APPENDIX

1. DATA SOURCES

The study used data available in a patient research database from several Swedish national and local registers. Each included register is described in detail in the following sections. Data from different sources were linked on patient level via the national ID personalized for each citizen. Due to a closed data system, patients are not lost to follow-up. The national administrative registers in Sweden have a nation-wide coverage and collect detailed information (patient level data) on the provision of care.

1.1 RAY

A local SCS register named "RAY" was initiated in 2009 by physicians at the Pain Centre (Smärtcentrum) at the Uppsala University Hospital, Sweden. It includes patients treated with invasive neurostimulation at the Uppsala University Hospital and collects information at the time of initiating treatment and at annual follow-ups.

1.2 The National Patient Register

The National Patient Register contains patient data, geographical data, administrative data and medical data for both inpatient and outpatient hospital care (i.e. patient visits in non-primary outpatient care) in Sweden. The register contains main and secondary diagnosis codes for each admission and outpatient visit as well as procedure codes. Complete in- and outpatient data from the register between January 1, 2000 and December 31, 2017 were available for analysis for all patients included in the study population.

1.3 The Swedish Social Insurance Agency

All people who live or work in Sweden are automatically covered by the Swedish social insurance. Statistics are available on all sick leave (episodes >14 days, dates of start and end of episode and cause of sick leave) covered by the social insurance at an individual level. Moreover, individual data are available on episodes of early retirement (disability pension). The National Social Insurance Agency is the sole administrator of sick leave and long-term disability in Sweden and thus allows for complete coverage of productivity loss of the study population. Extracted data include start and end of sick episodes, amounts paid, proportion of a patient's working time covered by a benefit and more.

1.4 The LISA Register

The LISA register integrates existing data from the labour market, educational and social sectors and is updated each year with a new annual register. Extracted data include disposable income, country of birth, immigration, place of residence, and highest level of education. The data included in the research database covers the years 2000–2015.

1.5 The Cause of Death Register

Date and cause of death will be obtained from The Cause of Death Register held by the National Board of Health and Welfare. Complete data from the register between January 1, 2000 and December 31, 2017 will be available for analysis for all patients included in the study population.

1.6 The Prescribed Drug Register

The prescribed drugs register covers all medicines and consumables (such as stoma products and special diet foods) dispensed on prescription at pharmacies. The number of items in the register amounts to over 100 million per year. The prescribed drug register with personal identity numbers started in July 2005.

1.7 SWESPINE

SWESPINE is administered by a steering group appointed by the Swedish Spine Surgery Association. Currently, about 95% of Sweden's clinics report to SWESPINE [1]. SWESPINE includes spine surgery clinical information at baseline (surgery) and follow-up conducted at 1, 2, 5, and 10 years after surgery. SWESPINE also includes patient-reported outcome measures (PROMs).

1.8 The Register of the Total Population

The register of the total population, held by Statistics Sweden, was used to construct a control group. The register covers the entire Swedish population and contains basic demographic and socioeconomic information on the individual level. A random sample of individuals from the register was used to construct the control cohort. The control cohort was matched 5:1 to the SCS and spine surgery study population using exact matching without replacement. Cases and controls were matched on age, gender and region of residence.

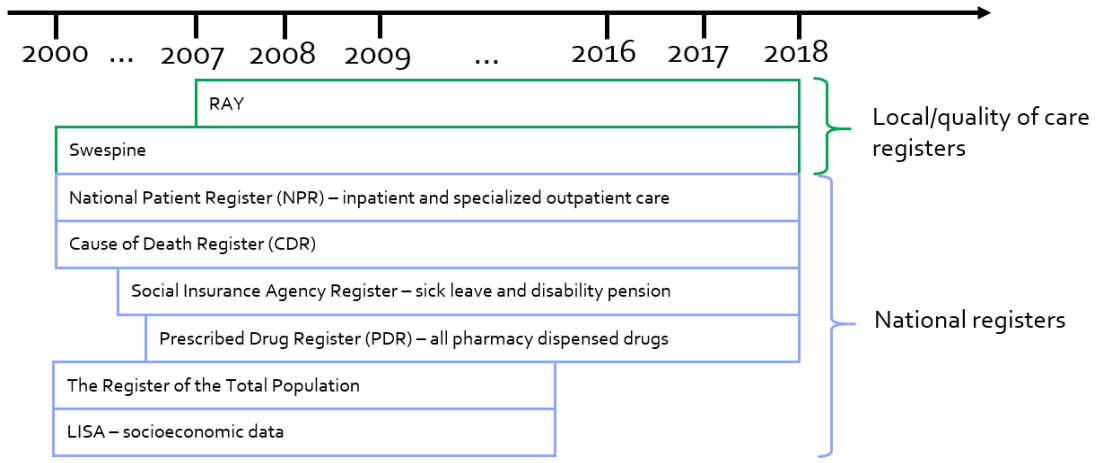

Figure A1: Time frames and data sources in the aggregated database.

2. Censoring for analysis of explantation due to insufficient analgesic effect (objective 1)

Risk of explantation was analyzed from index date, and continuously over time, until death or end of data availability, using a time-to-event analysis with first explantation due to insufficient analgesic effect as failure event. Patients were censored at change of therapy type (e.g., change from SCS to dorsal root ganglion stimulation), death or end of data availability. Patients were continuously followed through all other changes in (e.g., change of battery).

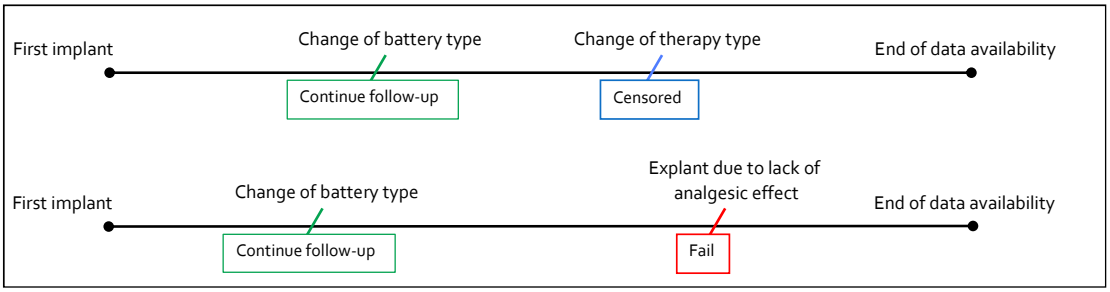

Figure A2. Example of two patients, one censored at the change of therapy type and one with failure event at explant due to lack of analgesic effect.

3. Supplementary tables

Table A1
Variables associated with explantation due to insufficient analgesia (objective 2)

	HR	SE	Statistic	P-value	Lower CI	Upper CI
Age (reference: 18-40)						
41-60	2.048	0.912	1.609	0.108	0.855	4.904
60+	2.769	1.379	2.044	0.041	1.043	7.351
Male gender (reference: female)	0.878	0.236	-0.483	0.629	0.518	1.488
Elixhauser comorbidity index	0.954	0.098	-0.452	0.651	0.78	1.168

Birth country (reference: Sweden)						
Other	0.97	0.39	-0.07	0.94	0.45	2.12
Income (EUR in thousands)	1.006	0.013	0.456	0.648	0.981	1.031
Education level (reference: primary education)						
Secondary education	0.686	0.22	-1.178	0.239	0.366	1.285
Post-secondary/post-graduate education	0.59	0.25	-1.245	0.213	0.257	1.353
Employment status (reference: employed)						
Not employed	1.21	0.362	0.637	0.524	0.673	2.175
Non-opioid pain drug usage (reference: 0 DDD)						
1-200 DDD	0.765	0.247	-0.833	0.405	0.406	1.438
201+ DDD	0.719	0.251	-0.945	0.345	0.363	1.426
Opioid usage (reference: 0 DDD)						
1-200 DDD	2.192	0.853	2.017	0.044	1.022	4.7
201+ DDD	1.984	0.814	1.67	0.095	0.888	4.432
Depression medicine (reference: 0 DDD)						
1-200 DDD	0.892	0.305	-0.334	0.739	0.456	1.744
201+ DDD	1.232	0.377	0.683	0.495	0.677	2.243
Number of previous spine surgeries	1.244	0.294	0.924	0.355	0.783	1.977
Indication group other (reference: back/leg pain)	0.705	0.215	-1.147	0.251	0.387	1.282
Pain duration (years)	0.989	0.018	-0.611	0.541	0.954	1.025
Battery (reference: non-rechargeable)	0.835	0.282	-0.534	0.593	0.431	1.617
Waveform (reference: Tonic)						
Burst	1.693	0.595	1.497	0.134	0.85	3.371
HF10	3.327	1.356	2.95	0.003	1.497	7.395

Table format of data presented in manuscript figure 3.
HR, Hazard ration; SE, Standard error

Table A2
Subgroup analysis: Cox regression of risk factors for explantation due to insufficient analgesic effect in patients with BMI-data (N=99)

	HR	SE	Statistic	P-value	Lower CI	Upper CI
Age	1.055	0.032	1.775	0.076	0.994	1.120
Gender (male)	3.373	1.858	2.207	0.027	1.146	9.928
Elixhauser comorbidity index	0.770	0.175	-1.149	0.251	0.493	1.203
Birth country						
Sweden	1.00 (reference value)					
Other	2.656	2.135	1.215	0.224	0.549	12.838
Income (closest to index date, EUR in thousands)	0.993	0.024	-0.296	0.767	0.947	1.041
Education level						
Primary education	2.821	1.837	1.593	0.111	0.787	10.111
Secondary education	1.00 (reference value)					
Post-secondary/post-graduate education	1.640	1.274	0.637	0.524	0.358	7.517
Employment status						
Employed	1.00 (reference value)					
Not employed	1.175	0.700	0.271	0.787	0.365	3.779
Non-opioid pain drug usage (Total DDD dispensed prior 12 months)	0.998	0.002	-0.770	0.441	0.994	1.003

Opioid usage (Total DDD dispensed prior 12 months)	1.000	0.001	0.582	0.561	0.999	1.002
Depression medicine (Total DDD dispensed prior 12 months)	1.000	0.001	-0.050	0.960	0.998	1.002
Previous spine surgery	1.287	0.395	0.822	0.411	0.705	2.347
Indication group (back and leg pain/other)	1.471	1.751	0.324	0.746	0.142	15.178
Pain duration	0.929	0.051	-1.328	0.184	0.833	1.036
Waveform						
Tonic	1.00 (reference value)					
Burst	0.938	0.854	-0.070	0.944	0.157	5.588
HF10	1.962	1.345	0.983	0.326	0.512	7.523
BMI						
Severely underweight	(no observations)					
Underweight	(no observations)					
Normal weight	0.193	0.228	-1.391	0.164	0.019	1.961
Overweight	1.00 (reference value)					
Obese	0.790	0.427	-0.436	0.663	0.274	2.278

Variables analysed for association of explantation of SCS-system due to insufficient analgesia in a subgroup of 99 patients with available BMI-data.

Table A3
Variables analyzed for association with successful or unsuccessful outcome of SCS-treatment (objective 4)

	Coefficient	SE	Statistic	P-value	Lower CI	Upper CI
Age (reference: 18-40)						
41-60	0.446	0.287	1.552	0.121	-0.117	1.009
60+	0.672	0.334	2.014	0.044	0,018	1.326
Male gender (reference: female)	-0.07	0.209	-0.335	0.738	-0.48	0.34
Elixhauser comorbidity index	-0.151	0.079	-1.909	0.056	-0.305	0.004
Birth country (reference: Sweden)						
Other	0.085	0.34	0.251	0.802	-0.58	0.0751
Income (EUR in thousands)	0.005	0.01	0.543	0.587	-0.014	0.025
Education level (reference: primary education)						
Secondary education	-0.578	0.267	-2.164	0.03	-1.102	-0.055
Post-secondary/post-graduate education	-1.054	0.321	-3.289	0.001	-1.682	-0.426
Employment status (reference: employed)						
Not employed	0.575	0.228	2.518	0.012	0.127	1.022
Non-opioid pain drug usage (reference: 0 DDD)						
1-200 DDD	0.164	0.248	0.661	0.509	-0.323	0.651
201+ DDD	-0.117	0.266	-0.439	0.66	-0.638	0.404
Opioid usage (reference: 0 DDD)						
1-200 DDD	0.355	0.255	1.39	0.164	-0.145	0.855
201+ DDD	0.5	0.284	1.764	0.078	-0.056	1.056
Anti-depression medication use (reference: 0 DDD)						
1-200 DDD	0.229	0.247	0.927	0.354	-0.255	0.712
201+ DDD	0.357	0.249	1.431	0.152	-0.132	0.846
Number of previous spine surgeries	0.344	0.19	1.811	0.07	-0.028	0.717
Indication group other (reference: back/leg pain)	-0.378	0.231	-1.637	0.102	-0.831	0.075
Pain duration (years)	-0.008	0.014	-0.614	0.539	-0.036	0.019
IPG type (reference: non-rechargeable)	0.199	0.265	0.751	0.452	-0.32	0.719
Waveform (reference: Tonic)						

Burst	0.144	0.244	0.591	0.555	-0.334	0.622
HF10	0.543	0.383	1.417	0.157	-0.208	1.294

Table format of data presented in manuscript figure 6. Negative coefficient values indicate increased probability of successful outcome.

4 Validation of combining BPI and NRS in analysis of stimulation effect (objective 3)

In objective 3, we analyzed the patient reported analgesic and global effect of SCS. The use of the survey question "What is the effect of stimulation?" to measure the global effect was validated by comparing changes in pain intensity and pain interference against the reported effect of stimulation (EoS). As shown in section 3.4, effect of stimulation is highly correlated with pain intensity and interference which validates the use of the effect of stimulation measure. In this validation exercise, pain intensity was based on patients' answers on Brief Pain Inventory (BPI) and Numerical Rating Scale (NRS). Depending on when patients were included in the RAY register, BPI or NRS for global pain was used at baseline and follow-up. We had three combinations of scales in the register: 1) BPI at baseline and follow-up, 2) NRS at baseline and follow-up, and 3) NRS at baseline and BPI at follow-up.

We hypothesized that the change from baseline to follow up in either of the two scales, BPI and NRS, was comparable. A t-test for equal means in percentage change was conducted to test each scale combination against each other. The t-test BPI-BPI (BPI at baseline and follow-up) and NRS-NRS (NRS at baseline and follow-up) indicate that the scales do not statistically differ in mean percentage change (Table 5, p=0.259). Therefore, it was deemed that change in BPI and NRS could be merged into one variable expressing the reported change in pain intensity from baseline to follow up.

Table A4

T-test for equal means in change (%) for BPI-BPI and NRS-NRS

	Ha: diff < 0	Ha: diff ≠ 0	Ha: diff > 0
P-value	0.8703	0.2594	0.1297