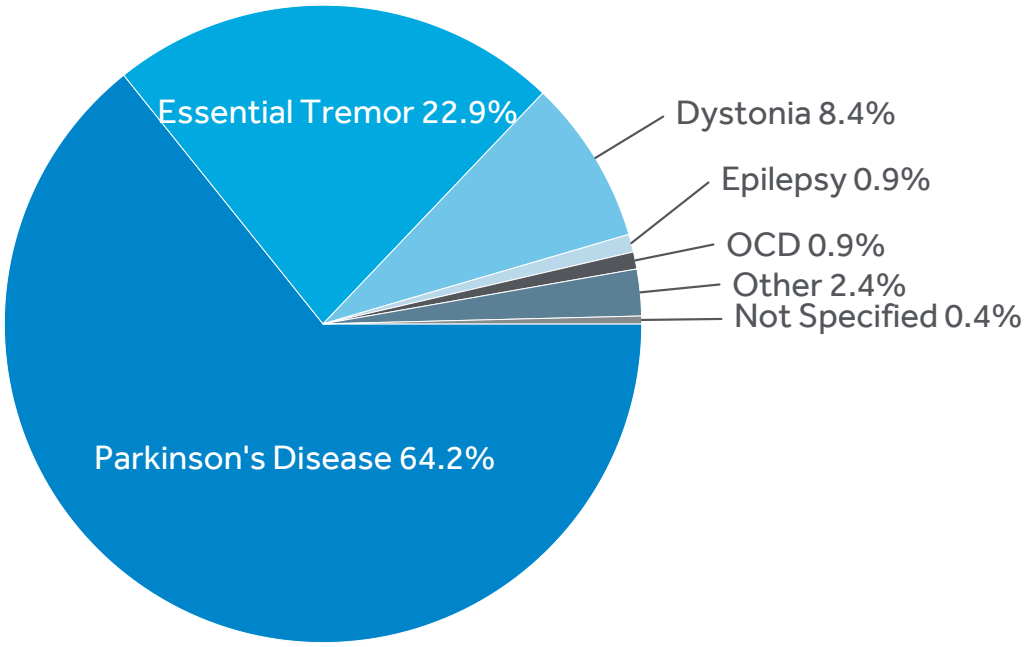


Figure 5.1: Deep Brain Stimulation Primary Treatment Indications

Table 5.1: Deep Brain Stimulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Parkinson's Disease	1,630 (64.2%)
Essential Tremor	580 (22.9%)
Dystonia	212 (8.4%)
Epilepsy	23 (0.9%)
OCD	22 (0.9%)
Other	60 (2.4%)
Not Specified[b]	10 (0.4%)
Total Patients	**2,537(100%)**

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

[b] Includes 8 patients exited prior to baseline and 2 patients with pending further information at time of data cut-off.

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 296 product performance events reported between July 2009 and October 31, 2018, in patients with deep brain stimulation systems. These events represent 19.3% of the total reported events (296/1,533), occured in 177 of the 2,537 (7.0%) 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 1,235 non-product performance events that were collected to understand patient experience (clinical signs and symptoms) with the deep brain stimulation systems (see Table 5.5 and Table 5.6). As an ongoing registry, events not coded at the time of the data snapshot (waiting on further information) will be included in future reports (n=2).

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

5.2.1 Product Performance Events

Table 5.2: Deep Brain Stimulation System Product Performance Events

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%)[b]
RPA Determination	**2**	**0.03**	**2 (0.08%)**
Premature Battery Depletion	2	0.03	2 (0.08%)
Physician's Determination	**294**	**4.51**	**176 (6.94%)**
High Impedance	155	2.38	85 (3.35%)
Lead Migration/Dislodgement	34	0.52	27 (1.06%)
Device Malfunction	20	0.31	15 (0.59%)
Lead Fracture	20	0.31	15 (0.59%)
Low Impedance	14	0.21	10 (0.39%)
Extension Migration	12	0.18	8 (0.32%)
Medical Device Complication	11	0.17	9 (0.35%)
Neurostimulator Unable To Recharge[c]	9	0.14	9 (0.35%)
Device Breakage	5	0.08	5 (0.20%)
Extension Fracture	4	0.06	4 (0.16%)

...continued

Product Performance Events[a]	Event Counts	Events Per 100 Patient Years	Patients with Events (%)[b]
Premature Battery Depletion	3	0.05	3 (0.12%)
Device Connection Issue	2	0.03	2 (0.08%)
Device Material Issue	2	0.03	1 (0.04%)
Other[d]	3	0.05	3 (0.12%)
Total	**296**	**4.55**	**177 (6.98%)**

[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 413 patients that used rechargeable neurostimulators for DBS in the registry. A total of 2.18% (9/413) 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 134 (45.3%) of the 296 product performance events were related to the lead, 54 (18.2%) were related to the extension, 48 (16.2%) were related to the neurostimulator, 19 (6.4%) were related to multiple etiologies, which includes events where at least one device and one non-device etiology was indicated, 21 (7.1%) were related to other component, 11 (3.7%) were related to surgery/anesthesia, 5 (1.7%) were related to recharging process, 3 (1.0%) were related to programming/stimulation, and 1 (0.3%) was related to incisional site/device tract (see Figure 5.2). Events could have more than one etiology.

Relatedness is reported by the physician. In cases where the 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.

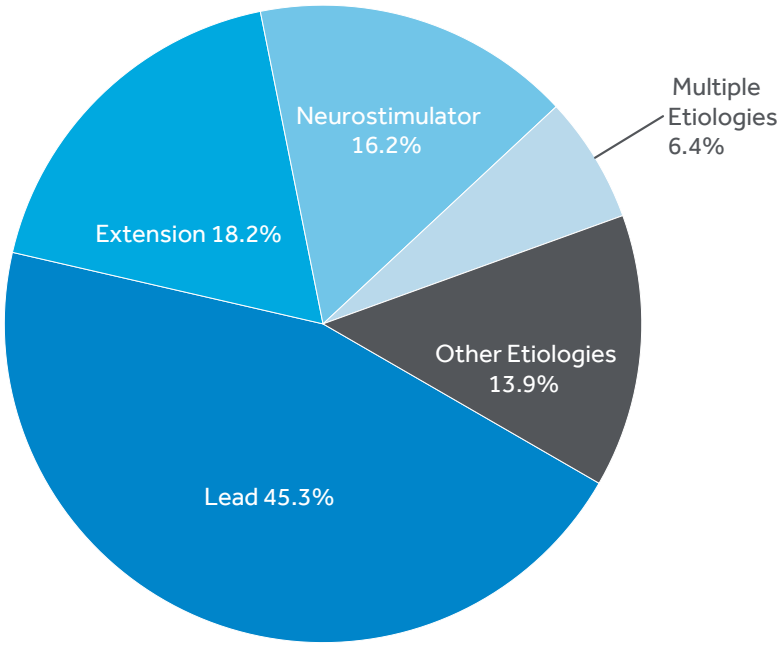


Figure 5.2: Deep Brain Stimulation System Product Performance Events by Relatedness

Table 5.3 and Table 5.4 describe the interventions taken for reported impedance events. In 42.6% and 21.4% of the high and low impedance events, the action taken was a surgical intervention. However, impedance could be used as a diagnostic measurement and may not result in any intervention or clinical impact. The majority of events required no intervention or device reprogramming only (57.4% for high impedance and 78.6% for low impedance). All events are reflected in lead survival curves.

Table 5.3: Deep Brain Stimulation System High Impedance Event by Last Intervention

Intervention	N (%) of High Impedance Events
Surgical Intervention	66 (42.6%)
No Action Taken	51 (32.9%)
Reprogramming	38 (24.5%)
Total High Impedance Events	**155 (100%)**

Table 5.4: Deep Brain Stimulation System Low Impedance Event by Last Intervention

Intervention	N (%) of Low Impedance Events
No Action Taken	7 (50.0%)
Reprogramming	4 (28.6%)
Surgical Intervention	3 (21.4%)
Total Low Impedance Events	**14 (100%)**

5.2.2 Non-Product Performance Events

Adverse events and device events that were not related to a product performance event are categorized in Table 5.5 and Table 5.6 by event group term. The 'other' code is composed of event codes with fewer than 5 events each. These events do not include deaths (see Section 5.2.3) or normal battery depletions. As explained in the Methodology section of this report, this registry's event reporting has evolved over time. Therefore, the event counts are strictly the sum of the events collected up to the October 31, 2018 data cut-off. **All 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 Non-Behavioral Non-Product Performance Events

Non-Behavioral Non-Product Performance Events	Event Counts
Movement disorders (including parkinsonism)	**251**
Tremor	110
Dyskinesia	61
Dystonia	30
Freezing Phenomenon	13
Parkinson's Disease	8
Bradykinesia	7
Resting Tremor	5
Other	17
Neurological disorders NEC	**173**
Dysarthria	50
Speech Disorder	43
Paraesthesia	30
Balance Disorder	28
Sensory Disturbance	7
Other	15
Infections - pathogen unspecified	**122**
Medical Device Site Infection	88
Wound Infection	19
Other	15

...continued

Non-Behavioral Non-Product Performance Events	Event Counts
Complications associated with device	**81**
Medical Device Site Pain	18
Medical Device Site Erosion	17
Medical Device Site Inflammation	8
Medical Device Site Laceration	6
Medical Device Discomfort	5
Medical Device Site Erythema	5
Other	22
Device issues	**56**
Neurostimulator Migration	30
Device Extrusion	7
Neurostimulator Unable To Recharge (Patient Related)	6
Other	13
General system disorders NEC	**47**
Gait Disturbance	36
Other	11
Procedural related injuries and complications NEC	**37**
Wound Dehiscence	19
Other	18
Injuries NEC	**27**
Fall	9
Subdural Haematoma	8
Other	10
Central nervous system vascular disorders	**25**
Cerebral Haematoma	9
Other	16
Musculoskeletal and connective tissue disorders NEC	**15**
Mobility Decreased	5
Musculoskeletal Stiffness	5
Other	5
Bacterial infectious disorders	**14**
Staphylococcal Infection	10
Other	4
Physical examination and organ system status topics	**13**
Weight Increased	13
Seizures (including subtypes)	**12**
Seizure	6
Other	6
Muscle disorders	**10**
Other	10

...continued

Non-Behavioral Non-Product Performance Events	Event Counts
Therapeutic and nontherapeutic effects (excluding toxicity)	**10**
Therapeutic Product Ineffective	5
Other	5
Medication errors and other product use errors and issues	**9**
Other	9
Personality disorders and disturbances in behaviour	**7**
Other	7
Gastrointestinal signs and symptoms	**6**
Dysphagia	5
Other	1
Headaches	**6**
Other	6
Vascular haemorrhagic disorders	**5**
Other	5
Other	**43**
Total	**969**

Table 5.6: Deep Brain Stimulation System Behavioral Non-Product Performance Events

Behavioral Non-Product Performance Events	Event Counts
Depressed mood disorders and disturbances	**75**
Depression	64
Other	11
Anxiety disorders and symptoms	**35**
Anxiety	26
Other	9
Disturbances in thinking and perception	**29**
Hallucination	26
Other	3
Mood disorders and disturbances NEC	**22**
Apathy	8
Affect Lability	7
Other	7
Deliria (including confusion)	**21**
Confusional State	14
Delirium	7
Psychiatric and behavioural symptoms NEC	**20**
Abnormal Behaviour	18
Other	2

...continued

Behavioral Non-Product Performance Events	Event Counts
Suicidal and self-injurious behaviours NEC	**17**
Suicidal Ideation	10
Suicide Attempt	7
Mental impairment disorders	**12**
Cognitive Disorder	8
Other	4
Psychiatric disorders NEC	**11**
Mental Disorder	6
Mental Status Changes	5
Manic and bipolar mood disorders and disturbances	**6**
Other	6
Other	**18**
Total	**266**

5.2.3 Patient Deaths

There were 171 deaths reported for patients with deep brain stimulation systems, none of which were reported as a direct result of a product performance event. Since 2009, a total of 137 (80.1%) deaths have been reported in this patient registry study based upon patients receiving therapy for Parkinson's Disease, 27 (15.8%) for essential tremor, 6 (3.5%) for dystonia, and 1 (0.6%) for other indication (see Table 5.7). The percentage is based upon the total patient death events and not based upon the rate of occurrence. As mentioned previously, **all tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

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

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Parkinson's Disease	137 (80.1%)
Essential Tremor	27 (15.8%)
Dystonia	6 (3.5%)
Other	1 (0.6%)
Total	**171 (100%)**

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

5.3 Neurostimulators

From July 2009 to the report cut-off date of October 31, 2018, there were 3,562 neurostimulators followed in the registry. The difference between the total number of patients (n=2,537) versus the number of neurostimulators (n=3,562) 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 83,787 months (6,982 years). Table 5.8 provides the number and percentage of neurostimulators by model.

Table 5.8: Deep Brain Stimulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	
Activa PC	2,131 (59.9%)
Activa SC	901 (25.3%)
Activa RC	420 (11.8%)
Other/Unspecified[a]	31 (0.9%)
No longer manufactured	
Soletra	67 (1.9%)
Kinetra	12 (0.3%)
Total	**3,562 (100%)**

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

5.3.1 Neurostimulator Events

Of the total of 2537 product performance-related events, there were 50 product performance-related events with an underlying reported etiology related to neurostimulator function. This includes 48 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 6.0% (66/1,096). 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 50 neurostimulator events, 96.0 % (48/50) were assigned as device related by the physician, not returned to Medtronic RPA (see Table 5.9).

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

Product Performance Events	N (%)
RPA Determination	**2 (4.0%)**
Premature Battery Depletion	2 (4.0%)
Physician's Determination	**48 (96.0%)**
High Impedance	29 (58.0%)
Device Malfunction	9 (18.0%)
Medical Device Complication	3 (6.0%)
Premature Battery Depletion	3 (6.0%)
Low Impedance	2 (4.0%)
Electromagnetic Interference	1 (2.0%)
Extension Migration	1 (2.0%)
Total	**50 (100%)**

The neurostimulator product performance-related events are summarized by model in Table 5.10, Table 5.11, and Table 5.12. Events of other/unspecified models and discontinued models are not shown.

Table 5.10: Event Summary Table: Model Activa PC

Neurostimulator Event	N
High impedance	19
Device malfunction	6
Premature battery depletion	4
Low impedance	2
Medical device complication	2
Electromagnetic interference	1
Total	**34**

Table 5.11: Event Summary Table: Model Activa SC

Neurostimulator Event	N
High impedance	4
Device malfunction	1
Medical device complication	1
Premature battery depletion	1
Total	**7**

Table 5.12: Event Summary Table: Model Activa RC

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

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.
- 1,727 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.
- 1,788 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.

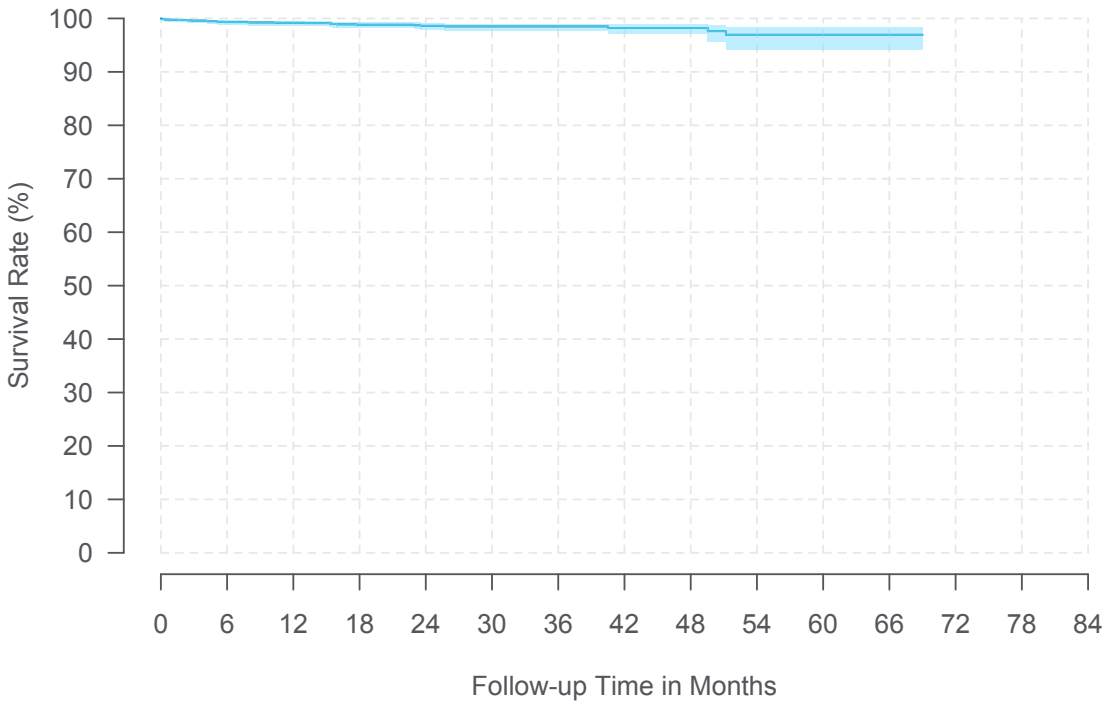
5.3.2 Neurostimulator Survival

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

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

Model Activa PC

Model Name	Activa PC
FDA Approval Date	April 2009
Neurostimulators Enrolled	2,131
Neurostimulators Currently Active in Study	1,116
Device Events	34
Cumulative Months of Follow-up	50,248



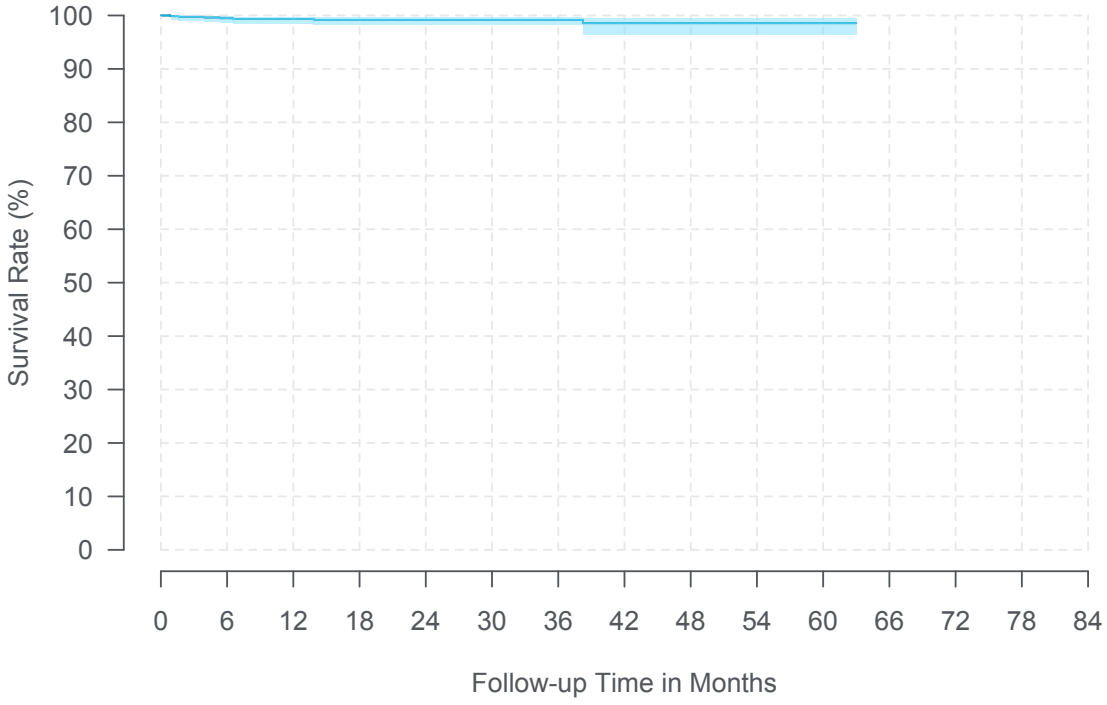
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.2% (98.7%, 99.5%)	98.6% (97.9%, 99.1%)	98.5% (97.7%, 99.0%)	98.2% (97.2%, 98.9%)	96.9% (94.2%, 98.4%)
Sample Size	1,503	943	488	183	64

Time Interval	At 69 Months
Survival (95% CI)	96.9% (94.2%, 98.4%)
Sample Size	24

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	$\leq$ 4 cm

Model Activa SC

Model Name	Activa SC
FDA Approval Date	January 2011
Neurostimulators Enrolled	901
Neurostimulators Currently Active in Study	397
Device Events	7
Cumulative Months of Follow-up	20,699



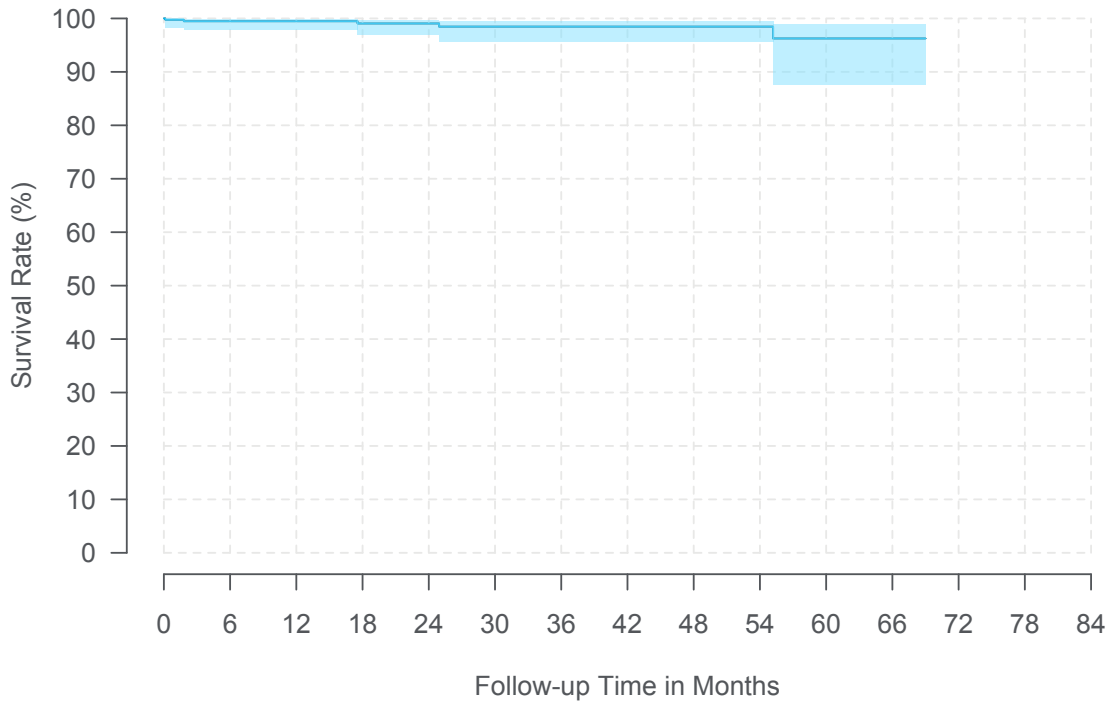
Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.3% (98.4%, 99.7%)	99.2% (98.2%, 99.6%)	99.2% (98.2%, 99.6%)	98.6% (96.3%, 99.4%)	98.6% (96.3%, 99.4%)
Sample Size	620	397	185	77	28

Time Interval	At 63 Months
Survival (95% CI)	98.6% (96.3%, 99.4%)
Sample Size	21

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	$\leq$ 4 cm

Model Activa RC

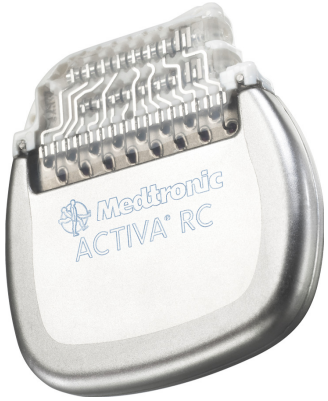
Model Name	Activa RC
FDA Approval Date	March 2009
Neurostimulators Enrolled	420
Neurostimulators Currently Active in Study	273
Device Events	5
Cumulative Months of Follow-up	10,410



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (97.9%, 99.9%)	99.1% (97.0%, 99.7%)	98.5% (95.7%, 99.5%)	98.5% (95.7%, 99.5%)	96.3% (87.6%, 98.9%)
Sample Size	296	175	102	56	38

Time Interval	At 69 Months
Survival (95% CI)	96.3% (87.6%, 98.9%)
Sample Size	23

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	≤ 1 cm



5.3.3 Neurostimulator Survival Summary

Table 5.13: Deep Brain Stimulation Neurostimulator Characteristics

Model Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Cumulative Follow-up Months
Activa PC	April 2009	2,131	1,116	34	50,248
Activa SC	January 2011	901	397	7	20,699
Activa RC	March 2009	420	273	5	10,410

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

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
Activa PC	99.2% (98.7%, 99.5%)	98.6% (97.9%, 99.1%)	98.5% (97.7%, 99.0%)	98.2% (97.2%, 98.9%)	96.9% (94.2%, 98.4%)
Activa SC	99.3% (98.4%, 99.7%)	99.2% (98.2%, 99.6%)	99.2% (98.2%, 99.6%)	98.6% (96.3%, 99.4%)	98.6% (96.3%, 99.4%)
Activa RC	99.5% (97.9%, 99.9%)	99.1% (97.0%, 99.7%)	98.5% (95.7%, 99.5%)	98.5% (95.7%, 99.5%)	96.3% (87.6%, 98.9%)

5.4 Leads

From July 2009 to the report cut-off date of October 31, 2018, there were 4,286 leads followed in the registry. The difference between the total number of leads (n=4,286) versus neurostimulators (n=3562) were 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 132,828 months (11,069 years). Table 5.15 provides the number and percentage of leads by model.

Table 5.15: Deep Brain Stimulation Lead Counts by Model

Model Name	N (%)
3389 (compact electrode spacing)	2,439 (56.9%)
3387 (standard electrode spacing)	1,805 (42.1%)
3391 (large electrodes and wide spacing)	27 (0.6%)
Other/Unspecified[a]	15 (0.3%)
Total	**4,286 (100%)**

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

5.4.1 Lead Events

Of the total of 2537 product performance-related events, there were 146 product performance-related events with an underlying reported etiology related to lead function. This includes 134 events with a lead etiology and 12 events with both a lead and other etiology (including device and non-device etiologies). Of these, 119 were the initial product performance event that affected lead survival estimates.

The lead product performance-related events are summarized by model in Table 5.16 and Table 5.17. Events of other/unspecified models are not shown. Model 3391 did not have any product performance-related events.

Table 5.16: Event Summary Table: Model 3387

Lead Event	N
High impedance	13
Lead migration/dislodgement	8
Lead fracture	3
Low impedance	3
Medical device complication	1
Total	**28**

Table 5.17: Event Summary Table: Model 3389

Lead Event	N
High impedance	55
Lead migration/dislodgement	14
Lead fracture	8
Low impedance	6
Device material issue	2
Device malfunction	1
Total	**86**

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:

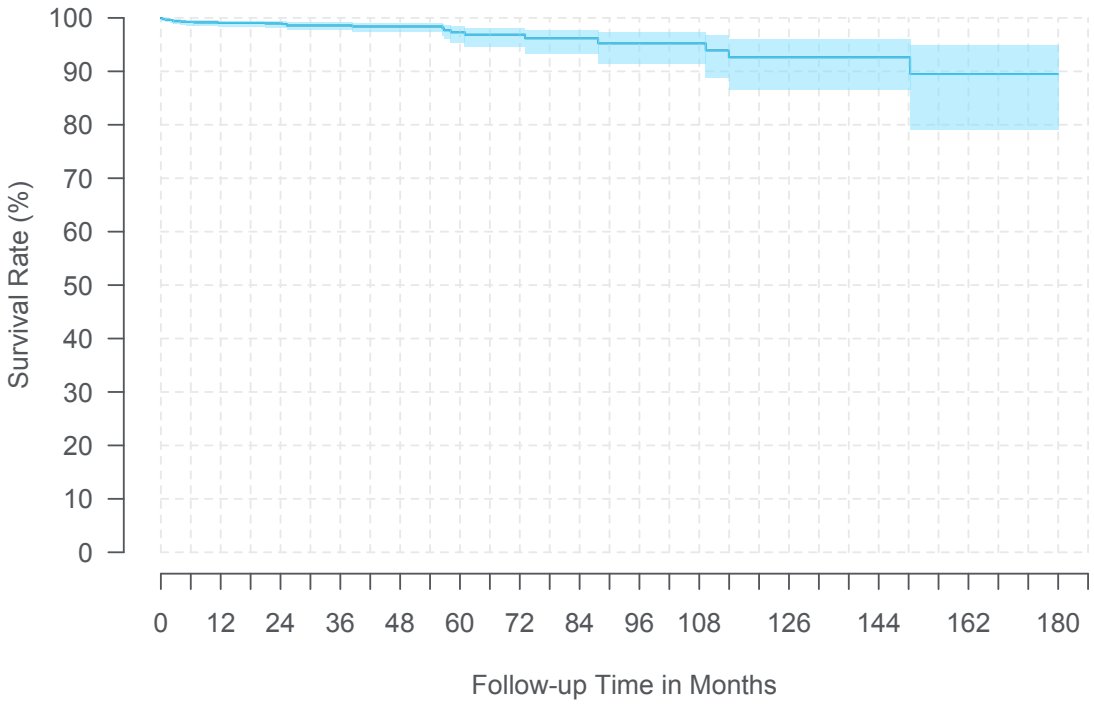
- 119 had follow-up time cut-off due to product performance-related events.
- 1,360 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,807 were free 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 Survival

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.

Model 3387

Model Name	3387
FDA Approval Date	July 1997
Leads Enrolled	1,805
Leads Currently Active in Study	1,138
Device Events	28
Cumulative Months of Follow-up	54,672



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.1% (98.4%, 99.5%)	99.0% (98.2%, 99.4%)	98.6% (97.7%, 99.1%)	98.4% (97.4%, 99.0%)	97.3% (95.4%, 98.4%)
Sample Size	1,194	800	550	371	236

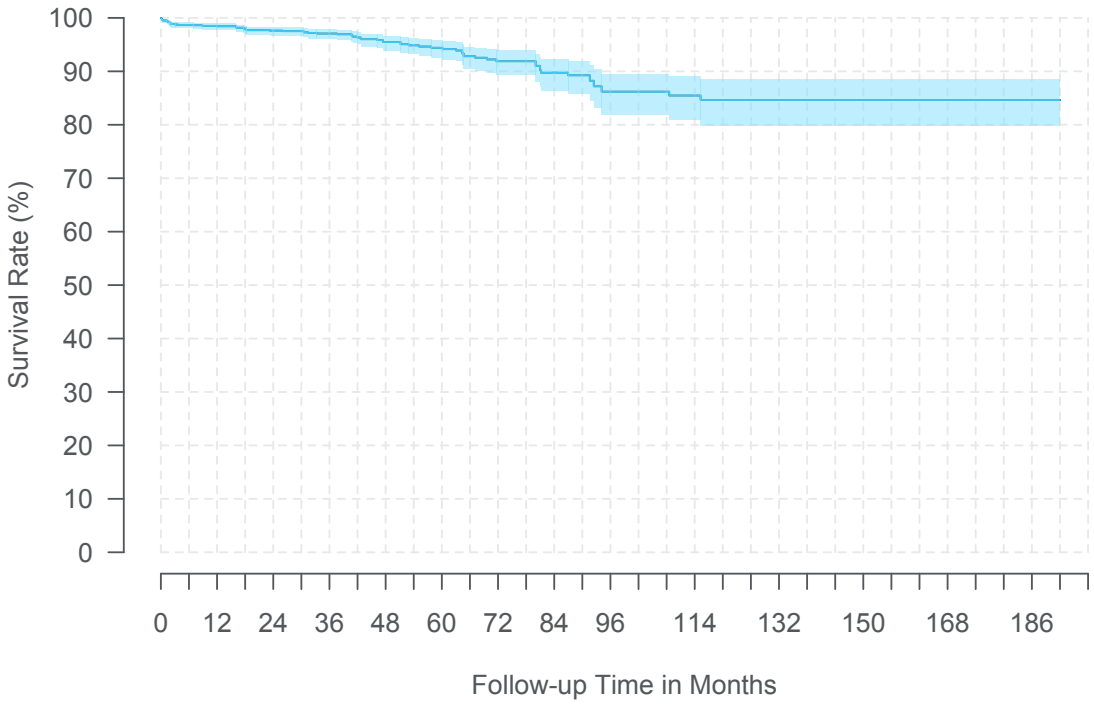
Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	96.9% (94.6%, 98.2%)	96.2% (93.3%, 97.8%)	95.2% (91.5%, 97.4%)	95.2% (91.5%, 97.4%)	92.6% (86.6%, 96.0%)
Sample Size	143	113	81	68	62

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	92.6% (86.6%, 96.0%)	92.6% (86.6%, 96.0%)	89.5% (79.1%, 94.9%)	89.5% (79.1%, 94.9%)	89.5% (79.1%, 94.9%)
Sample Size	42	27	22	24	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

Model 3389

Model Name	3389
FDA Approval Date	September 1999
Leads Enrolled	2,439
Leads Currently Active in Study	1,705
Device Events	86
Cumulative Months of Follow-up	76,767



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.4% (97.8%, 98.9%)	97.6% (96.7%, 98.3%)	97.1% (96.0%, 97.8%)	95.5% (94.0%, 96.6%)	94.4% (92.6%, 95.8%)
Sample Size	1,517	1,098	768	513	380

Time Interval	6 Years	7 Years	8 Years	9 Years	10 Years
Survival (95% CI)	91.9% (89.3%, 93.9%)	89.8% (86.5%, 92.3%)	86.2% (81.9%, 89.5%)	86.2% (81.9%, 89.5%)	84.6% (79.8%, 88.4%)
Sample Size	274	188	162	121	83

Time Interval	11 Years	12 Years	13 Years	14 Years	15 Years
Survival (95% CI)	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)
Sample Size	76	56	52	47	31

Time Interval	16 Years
Survival (95% CI)	84.6% (79.8%, 88.4%)
Sample Size	20

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

5.4.3 Lead Survival Summary

Table 5.18: Deep Brain Stimulation Lead Characteristics

Model Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Cumulative Follow-up Months
3387	July 1997	1,805	1,138	28	54,672
3389	September 1999	2,439	1,705	86	76,767

Table 5.19: Deep Brain Stimulation Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
3387	99.1% (98.4%, 99.5%)	99.0% (98.2%, 99.4%)	98.6% (97.7%, 99.1%)	98.4% (97.4%, 99.0%)	97.3% (95.4%, 98.4%)
3389	98.4% (97.8%, 98.9%)	97.6% (96.7%, 98.3%)	97.1% (96.0%, 97.8%)	95.5% (94.0%, 96.6%)	94.4% (92.6%, 95.8%)

Model Name	6 Years	7 Years	8 Years	9 Years	10 Years
3387	96.9% (94.6%, 98.2%)	96.2% (93.3%, 97.8%)	95.2% (91.5%, 97.4%)	95.2% (91.5%, 97.4%)	92.6% (86.6%, 96.0%)
3389	91.9% (89.3%, 93.9%)	89.8% (86.5%, 92.3%)	86.2% (81.9%, 89.5%)	86.2% (81.9%, 89.5%)	84.6% (79.8%, 88.4%)

Model Name	11 Years	12 Years	13 Years	14 Years	15 Years
3387	92.6% (86.6%, 96.0%)	92.6% (86.6%, 96.0%)	89.5% (79.1%, 94.9%)	89.5% (79.1%, 94.9%)	89.5% (79.1%, 94.9%)
3389	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)	84.6% (79.8%, 88.4%)

Model Name	16 Years				
3387					
3389	84.6% (79.8%, 88.4%)				

5.5 Extensions

From July 2009 to the report cut-off date of October 31, 2018, there were 4,332 extensions followed in the registry. The difference between the total number of extensions (n=4,332) versus neurostimulators (n=3,562) were 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 130,539 months (10,878 years). The table below provides the number and percentage of extensions by model. Table 5.20 provides the number and percentage of extensions by model.

Table 5.20: Deep Brain Stimulation Extension Counts by Model

Model Name	N (%)
Currently manufactured	
37085/37086 (quadripolar stretch)	3,730 (86.1%)
Other/Unspecified[a]	115 (2.7%)
No longer manufactured	
7482[b] (quadripolar)	487 (11.2%)
Total	**4,332 (100%)**

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

5.5.1 Extension Events

Of the total of 2537 product performance-related events, there were 58 product performance-related events with an underlying reported etiology related to extension function. This includes 54 events with an extension etiology and 4 events with both an extension and other etiology (including device and non-device etiologies). Of these, 54 were the initial product performance event that affected extension survival estimates.

The extension product performance-related events are summarized by model in Table 5.21. Events of other/unspecified models and discontinued models are not shown.

Table 5.21: Event Summary Table: Model 37085/37086

Extension Event	Total
High impedance	25
Extension migration	8
Medical device complication	4
Extension fracture	2
Low impedance	2
Device malfunction	1
Total Extension Events	**42**

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:

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

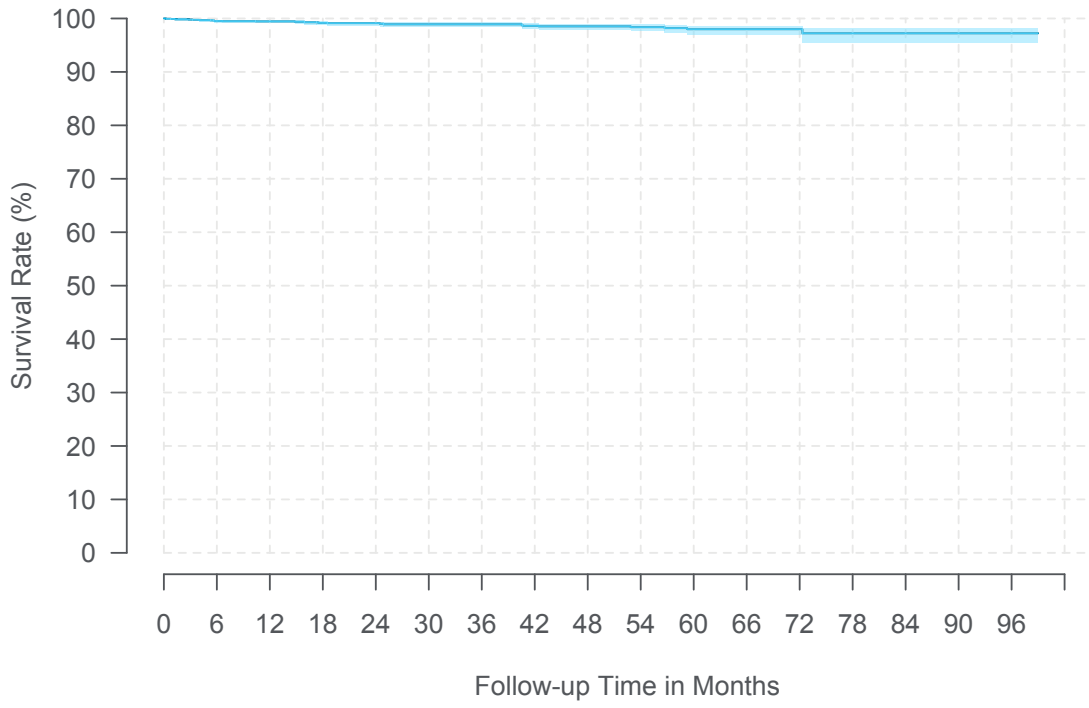
- 1,434 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 2,844 were free from product performance-related events and censoring events, and were censored at the last follow-up visit prior to the report cut-off.

5.5.2 Extension Survival

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

Model 37085/37086

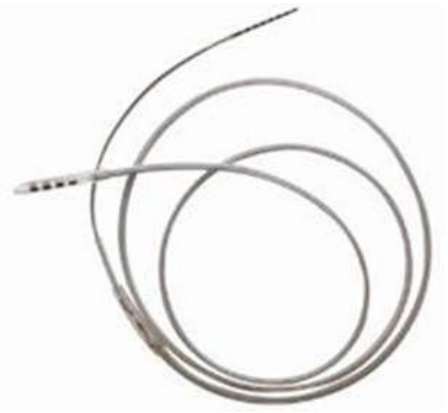
Model Name	37085/37086
FDA Approval Date	March 2009
Extensions Enrolled	3,730
Extensions Currently Active in Study	2,501
Device Events	42
Cumulative Months of Follow-up	109,729



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	99.5% (99.1%, 99.7%)	99.1% (98.7%, 99.4%)	98.9% (98.4%, 99.2%)	98.5% (97.9%, 99.0%)	98.0% (97.0%, 98.7%)
Sample Size	2,696	1,867	1,259	775	463

Time Interval	6 Years	7 Years	8 Years	At 99 Months	
Survival (95% CI)	98.0% (97.0%, 98.7%)	97.2% (95.5%, 98.3%)	97.2% (95.5%, 98.3%)	97.2% (95.5%, 98.3%)	
Sample Size	260	117	44	31	

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



5.5.3 Extension Survival Summary

Table 5.22: Deep Brain Stimulation Extension Characteristics

Model Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Device Events	Cumulative Follow-up Months
37085/37086	March 2009	3,730	2,501	42	109,729

Table 5.23: Deep Brain Stimulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
37085/37086	99.5% (99.1%, 99.7%)	99.1% (98.7%, 99.4%)	98.9% (98.4%, 99.2%)	98.5% (97.9%, 99.0%)	98.0% (97.0%, 98.7%)
Model Name	**6 Years**	**7 Years**	**8 Years**		
37085/37086	98.0% (97.0%, 98.7%)	97.2% (95.5%, 98.3%)	97.2% (95.5%, 98.3%)		

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, 2018. Twenty centers in North America and South America, have enrolled and contributed patients to the sacral neuromodulation systems section of this report.

6.1.2 Patients

Of the 1,098 sacral neuromodulation patients enrolled, the primary indications for implant were as follows: 43.4% were implanted for the treatment of urinary urge incontinence, 31.1% were implanted for the treatment of urgency-frequency, 12.8% were implanted for the treatment of urinary retention, 5.0% were implanted for the treatment of fecal incontinence, 3.0% were implanted for the treatment of bladder pain syndrome, 4.0% 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).

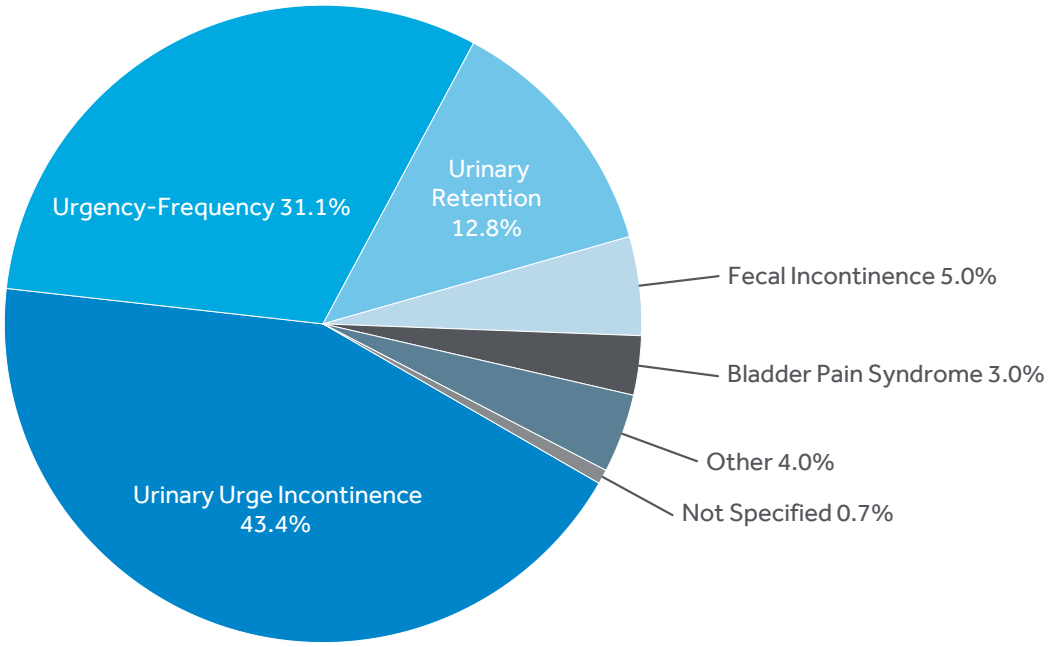


Figure 6.1: Sacral Neuromodulation Primary Treatment Indications

Table 6.1: Sacral Neuromodulation Primary Treatment Indications

Primary Treatment Indication[a]	Enrolled Patients (%)
Urinary Urge Incontinence	477 (43.4%)
Urgency-Frequency	341 (31.1%)
Urinary Retention	140 (12.8%)
Fecal Incontinence	55 (5.0%)
Bladder Pain Syndrome	33 (3.0%)
Other	44 (4.0%)
Not Specified	8 (0.7%)
Total Patients	**1,098 (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 124 product performance events reported between April 2010 and October 31, 2018, in patients with sacral neuromodulation systems. These events represent 15.3% of the total reported events (124/813), occured in 102 (9.3%) of the 1,098 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 685 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=4).

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 22 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 (%)[b]
RPA Determination	**0**	**0.00**	**0 (0.00%)**
Physician's Determination	**124**	**6.34**	**102 (9.29%)**
High Impedance	44	2.25	37 (3.37%)
Lead Migration/Dislodgement	28	1.43	25 (2.28%)
Lead Fracture	15	0.77	14 (1.28%)
Device Malfunction[c]	9	0.46	8 (0.73%)
Low Impedance	9	0.46	9 (0.82%)
Device Lead Issue	6	0.31	4 (0.36%)
Device Battery Issue	5	0.26	4 (0.36%)
Device Electrical Impedance Issue	2	0.10	1 (0.09%)
Device Failure	2	0.10	1 (0.09%)
Device Lead Damage	1	0.05	1 (0.09%)
Device Stimulation Issue	1	0.05	1 (0.09%)
Device Telemetry Issue	1	0.05	1 (0.09%)
Premature Battery Depletion	1	0.05	1 (0.09%)
Total	**124**	**6.34**	**102 (9.29%)**

[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 92 (74.2%) of the 124 product performance events were related to the lead, 20 (16.1%) were related to the neurostimulator, 4 (3.2%) were related to programming/stimulation, 3 (2.4%) were related to "multiple etiologies" (which includes events where at least one device and one non-device etiology was indicated), 2 (1.6%) were related to the extension, 2 (1.6%) were related to "other component", and 1 (0.8%) was related to "other etiology". Relatedness is determined by the physician.

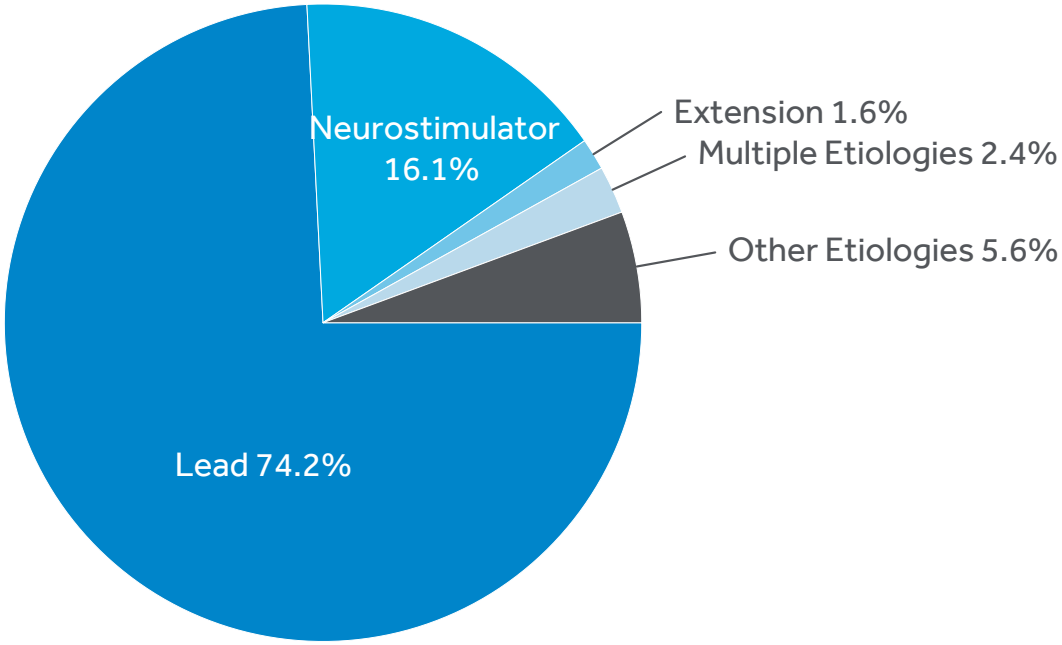


Figure 6.2: Sacral Neuromodulation System Product Performance Events by Relatedness

Table 6.3 and Table 6.4 describe the interventions taken for reported impedance events. In 50.0% and 33.3% of the high and low impedance events, the action taken was a surgical intervention. However, impedance could be used as a diagnostic measurement and may not result in any intervention or clinical impact. The majority of events required no intervention or device reprogramming only (45.5% for high impedance and 55.6% for low impedance). All events are reflected in lead survival curves.

Table 6.3: Sacral Neuromodulation System High Impedance Event by Last Intervention

Intervention	N (%) of High Impedance Events
Surgical Intervention	22 (50.0%)
Reprogramming	16 (36.4%)
No Action Taken	4 (9.1%)
Other[a]	2 (4.5%)
Total High Impedance Events	**44 (100%)**

[a] Includes 1 medication adjustment and 1 device reset.

Table 6.4: Sacral Neuromodulation System Low Impedance Event by Last Intervention

Intervention	N (%) of Low Impedance Events
Surgical Intervention	3 (33.3%)
Reprogramming	3 (33.3%)
No Action Taken	2 (22.2%)
Other[a]	1 (11.1%)
Total Low Impedance Events	**9 (100%)**

[a] Includes 1 device reset.

6.2.2 Non-Product Performance Events

Adverse events and device events that were not related to a product performance event are categorized in Table 6.5 by event group term. These events do not include deaths (see Section 6.2.3) or normal battery depletions. As explained in the Methodology section of this report, this registry's event reporting has evolved over time. Therefore, the event counts are strictly the sum of the events collected up to the October 31, 2018 data cut-off. **All 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 Non-Product Performance Events

Non-Product Performance Events	Event Counts
Infections - pathogen unspecified	**317**
Urinary Tract Infection[a]	285
Medical Device Site Infection	16
Wound Infection	12
Other[b]	4
Therapeutic and nontherapeutic effects (excluding toxicity)	**121**
Therapeutic Product Ineffective	104
Therapeutic Response Decreased	17

...continued

Non-Product Performance Events	Event Counts
Complications associated with device	**65**
Medical Device Site Pain	55
Medical Device Site Discomfort	5
Other[b]	5
Urinary tract signs and symptoms	**44**
Urge Incontinence	9
Urinary Incontinence	9
Pollakiuria	7
Incontinence	5
Micturition Urgency	5
Other[b]	9
Device issues	**28**
Device Stimulation Issue	15
Neurostimulator Migration	5
Other[b]	8
Neurological disorders NEC	**23**
Paraesthesia	18
Other[b]	5
Bladder and bladder neck disorders (excluding calculi)	**15**
Hypertonic Bladder	14
Other[b]	1
Musculoskeletal and connective tissue disorders NEC	**12**
Pain In Extremity	6
Other[b]	6
Administration site reactions	**9**
Medical Device Site Pain	9
General system disorders NEC	**7**
Other[b]	7
Vulvovaginal disorders (excluding infections and inflammations)	**7**
Vulvovaginal Pain	6
Other[b]	1
Bacterial infectious disorders	**6**
Other[b]	6
Injuries NEC	**6**
Wound Secretion	6
Reproductive tract disorders NEC	**5**
Other[b]	5
Other[b]	**20**
Total	**685**

[a] Condition relevant event collected per registry protocol but not device related.
[b] Composed of event codes with fewer than 5 events each.

6.2.3 Patient Deaths

There were 22 deaths reported for patients with sacral neuromodulation systems, none of which were reported as a direct result of a product performance event.

Since 2010, a total of 10 (45.5%) deaths have been reported in this patient registry study based upon patients receiving therapy for urgency-frequency, 4 (18.2%) for urinary urge incontinence, 3 (13.6%) for urinary retention, 1 (4.5%) for fecal incontinence, and 4 (18.2%) for other indications (see Table 6.6). The percentage is based upon the total patient death events and not based upon the rate of occurrence. As mentioned previously, **all tables depicted without a patient denominator should not be interpreted using other numbers within this report to calculate event rates**.

Table 6.6: Sacral Neuromodulation System Patient Deaths by Primary Indication

Number of Reports of Death by Primary Indication[a]	N (%) of Deaths
Urgency-Frequency	10 (45.5%)
Urinary Urge Incontinence	4 (18.2%)
Urinary Retention	3 (13.6%)
Fecal Incontinence	1 (4.5%)
Other Indications	4 (18.2%)
Total	**22 (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, 2018, there were 1,051 neurostimulators followed in the registry. The difference between the total number of patients (n=1,098) versus the total number of neurostimulators (n=1,051) is due to the fact that patients could enroll prior to implant but may not have received an implanted device, or patients were enrolled but not implanted before the data cut-off.

In total, 90.4% (950/1,051) of neurostimulators were InterStim II, and 9.6% (101/1,051) were InterStim. The aggregate prospective follow-up time for all neurostimulators was 22,703 months (1,892 years).

6.3.1 Neurostimulator Events

There were 21 product performance-related events with an underlying reported etiology related to neurostimulator function. This includes 20 events with a neurostimulator etiology and 1 event with both a neurostimulator and other etiology (including device and non-device etiologies). Of these, 20 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 14.6% (27/185). 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 21 neurostimulator events, 100.0 % (21/21) 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	**21 (100%)**
Device Malfunction[a]	6 (28.6%)
Device Battery Issue	4 (19.0%)
High Impedance	4 (19.0%)
Device Lead Issue	2 (9.5%)
Device Electrical Impedance Issue	1 (4.8%)
Device Failure	1 (4.8%)
Device Stimulation Issue	1 (4.8%)
Lead Migration/Dislodgement	1 (4.8%)
Premature Battery Depletion	1 (4.8%)

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

The neurostimulator product performance-related events are summarized by model in Table 6.8 and Table 6.9.

Table 6.8: Event Summary Table: InterStim II (model 3023)

Neurostimulator Event	N
Device Battery Issue	1
Device Malfunction[a]	1
Total	**2**

[a] Device intermittently turning off.

Table 6.9: Event Summary Table: InterStim II (model 3058)

Neurostimulator Event	N
Device Malfunction	5
High Impedance	4
Device Battery Issue	2
Device Lead Issue	2
Device Electrical Impedance Issue	1
Device Failure	1
Device Stimulation Issue	1
Lead Migration/Dislodgement	1
Premature Battery Depletion	1
Total	**18**

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:

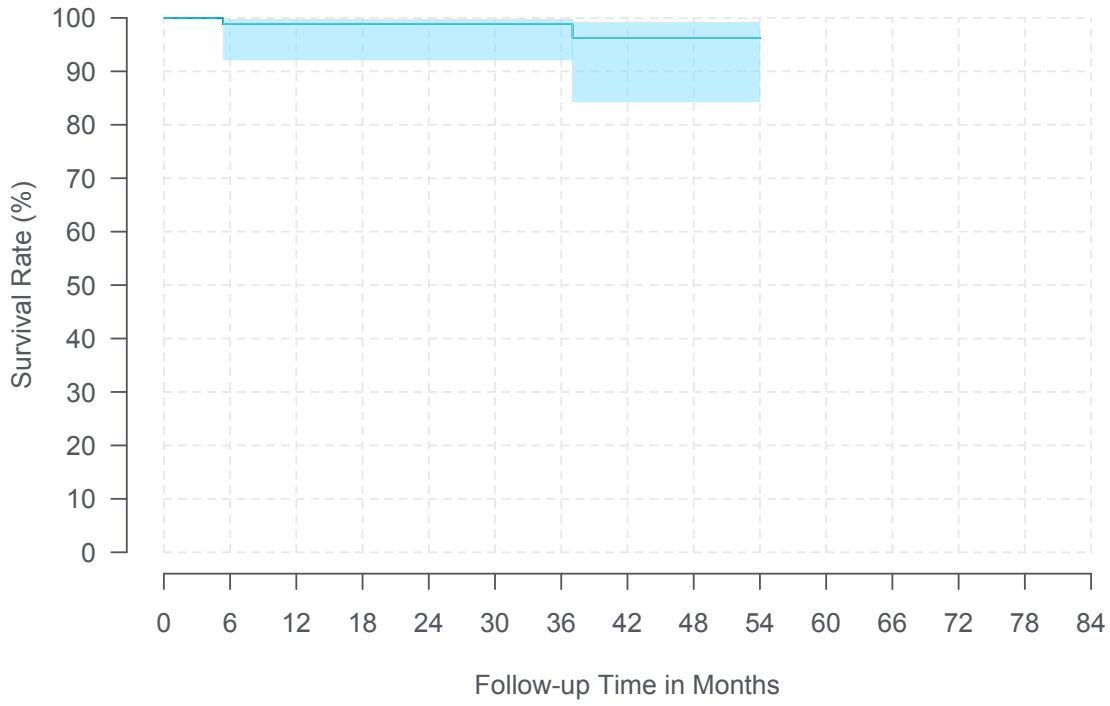
- 20 had follow-up time cut-off due to product performance-related events.
- 492 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 539 were free from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

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

Model 3023

Model Name	InterStim
FDA Approval Date	July 1998
Neurostimulators Enrolled	101
Neurostimulators Currently Active in Study	24
Device Events	2
Cumulative Months of Follow-up	3,144

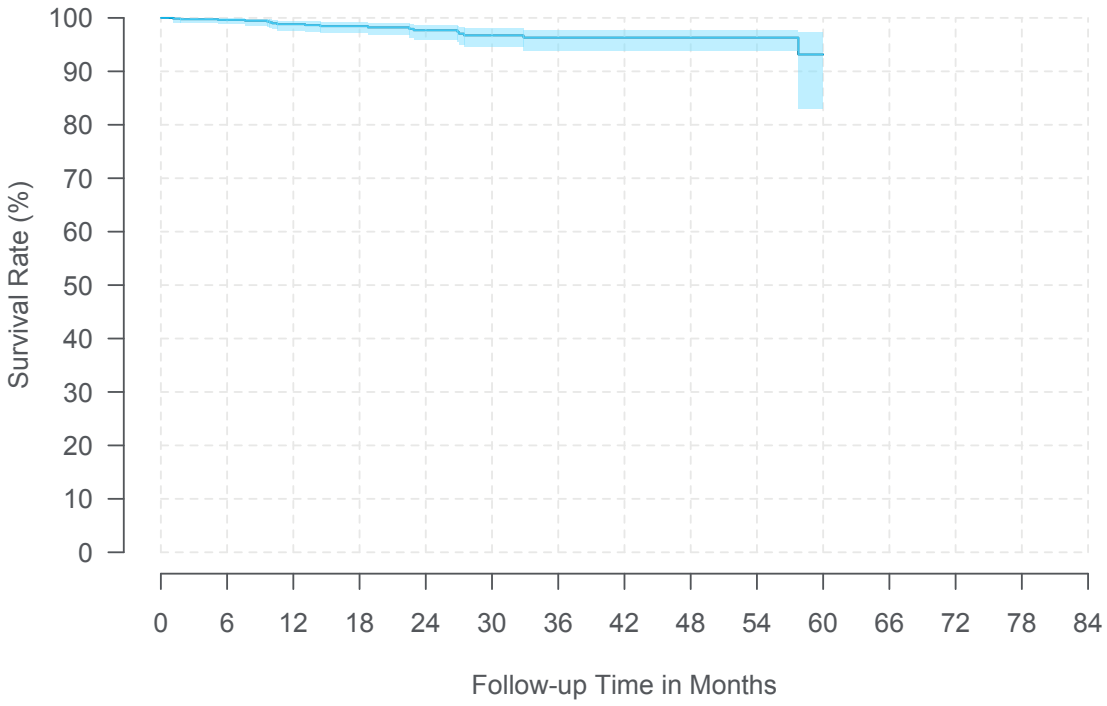


Time Interval	1 Year	2 Years	3 Years	4 Years	At 54 Months
Survival (95% CI)	98.9% (92.2%, 99.8%)	98.9% (92.2%, 99.8%)	98.9% (92.2%, 99.8%)	96.2% (84.2%, 99.1%)	96.2% (84.2%, 99.1%)
Sample Size	69	56	37	24	20

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

Model 3058

Model Name	InterStim II
FDA Approval Date	June 2006
Neurostimulators Enrolled	950
Neurostimulators Currently Active in Study	518
Device Events	18
Cumulative Months of Follow-up	19,559



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	98.8% (97.7%, 99.4%)	97.7% (96.0%, 98.7%)	96.3% (93.9%, 97.8%)	96.3% (93.9%, 97.8%)	93.2% (83.1%, 97.3%)
Sample Size	569	345	196	84	21

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	$\leq$ 2.5 cm

6.3.3 Neurostimulator Survival Summary

Table 6.10: Sacral Neuromodulation Neurostimulator Characteristics

Model Name	FDA Approval Date	Neurostimulators Enrolled	Neurostimulators Active	Device Events	Cumulative Follow-up Months
InterStim	July 1998	101	24	2	3,144
InterStim II	June 2006	950	518	18	19,559

Table 6.11: Sacral Neuromodulation Neurostimulator Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
InterStim	98.9%	98.9%	98.9%	96.2%	
	(92.2%, 99.8%)	(92.2%, 99.8%)	(92.2%, 99.8%)	(84.2%, 99.1%)	
InterStim II	98.8%	97.7%	96.3%	96.3%	93.2%
	(97.7%, 99.4%)	(96.0%, 98.7%)	(93.9%, 97.8%)	(93.9%, 97.8%)	(83.1%, 97.3%)

6.4 Leads

From April 2010 to the report cut-off date of October 31, 2018, there were 1,028 leads followed in the registry. The difference between the total number of leads (n=1,028) versus the total number of neurostimulators (n=1,051) 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 22,817 months (1,901 years). Table 6.12 provides the number and percentage of leads by model.

Table 6.12: Sacral Neuromodulation Neurostimulator Counts by Model

Model Name	N (%)
Currently manufactured	**927 (90.2%)**
InterStim Quad Lead Tined (3889)	927 (90.3%)
No longer manufactured	**100 (9.7%)**
InterStim Extended Electrode Quad Lead Tined (3093)	95 (9.3%)
InterStim Quad Lead (3080)	3 (0.3%)
InterStim Extended Electrode Quad Lead (3092)	2 (0.2%)
Other/Unspecified	**1 (0.1%)**
Total	**1,028 (100%)**

6.4.1 Lead Events

There were 94 product performance-related events with an underlying reported etiology related to lead function. This includes 92 events with a lead etiology and 2 events with both a lead and other etiology (including device and non-device etiologies). Of these, 86 were the initial product performance event that affected lead survival estimates.

The lead product performance-related events are summarized by model in Table 6.13 and Table 6.14. Events of other/unspecified models and discontinued models are not shown.

Table 6.13: Event Summary Table: InterStim Extended Electrode Quad Lead Tined (model 3093)

Lead Event	N
High Impedance	3
Device Lead Damage	1
Lead Fracture	1
Lead Migration/Dislodgement	1
Total	**6**

Table 6.14: Event Summary Table: InterStim Quad Lead Tined (model 3889)

Lead Event	N
High Impedance	31
Lead Migration/Dislodgement	20
Lead Fracture	12
Low Impedance	7
Device Lead Issue	4
Device Battery Issue	1
Device Electrical Impedance Issue	1
Device Failure	1
Device Malfunction	1
Total	**78**

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:

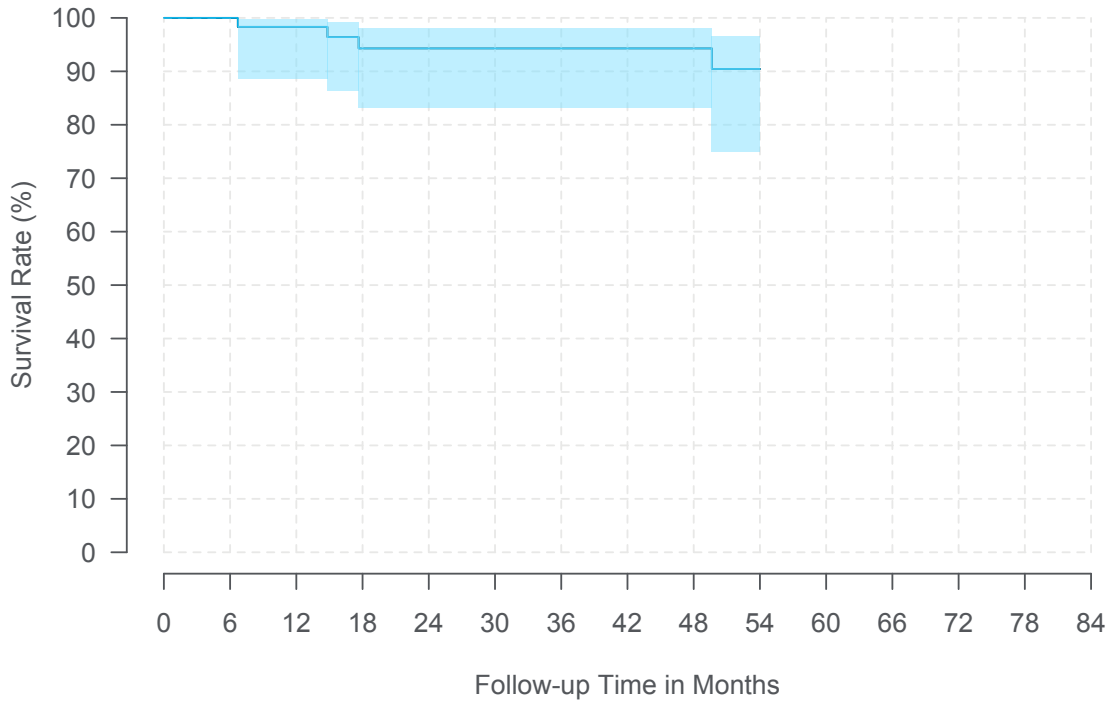
- 86 had follow-up time cut-off due to product performance-related events.
- 420 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 522 were free from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

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

Model 3093

Model Name	InterStim Extended Electrode Quad Lead Tined
FDA Approval Date	September 2002
Leads Enrolled	95
Leads Currently Active in Study	37
Device Events	6
Cumulative Months of Follow-up	2,743

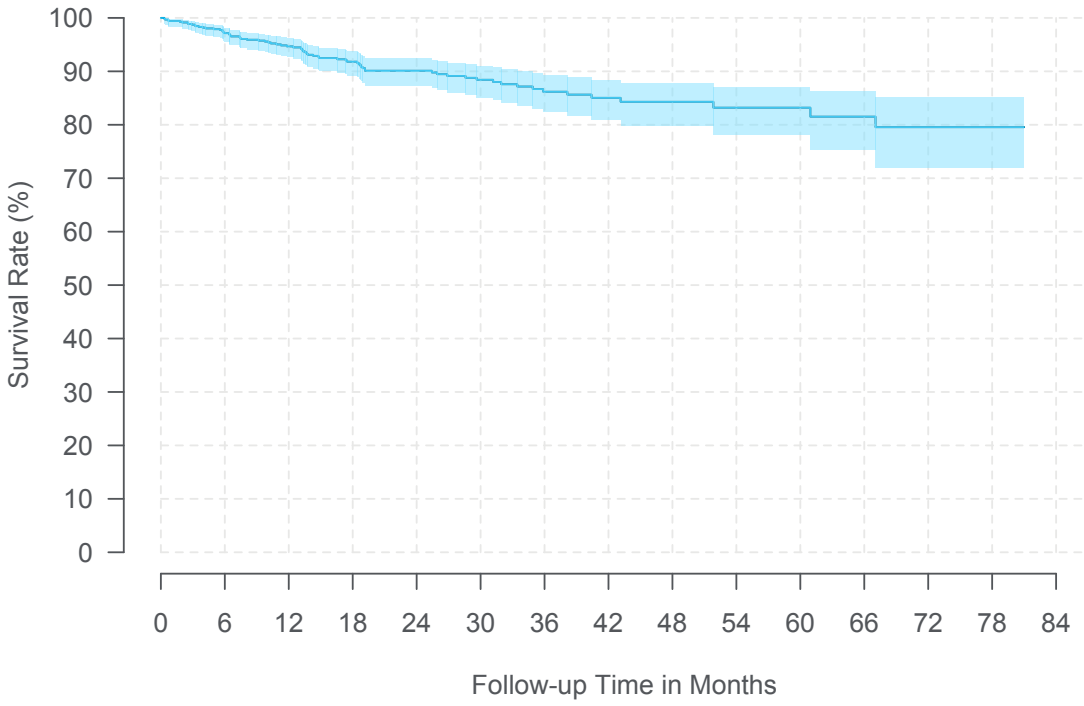


Time Interval	1 Year	2 Years	3 Years	4 Years	At 54 Months
Survival (95% CI)	98.3% (88.7%, 99.8%)	94.3% (83.2%, 98.1%)	94.3% (83.2%, 98.1%)	94.3% (83.2%, 98.1%)	90.4% (75.0%, 96.5%)
Sample Size	51	37	28	26	21

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

Model 3889

Model Name	InterStim Quad Lead Tined
FDA Approval Date	September 2002
Leads Enrolled	927
Leads Currently Active in Study	503
Device Events	78
Cumulative Months of Follow-up	19,924



Time Interval	1 Year	2 Years	3 Years	4 Years	5 Years
Survival (95% CI)	94.7% (92.6%, 96.1%)	90.1% (87.3%, 92.3%)	86.2% (82.4%, 89.2%)	84.3% (79.9%, 87.8%)	83.2% (78.2%, 87.2%)
Sample Size	502	301	172	92	51

Time Interval	6 Years	At 81 Months			
Survival (95% CI)	79.6% (72.1%, 85.2%)	79.6% (72.1%, 85.2%)			
Sample Size	40	24			

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

6.4.3 Lead Survival Summary

Table 6.15: Sacral Neuromodulation Lead Characteristics

Model Name	FDA Approval Date	Leads Enrolled	Leads Active	Device Events	Cumulative Follow-up Months
InterStim Extended Electrode Quad Lead Tined (model 3093)	September 2002	95	37	6	2,743
InterStim Quad Lead Tined (model 3889)	September 2002	927	503	78	19,924

Table 6.16: Sacral Neuromodulation Lead Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years	4 Years	5 Years
InterStim Extended Electrode Quad Lead Tined (model 3093)	98.3% (88.7%, 99.8%)	94.3% (83.2%, 98.1%)	94.3% (83.2%, 98.1%)	94.3% (83.2%, 98.1%)	
InterStim Quad Lead Tined (model 3889)	94.7% (92.6%, 96.1%)	90.1% (87.3%, 92.3%)	86.2% (82.4%, 89.2%)	84.3% (79.9%, 87.8%)	83.2% (78.2%, 87.2%)

Model Name	6 Years
InterStim Extended Electrode Quad Lead Tined (model 3093)	
InterStim Quad Lead Tined (model 3889)	79.6% (72.1%, 85.2%)

6.5 Extensions

From April 2010 to the report cut-off date of October 31, 2018, 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=1,051) 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 3,211 months (268 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.

The extension product performance-related events are summarized by model in Table 6.17.

Table 6.17: Event Summary Table: Quadripolar extension (model 3095)

Extension Event	N
Lead Fracture	1
Total	**1**

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:

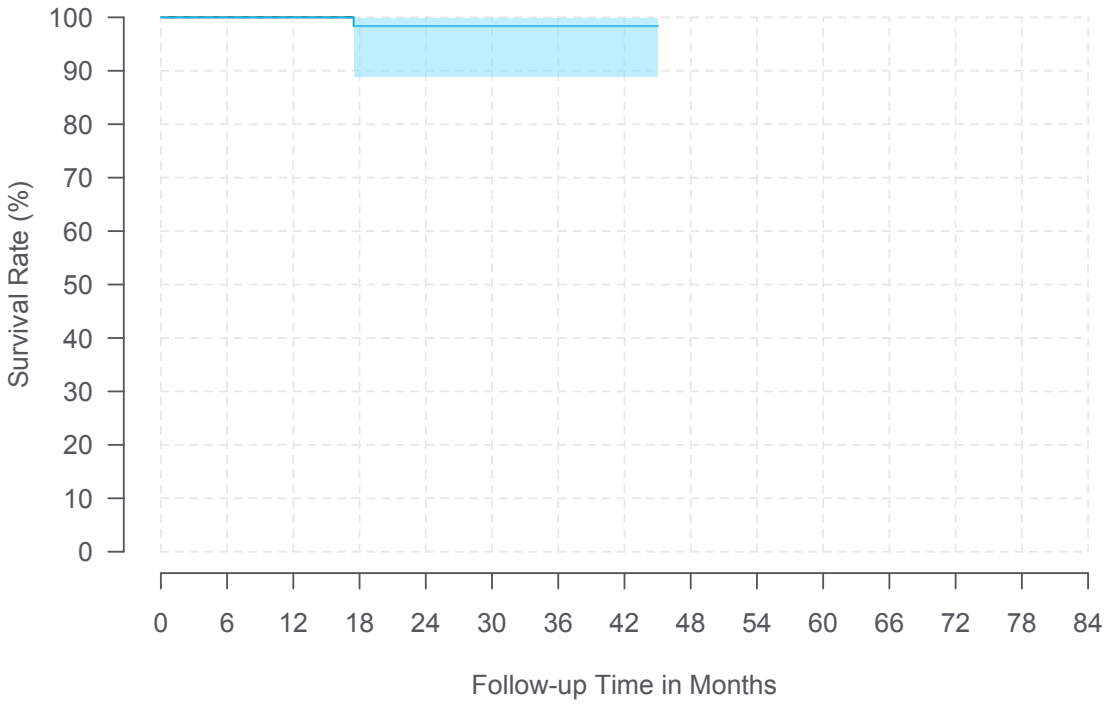
- 1 had follow-up time cut-off due to product performance-related events.
- 73 were censored in the survival analysis for the following reasons: patient expired, neurostimulator explanted, patient discontinued, therapy suspended, or site discontinued participation in the registry.
- 28 were free from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

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

Model 3095

Model Name	Quadripolar extension
FDA Approval Date	July 1998
Extensions Enrolled	102
Extensions Currently Active in Study	28
Device Events	1
Cumulative Months of Follow-up	3,211



Time Interval	1 Year	2 Years	3 Years	At 45 Months
Survival (95% CI)	100.0% (NA)	98.3% (88.8%, 99.8%)	98.3% (88.8%, 99.8%)	98.3% (88.8%, 99.8%)
Sample Size	63	48	30	23

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

6.5.3 Extension Survival Summary

Table 6.18: Sacral Neuromodulation Extension Characteristics

Model Name	FDA Approval Date	Extensions Enrolled	Extensions Active	Device Events	Cumulative Follow-up Months
Quadripolar extension (model 3095)	July 1998	102	28	1	3,211

Table 6.19: Sacral Neuromodulation Extension Survival Probability (95% Confidence Intervals)

Model Name	1 Year	2 Years	3 Years
Quadripolar extension (model 3095)	100.0%	98.3%	98.3%
	(NA)	(88.8%, 99.8%)	(88.8%, 99.8%)