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5-year longitudinal follow-up of patients treated for chronic mechanical low back pain using restorative neurostimulation

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ABSTRACT

Background Chronic mechanical low back pain (CLBP) often stems from dysfunction of the multifidus muscle, leading to impaired motor control and pain. Restorative neurostimulation has emerged as a novel treatment targeting this dysfunction by delivering electrical stimulation to the medial branches of the L2 dorsal rami to restore multifidus activation.

Methods This prospective, open-label, postmarket clinical follow-up study aimed to evaluate 5-year clinical outcomes and device utilization trends in a cohort of 42 patients with CLBP treated across five UK sites with restorative neurostimulation via an implanted ReActiv8 neurostimulation system. Patients were followed for 5 years, with assessments of pain (Numerical Rating Scale (NRS)), disability (Oswestry Disability Index (ODI)), and health-related quality of life (EuroQol-5 Dimension, 5 Level (EQ-5D-5L)) at baseline and regular intervals. Therapy utilization was collected via implantable device logs.

Results At 5 years, 34/42 patients (81%) completed follow-up. Significant and durable improvements were observed in pain (mean NRS reduced from 7.0 to 3.2), disability (mean ODI reduced from 46.6 to 26.1), and quality of life (EQ-5D index increased from 0.426 to 0.703). A total of 82% of patients achieved a minimally clinically important change in either pain or disability, and 62% were pain remitters (NRS ≤3). Device usage averaged 1106 hours over 5 years, with reductions in usage over time. Lower usage was associated with non-response, though causality could not be determined.

Conclusions Restorative neurostimulation provides robust, sustained improvements in pain, function, and quality of life in patients with CLBP associated with multifidus dysfunction. These results support its long-term efficacy and safety in real-world clinical practice.

Trial registration number ClinicalTrials.gov Identifier: NCT01985230.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Restorative neurostimulation for chronic low back pain had been demonstrated to be a highly effective treatment in randomized controlled trials with long-term follow-up.

WHAT THIS STUDY ADDS

This study demonstrates the clinical effect over 5 years in a cohort of patients selected from real-world clinical practice. It is also the first examination of the complex interaction between patient-directed therapy utilization and clinical outcome.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

The results presented here show generalizability to clinical practice beyond clinical trial conditions, supporting the adoption of the treatment for well-selected patients.

INTRODUCTION

The multifidus muscle is an essential component of the trunk musculature and is responsible for providing segmental stabilization and control.[1] It is especially important for control of lordosis during flexion and return from flexion. This muscle is highly adapted for this role, with an anatomical location providing a distinct biomechanical advantage as well as discrete proprioceptive sensory input into the central nervous system.[2] When functioning appropriately, the multifidus is the sensor and actuator within a motor control system, allowing for pain-free spinal motion.[3]

Degenerative changes of spinal structures in most people are an inevitable consequence of aging, with the timing of onset and eventual severity having both environmental and genetic components.[4] Structural changes, for example, Modic signs, disc degeneration, and facet arthropathy observed by various imaging modalities may not in and of themselves be painful but are closely associated with altered biomechanics contributing to and perpetuating painful motion.[5] Degeneration of these tissues is causal in activating neural inhibition of motor pathways to the paraspinal muscles, in particular the multifidus.[6] Mechanical consequences of multifidus inhibition manifest as losses of lumbar motor control, which can cause overloading of already degenerated structures, activating tissue nociceptors as a primary pain source. Poor motor control, reinforced by both pain and fear avoidance, can result in further inhibition and a self-reinforcing loop of negative outcomes.

Identifying specific pain generators among multifactorial degenerative processes, altered biomechanics, and the biopsychosocial complexity of a chronic mechanical low back pain (CLBP) patient is often rendered unproductive, resulting in many

failed treatments. Best efforts in managing these patients are often through palliative interventions attempting to quiet specific pain generators and tend to only provide temporary relief.[7] As symptoms persist and therapies become less effective, patients and physicians alike may be tempted to incorporate irreversible treatments, such as spinal fusion, that fall outside most clinical practice guidelines for patients with mechanical low back pain with no neuropathic involvement.

The past decade has seen the conceptualization and ultimate realization of restorative neurostimulation as a viable therapeutic option for CLBP in the presence of multifidus muscle dysfunction.[8 9] The practical implementation of restorative neurostimulation involves bilateral surgical implantation of two leads over the medial branches of the L2 dorsal rami connected to an implantable pulse generator (IPG) located over the buttock or flank. The nerves are stimulated with a waveform that induces smooth tetanic contractions of the multifidus muscle. This application of normalized muscle contractions of dysfunctional multifidi has demonstrated substantial, durable reductions in pain and disability as part of a long-term clinical trial to establish safety and efficacy.[10–15] Additionally, animal studies have shown that this stimulation paradigm is able to restore degenerate structures in the multifidus related to both muscle function and proprioceptive acuity.[16 17]

Industry-sponsored randomized controlled trials (RCTs) of neuromodulation have often yielded results that have not been replicated in clinical practice.[18] The generalizability of many RCTs can be limited due to the necessary control of patient eligibility, especially in trials designed for regulatory bodies. However, this study presents 5-year real-world outcomes of restorative neurostimulation for CLBP reflective of normal clinical practice from a postmarket registry in the UK reported as verification of the long-term efficacy of this therapy.

METHODS

Study design

The ReActiv8 postmarket clinical follow-up cohort was collected as part of an open-label 5-year prospective follow-up for the treatment of CLBP of nociceptive origin with restorative neurostimulation using the ReActiv8 (Mainstay Medical, Dublin, Ireland) device. This was undertaken independent of the original ReActiv8-A cohort with different patients and investigators, though registered under the same clinical trial (ClinicalTrials.gov Identifier: NCT01985230, original registration 11/15/2013). Patients were consented to participate between September 1, 2017, and September 28, 2018, then followed for 5 years. Data were collected at five sites across the UK. Outcomes were collected at baseline, 45, 90, 180, and 365 days, and thereafter annually near the date of the activation visit out to 5 years postactivation. Assessments of patient-reported outcomes were completed for pain (Numerical Rating Scale—NRS), disability (Oswestry Disability Index—ODI), and health-related quality of life (EuroQol-5 Dimension 5 Level—EQ5D-5 L) at baseline and each follow-up. The sample size was selected to fulfill the requirements of postmarket surveillance in Europe, following a change to the surgical technique from the original ReActiv8-A study. No substantive amendments were made to the protocol after commencement of the study. Ongoing safety reporting included actively collected serious device- or procedure-related adverse events, documented at each visit.

The analysis of all subjects who reached 5 years of therapy or exited the study is reported.

Patient selection

As previously described, this post market component of the study was conducted without formal inclusion or exclusion criteria. Patients were eligible if they met NHS guidelines, the instructions for use, and the indications of the CE Mark (Conformite Europeene) to better understand therapy efficacy in real-world clinical practice. The indications for this therapy have been reported in prior publications;[14 15] however, in essence, patients were indicated if they were adults with a significant history of severe, predominantly mechanical CLBP refractory to physiotherapy and medication. The application of this therapy is indicated for patients with evidence of multifidus dysfunction, and, although the study protocol did not specify a particular method, all physicians were trained and encouraged to do physical testing for multifidus dysfunction using the prone instability test.[19 20] The multifidus lift test, the aberrant movement patterns assessment, and observation of fatty infiltration of the multifidus by MRI imaging are also concordant clinical signs of multifidus dysfunction. The diagnosis of multifidus dysfunction per the label and the ultimate decision for inclusion or exclusion were made by the treating clinician. Prior to restorative neurostimulation, guideline-directed treatments such as pharmacological and physical therapies should have been attempted and deemed unsuccessful by criteria, including a temporary response or side effect limitations.

In the UK, it is a requirement that patients with back pain be assessed by a multidisciplinary team. This review team may include physical therapists, psychologists, neuromodulation nurses, and pain management specialists to evaluate and exclude serious comorbidities and to ensure appropriate education and expectation management. This team reviewed important features of the patient's history, including pain presentation, severity, and continuity of CLBP. These patients may then be formally diagnosed with chronic multifidus dysfunction corresponding with neuromuscular instability of the lumbar spine, resulting in symptoms of nociceptive low back pain and are suitable for treatment with a neuromodulation device in the NHS.

Device utilization

The initiation and duration of therapy sessions were automatically logged by the IPG operating system. These data were extracted and analyzed to classify the dose of therapy delivered, patient engagement with the therapy, and investigate correlations with clinical outcomes. Patient-specific weekly utilization and cumulative therapy doses were measured. Throughout the course of the COVID-19 pandemic (from 2020 to 2022), patients participated in telehealth visits that in some cases caused the buffer capacity of the IPGs to be exceeded, resulting in some data loss. The current IPG allows for the storage of data on approximately 9–12 months of therapy session-related data, which is continuously overwritten from oldest to newest. As the buffer capacity was exceeded through the COVID-19/telehealth period, old data were overwritten, resulting in some data gaps. To extrapolate for these missing data, we estimated system use based on usage patterns immediately prior to the data gap. A sensitivity analysis was used to impute missing data using an average of the system utilization for the 2 weeks or the 10 prior to the missing data.

Data analysis

Patient-reported outcomes over time were compared with baseline using repeated measures analysis of variance with Bonferroni

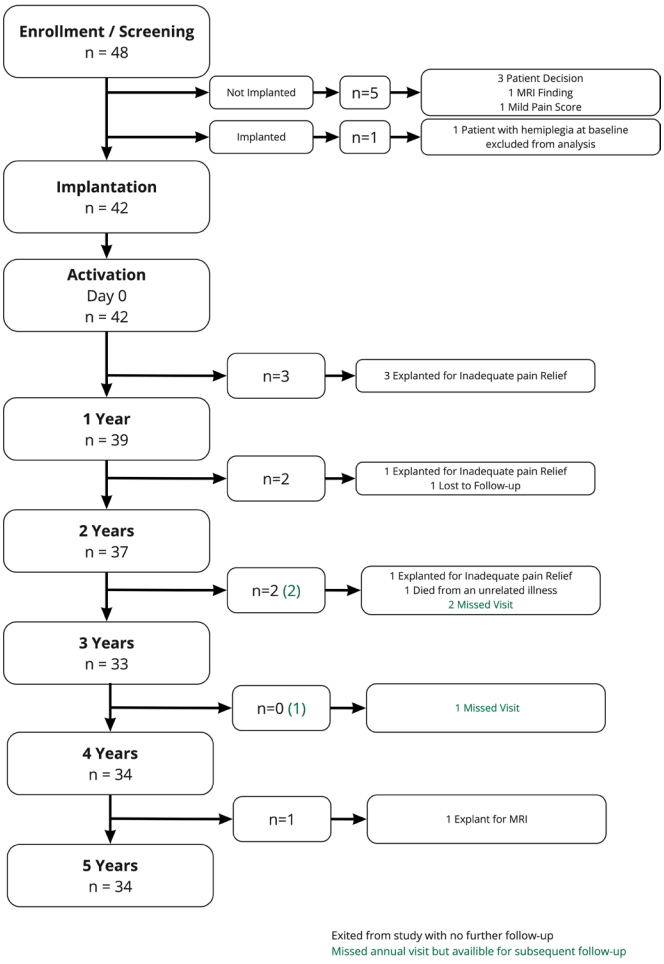

Figure 1 Patient disposition throughout 5 years.

correction for multiple comparisons conducted in R V.4.4.2 and RStudio V.2024.12.0+467.

To interpret the impact of incomplete follow-up, imputation was performed by applying different techniques depending on the reasoning for the incomplete patient record, similar to other publications.[11 21] Baseline observation carried forward was used for participants withdrawn for reported lack of efficacy at any time. For those withdrawn or who had missing data for other reasons (death, unavailable, or otherwise lost to follow-up), the mixed-effects model repeated measures (MMRM) approach was used to provide implicit imputations of missing data for continuous outcomes.[22] Parametric demographic data were compared using a two-sided t-test, and proportional data were compared using Fisher exact test.

RESULTS

Demographics and disposition

42 patients were eligible for the study and implanted with the stimulator. 34 (81%) were available at the 5-year closure of the study. The disposition of patients is shown in figure 1. Briefly, over the course of 5 years, 5/42 (11.9%) patients were explanted for inadequate pain relief. Three of these patients were explanted before 1 year of therapy; however, since this time, clinical opinion has evolved, and the interpretation of clinical evidence, including this study, suggests that this may be too early to definitively declare therapy failure.[11 14] Two patients were lost to follow-up, and one patient was explanted prior to the need for MRI. Since that time, the implantable system has received European Medical Device Regulation approval by the notified body for full-body 1.5 T MR (Magnetic Resonance Imagaing) conditionality, and explant as a safety precaution is no longer necessary. One patient died from an unrelated illness, and one patient missed their final visit.

The average age of the full cohort was 47 years, with 40% female and an average pain duration of almost 14 years. Prior to enrollment, 16/42 (38%) patients had medial branch radiofrequency ablation, 31% (13/42) reported a prior nerve block, and 24% (9/42) a prior epidural injection. There were no statistically significant differences in any baseline measure between the 34 patients who completed the 5-year follow-up and the eight non-completers (table 1).

Clinical outcomes

The 5-year outcomes in patients with (table 2) show statistically significant, clinically meaningful, and durable improvements

Table 1 Baseline patient demographics

		5 years		
Characteristic mean±SE or N (%)	**Full cohort** (n=42)	**Completers** (n=34)	**Non-completers** (n=8)	**P value**
Age	47.2±1.7	47.5±1.7	46.0±5.6	0.81*
BMI	29.7±0.9	29.7±1.0	29.8±2.5	0.98*
Sex (% female)	17 (40.5%)	12 (35.3%)	5 (62.5%)	0.23†
Pain duration (years)	13.8±1.6	13.9±1.7	13.5±4.6	0.94*
Previous rhizotomy	16 (38.0%)	14 (41.2%)	2 (25.0%)	0.69†
Non-smoker	34 (81.0%)	28 (82.0%)	6 (75.0%)	0.64†
Baseline NRS	7.0±0.2	7.0±0.2	7.1±0.7	0.89*
Baseline ODI	46.6±2.2	45.0±2.0	53.5±7.7	0.32*
Baseline EQ-5D	0.426±0.035	0.454±0.036	0.306±0.096	0.18*
DASS—depression (moderate or less)	31 (74%)	26 (76%)	5 (63%)	0.41†
DASS—anxiety (moderate or less)	33 (79%)	28 (82%)	5 (63%)	0.34†
DASS—stress (moderate or less)	30 (71%)	25 (74%)	5 (63%)	0.67†

Depression, anxiety, and stress from their respective components of the DASS scale. Comparison between completer group and non-completer group; p<0.05 considered to be statistically significant.
*Parametric data compared using two-sided t-test.
†Proportional data compared using Fisher exact test.
BMI, body mass index; EQ-5D, EuroQol-5 Dimension; NRS, Numerical Rating Scale; ODI, Oswestry Disability Index.

Table 2 Analysis of patient-reported outcomes, including 'As Completed' and 'As Treated' with imputation for missing data

Completer analysis					AT/MMRM			
Study visit	N	NRS mean (SE)	ODI mean (SE)	EQ-5D mean (SE)	N	NRS mean (SE)	ODI mean (SE)	EQ-5D mean (SE)
Baseline	**42**	7.0 (0.2)	46.6 (2.2)	0.426 (0.035)	**42**	7.0 (0.3)	46.6 (2.9)	0.426 (0.036)
Year 1	**39**	4.7 (0.4)	32.0 (3.2)	0.620 (0.040)	**42**	4.7 (0.4)	32.3 (2.9)	0.611 (0.037)
Year 2	**37**	3.5 (0.3)	29.2 (3.1)	0.675 (0.030)	**42**	3.7 (0.4)	31.2 (2.9)	0.648 (0.038)
Year 3	**33**	2.7 (0.3)	26.0 (3.1)	0.705 (0.036)	**42**	2.8 (0.4)	27.2 (3.0)	0.687 (0.039)
Year 4	**34**	3.3 (0.5)	25.7 (3.2)	0.659 (0.038)	**42**	3.5 (0.4)	27.7 (3.0)	0.634 (0.039)
Year 5	**34**	3.2 (0.4)	26.1 (2.6)	0.703 (0.027)	**42**	3.5 (0.4)	28.9 (3.0)	0.663 (0.039)

Bold indicates the difference between the computer analysis and the treated analysis.
EQ-5D, EuroQol-5 Dimension; NRS, Numeric Rating Scale; ODI, Oswestry Disability Index.

in pain, disability, and healthcare-related quality of life (figure 2a–c). In the As Treated (AT) with MMRM, mean baseline pain reduced from 7.0±0.3 to 3.5±0.4, mean baseline ODI reduced from 46.6±2.9 to 28.9±3.0, and mean baseline EuroQol-5 Dimension (EQ-5D) increased from 0.426±0.036 to 0.663±0.039.

The completer analysis excluding patients exiting the study for reasons described above shows a slightly larger effect, as in the AT 5/42 had baseline observations carried forward. Those with outcomes observed (34/42) at the 5-year follow-up demonstrated a reduction in pain from 7.0±0.2 to 3.2±0.4, with 67% (23/34) and 62% (21/34) benefiting from a greater than 30% and 50% reduction in pain, respectively. Baseline disability dropped from 46.6±2.2 to 26.1±2.6, with 82% (28/34) and 56% (19/34) benefiting from a greater than 10- and 15-point reduction, respectively, and a mean difference in 5-year completers of 18.9±2.1. In combination, at 5 years, 82% of patients experienced a minimally clinically important change (MCIC) of a 30% reduction in NRS or a 15-point reduction in ODI, while 59% of patients achieved substantial improvements of 50% in NRS or 20 points in ODI. Healthcare-related quality of life improved from an index score of 0.426, representative of multidimensional moderate to severe health issues, to an index of 0.703, representative of negligible to mild impact likely only in a single dimension. There were 21/34 (62%) pain remitters (defined as a residual NRS≤3) at 5 years postimplant.

Univariate correlation between demographic factors was performed to assess the relationship with a reduction in pain at 5 years (figure 3a–c). There was no significant correlation between age at implant (r=−0.21, p=0.23), body mass index (BMI) (r=−0.16, p=0.36), or duration of lower back pain (LBP) symptoms (r=−0.09, p=0.60), suggesting that these variables are not specifically predictive of response to the therapy.

System utilization

Estimation of the missing usage data was not impacted by the size of the extrapolation average from 2 or 10 weeks prior to the missing data (figure 4a). Subsequent analysis was performed using a 2-week extrapolation.

The heat map of device utilization in figure 4b–c shows variation of usage patterns among patients with and without extrapolated data. On average, a reduction from 312 hours/patient of therapy in the first year to an average of 166 hours by the fifth year was noted. Over the entire follow-up period, on average, patients delivered a total of 1106 hours of therapy, or the equivalent of over 132 000 strong and isolated multifidus muscle contractions. This quantity of musculoskeletal activation is not possible nor practical to achieve by other methods.

The correlation between system utilization and outcomes (figure 4d) showed there was a reduction in average system utilization, even as early as year 1, in patients who failed to achieve an MCIC in either pain (ΔNRS <30%) or disability (ΔODI <15) (n=6). Patients who benefited by more than the MCIC in pain and/or disability but less than 50% change in NRS or 30 points in ODI have similar usage patterns to those attaining substantial benefit.

Safety outcomes

The safety profile for years 1–3 has been previously reported.[14 15] Throughout years 4 and 5, there were no serious adverse events reported and one report of tissue overstimulation/uncomfortable muscle activation that was resolved through reprogramming the stimulation parameters.

DISCUSSION

This report presents the 5-year clinical outcomes from a cohort of patients selected from real-world clinical practice and is a continuation of efforts to understand the long-term clinical utility of direct multifidus muscle motor stimulation in CLBP patients. Additionally, this is the first detailed examination of the amounts of stimulation being applied by patients over extended periods. The 'As Treated' analysis showed that response to the therapy was robust and durable in most patients. When MMRM imputation for missing data was applied, mean baseline pain reduced from 7.0±0.3 to 3.5±0.4, mean baseline ODI reduced from 46.6±2.9 to 28.9±3.0, and mean baseline EQ-5D increased from 0.426±0.036 to 0.663±0.039. 82% (28/34) of patients completing 5-year follow-up responded by more than an MCIC in pain or disability, 65% (22/34) of patients achieving substantial improvements (ΔNRS ≥50% and/or ΔODI ≥20 points) in pain or disability, and 62% (21/34) pain remitters (residual NRS≤3) at 5 years postimplant. This cohort was comprised of patients who had very few options available to them, having exhausted current National Institute for Health and Care Excellence (NICE) guidelines for management of CLBP. There was no statistically significant correlation between outcome and age, BMI, or pain duration (figure 3), though a larger sample may be more instructive.

Reports of long-term outcomes of neuromodulation for low back pain are infrequent. Notably, the ReActiv8-B trial reported[11] outcomes on 126 participants at year 5, accounting for missing data using similar imputation methods as this study. The results of the current study are consistent with the long-term data from Gilligan *et al*[11] demonstrating improvements in pain disability and quality of life (table 3). These outcomes are also consistent with the conclusion of a recent systematic

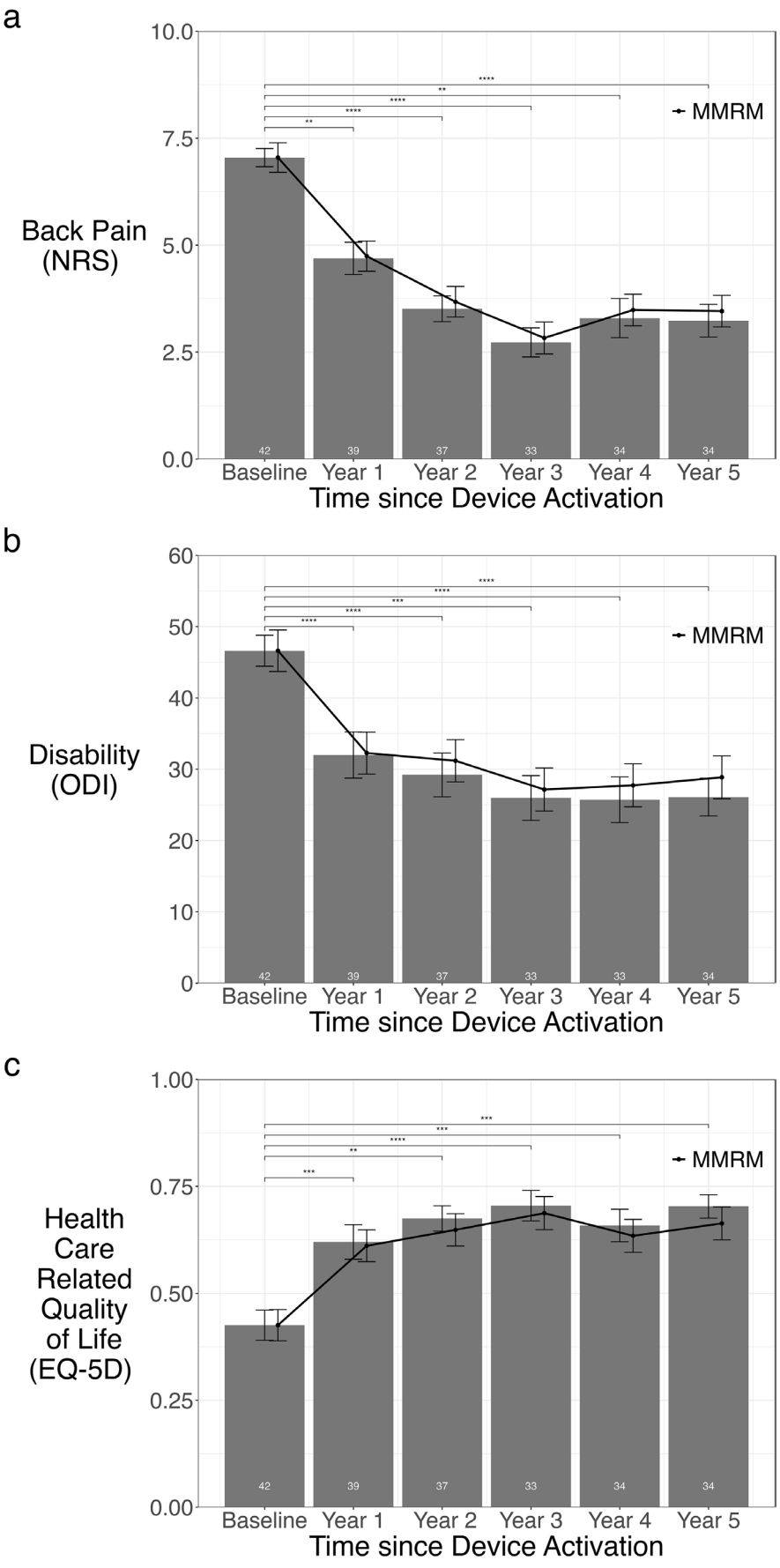

Figure 2 Mean patient-reported outcomes over time for (a) low back pain Numeric Rating Scale (NRS), (b) Oswestry Disability Index (ODI), and (c) quality of life via EQ-5D-5L index. A bar plot shows completers for each time point. The red line indicates the imputation for missing data using mixed method of repeated measures (MMRM). Error bars represent the SE of the mean. EQ-5D-5L, EuroQol-5 Dimension, 5 Level.

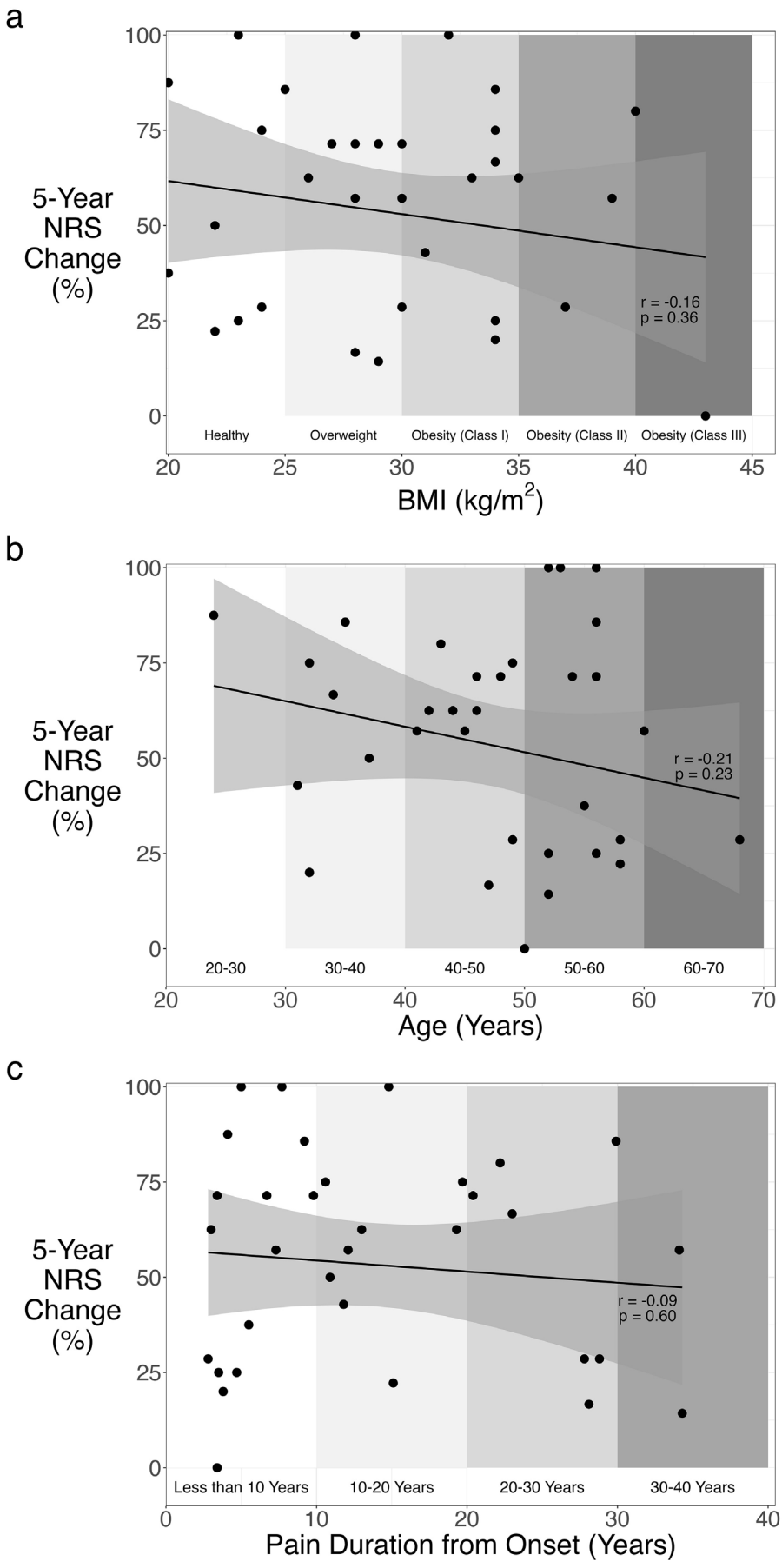

Figure 3 Correlation between reduction in pain score at 5 years and select demographics: (a) age, (b) body mass index (BMI), and (c) pain duration from LBP onset. NRS, Numeric Rating Scale.

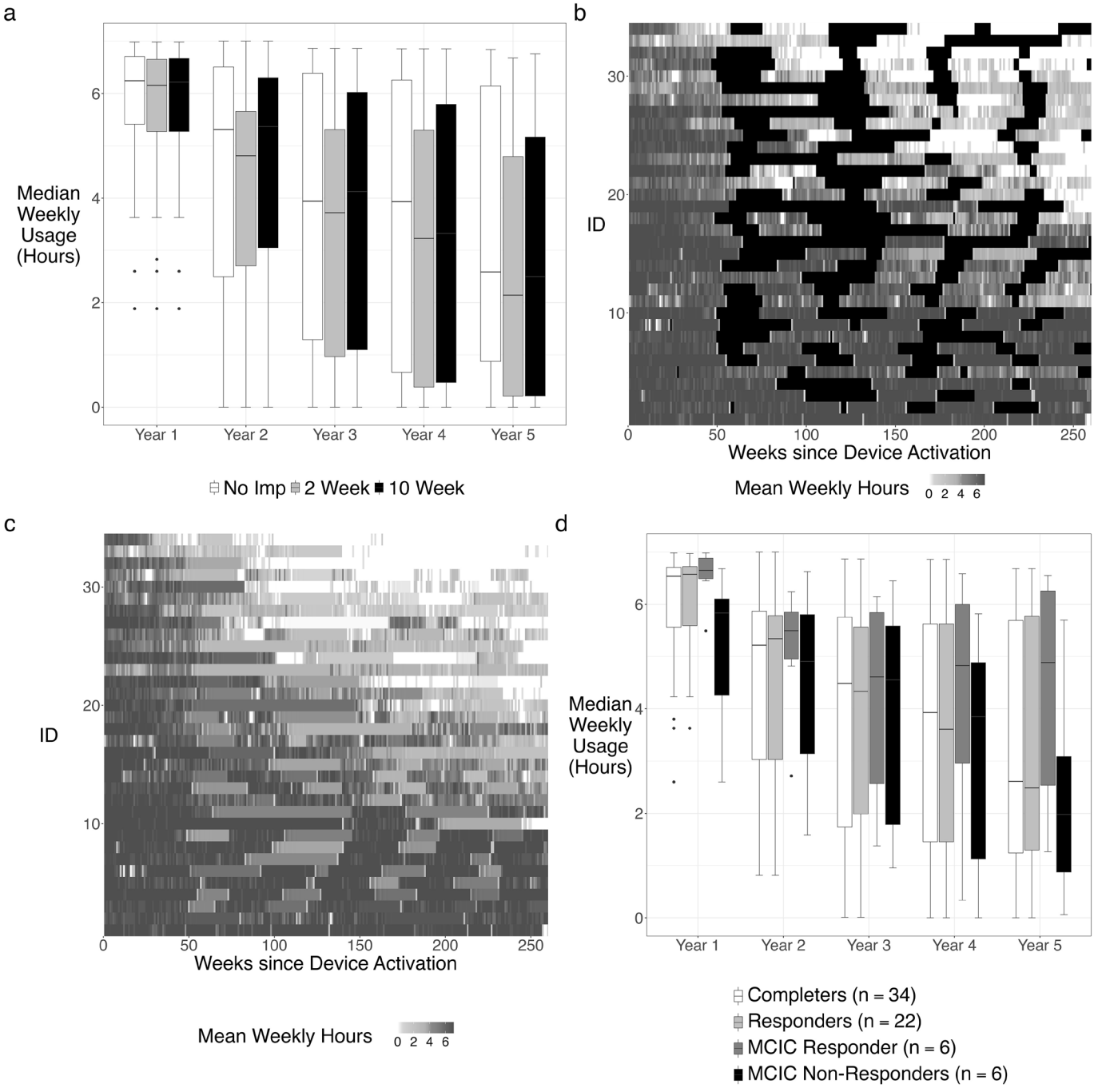

Figure 4 (a) Sensitivity analysis of missing utilization data extrapolation on median weekly device usage per year, with estimates for missing data based on previous 2 and 10 average weekly use. (b) Heat map of weekly device utilization of 34 patients reaching 5-year follow-up, no imputed data (c) 2-week prior average imputation (d) Median weekly device usage per year, for completers (n=34) with subsets of substantial responders (n=22)—patients with substantial improvement (NRS ≥50% and/or ODI ≥20 points), MCIC responders (n=6) patients benefiting by at least MCIC in pain or disability, but less than the threshold for substantial improvement (change in NRS ≥30% and ≤50% and/or ODI ≥15 and ≤30) and non-responders (n=6) patients who did not sustain any change greater than MCIC in NRS <30% and ODI <15. With all outcomes measured at 5 years. MCIC, minimally clinically important change; NRS, Numeric Rating Scale; ODI, Oswestry Disability Index.

review[23] and meta-analysis that determined 'longer duration of stimulation was associated with decreased low back pain intensities' as demonstrated here by the analysis of system utilization. A recent report[24] of a survey of responders to 60-day peripheral nerve stimulation at longer than 4 years follow-up has also been recently published, though minimal data were presented and complete patient disposition was limited by the retrospective methodology.

There is strong evidence of the association between mechanical CLBP and motor control dysfunction of the multifidus muscle, with multiple studies correlating changes in structure, function, and appearance with the onset and maintenance of low back pain.[1 25 26] As a result, therapies aimed at improving motor control have been deployed to clinical practice with mixed efficacy. Motor control exercises remain the standard of care for a physical medicine approach to CLBP, and this has been the focus

Table 3 Results of long-term follow-up of medial branch stimulation for CLBP

	Study	Gilligan et al[24]		Gilmore et al[24]	Current study	
	Follow-up length	5 years		4+ years	5 years	
	Follow-up methodology	Prespecified prospective follow-up		Ad-hoc survey	Prespecified prospective follow-up	
	Available population	As Treated with imputation	All completers	Therapy responders only	As Treated with imputation	All completers
	N	204	126	23	42	34
Baseline	*Mean Pain* (SE)*	7.3 (0.05)		6.6 (0.3)	7.0 (0.2)	
	Mean ODI (SE)	39.1 (0.7)		NR	46.6 (2.2)	
	Mean EQ-5D (SE)	0.585 (0.012)		NR	0.426 (0.035)	
Outcomes at longest follow-up	*Mean Pain* (SE)*	3.3 (0.2)	2.4 (0.2)	NR	3.5 (0.4)	3.2 (0.4)
	Mean ODI (SE)	20.3 (1.1)	16.5 (1.3)	NR	28.9 (3.0)	26.1 (2.6)
	Mean EQ-5D (SE)	0.768 (0.013)	0.807 (0.015)	NR	0.663 (0.039)	0.703 (0.027)
	30% pain reduction	66.1% (3.7)†	81.5% (101/124)	65% (15/23)	NR	67% (23/34)
	50% pain reduction	57.6% (3.8) †	71.8% (89/124)	NR	NR	62% (21/34)
	Reduction in ODI	18.7 (1.1)	22.7 (1.4)	11.5 (3.0)	17.7 (3.0)	18.9 (2.1)
	10-point ODI reduction	NR	NR	70% 1 (6/23)	NR	82% (28/34)
	15-point ODI reduction	59.7% (3.7)†	73.0% (92/126)	NR	NR	56% (19/34)

*Visual Analog Score (VAS)—Gilligan *et al*/Brief Pain Inventory (BPI)—Gilmore *et al*/Numerical Rating Scale (NRS)—this study.
†Proportions estimated by imputation presented with 95% CIs. NR—not reported in the manuscript
CLBP, chronic mechanical low back pain; EQ-5D, EuroQol-5 Dimension; ODI, Oswestry Disability Index.

of multiple clinical trials and systematic reviews[27–29] that conclude that motor control training can be beneficial for subacute cases where neurological activation can still be achieved, but in cases of CLBP associated with denser neurological inhibition/deficit, exercise alone may not be beneficial. Approaches that use volitional activation of discrete paraspinal muscles are inherently limited to muscle groups that maintain some level of neural integration. Unfortunately, in cases of chronic motor control loss, central reorganization of descending motor control results in a reliance on compensatory strategies that involve muscles that are less well adapted for the specific task of functional trunk stability.[30 31] For example, without discrete drive to the multifidus, activation of longissimus muscles occurs as a compensatory mechanism to account for deficits in the multifidus activation.[32] Both the anatomy and structure of the longissimus would suggest that the role of this muscle is for large movements of the trunk rather than the precise control required for segmental stability.[33] Simplistically, exercise in the presence of selective neural inhibition of the multifidus muscle results in a reinforcement of less well-adapted compensatory mechanisms, that is, stabilization via longissimus, rather than restoring the function of the primary motor control actuator.

The alternative to actively attempting volitional muscle activation, which often is impacted by neural inhibition, is specific muscle activation via direct motor stimulation of the neural structures innervating the multifidus muscle. This has been demonstrated through multiple clinical studies as an effective intervention for significant and durable pain relief in patients with low back pain from impaired multifidus motor control.[10–15] The clinical outcomes from this study support the prior work by demonstrating sustained clinical benefit at the 5-year follow-up.

This paper is the first to present a detailed analysis of how patient utilization changes over time. It was important to understand device ultilization since restorative neurostimulation therapy sessions are directly initiated by the patient, with stimulation being able to be applied in up to two daily sessions, with a maximum time of 30 min per session. It was hypothesized the patient system usage would decrease over time, which was on aggregate, confirmed by this analysis. Several different usage patterns emerged, namely, high users (two times per day on most days), intermediate users (less than once per day), infrequent users (periods of low use interspersed with periods of high use), and low users (fewer than three times per week). The regularity of stimulation sessions is highly patient-context-specific, and without formal qualitative assessment of their rationale, it is difficult to assign meaning to these patterns. For example, a high user, despite having a substantial response, may continue to be a high user because they need stimulation to maintain improvement, *believe* they need stimulation to maintain symptom response, prefer the sensation of stimulation, and/or have a highly compliant personality type. Alternatively, an intermittent user with substantial response may decide to initiate therapy sessions only in anticipation of strenuous activity or for recovery because of residual back pain following strenuous activity.

Therefore, the relationship between clinical outcome and therapy utilization (figure 4d) is complicated by patient motivation to start therapy sessions. This includes the observed lower utilization in patients who did not go on to achieve clinical benefit at 5 years. It is impossible to establish whether the lack of response was a result of the patient not using the stimulator or the patient responding to the therapy and stopping using the stimulator without contextual input from the patient. Care should be taken to not misinterpret this, as the number of patients not achieving MCIC for both ODI and NRS was small (n=6). Further analysis on larger data sets should be undertaken.

The diagnosis of chronic multifidus dysfunction is relatively new to the world of interventional pain medicine but is well established within academic musculoskeletal literature. It is a clinical diagnosis and has been described previously.[34 35]

To date, the approach of interventional pain medicine has been to methodically diagnose an underlying pain generator that may be amenable to treatment, such as neural ablation. Multifidus dysfunction is agnostic to any specific pain generator. If multifidus dysfunction is present, the majority of patients with low back pain respond durably to direct nerve/muscle activation. The diagnosis and therapy represent a disruption to the management of persistent low back pain. It does not replace palliative measures such as medial branch radiofrequency (MBRF)

neurolysis but prevents the need for other less effective therapies, such as repeat MBRF or spinal fusion. The authors have incorporated the treatment into their therapeutic algorithm. Time will tell if low back pain care guidelines will change as well. This cohort, from a more generalizable population of persistent low back pain patients, supports the previous published data.

Strengths and limitations

This study provides a 5-year clinical follow-up on patients treated with restorative neurostimulation. It is the only report of outcomes over this length of follow-up besides the pivotal ReActiv8-B trial. This therapy is patient-initiated, and this paper is the first to document long-term utilization trends alongside clinical outcomes. While the cohort is modest in size, retention in the study was good, with 81% (34/42) of patients available for the 5-year follow-up, and stringent collection of safety data was performed over the entire 5 years. This is an open-label study without a control arm and has the associated inherent limitations, such as comparisons to baseline rather than control.

CONCLUSIONS

Restorative neurostimulation continues to demonstrate sustained improvements in clinical outcomes in real-world settings. At 5 years postimplant, patients reported substantial and sustained improvements in pain, disability, and health-related quality of life. The outcomes presented here are consistent with the recent report of the 5-year results from the pivotal ReActiv8-B trial. The analysis of device utilization suggests most patients stimulate frequently, even after symptoms have resolved. Patient usage over time decreased from an average of 312 patient hours of therapy in year 1 to 166 hours by year 5, suggesting the potential of restoration in the function/strength of the muscle group being stimulated. Patients received, on average, a total of 1106 hours of therapy throughout the 5-year follow-up period. Overall, restorative neurostimulation is a safe and effective treatment for the vast majority of patients with CLBP associated with multifidus muscle dysfunction.

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