# Real-World Evidence for Restorative Neurostimulation in Chronic Low Back Pain—a Consecutive Cohort Study

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■ BACKGROUND: **Neuromuscular instability of the lumbar spine resulting from impaired motor control and degeneration of the multifidus muscle is a known root cause of refractory chronic low back pain (LBP). An implantable neurostimulation system that aims to restore multifidus motor control by stimulating the L2 medial branch of the dorsal ramus thereby relieving pain and reducing disability has demonstrated clinically significant benefits in the clinical trial setting. The 1-year results of a single-site real-world cohort study are presented.**

■ METHODS: **This study recruited 44 consecutive patients with refractory, predominantly nociceptive axial chronic LBP, evidence of multifidus dysfunction, and no surgical indications or history of surgical intervention for chronic LBP. Each patient was implanted with a neurostimulation device. Pain (numeric rating scale), disability (Oswestry Disability Index), and quality of life (5-level EuroQol 5-Dimension) outcomes were collected at baseline and 3, 6, and 12 months after activation.**

■ RESULTS: **Statistically significant improvements in pain, disability, and quality of life from baseline were seen at all assessment time points. At 12 months after activation, mean ± standard error of the mean numeric rating scale score was reduced from 7.6 ± 0.2 to 3.9 ± 0.4 ($P < 0.001$), Oswestry Disability Index score was reduced from 43.0 ± 2.8 to 25.8 ± 3.9 ($P < 0.001$), and 5-level EuroQol 5-Dimension index improved from 0.504 ± 0.034 to 0.755 ± 0.039 ($P < 0.001$). No lead migrations were observed. One patient required revision due to lead fracture.**

■ CONCLUSIONS: **Restorative neurostimulation is a new treatment option for well-selected patients with refractory chronic LBP. Clinically meaningful improvements in pain, disability, and quality of life demonstrated in routine clinical practice are consistent with published results of controlled trials.**

## INTRODUCTION

Low back pain (LBP) is the leading cause of years lived with disability globally and is endemic to both high- and low-income countries.[1] The prognosis for most patients with LBP is good, and the majority of patients will either not need to seek clinical care or recover rapidly with relatively minor noninvasive treatments. A few patients go on to develop chronic, disabling LBP. Currently, clinical practice guidelines from a number of international societies[2-4] provide limited recommendations for durable physiological treatments with small effect sizes. One reason for this is the heterogeneous nature of nonspecific LBP with a multifactorial presentation that typically involves physiological, psychological, and social factors. Educational and cognitive coping interventions are typically left as the last line of therapy in patients experiencing severe, refractory chronic LBP. The need for durable, effective therapies is well recognized, specifically therapies that focus on restorative or rehabilitative mechanisms.[5]

The initiation of the progression from acute to chronic LBP has been attributed to a short-term acute nociceptive stimulus that disrupts back muscle function. The resultant inhibition and inflammation lead to further changes to the structure and function

**Key words**
- Chronic low back pain
- Dorsal ramus stimulation
- Lumbar multifidus
- Motor control
- Restorative neurostimulation

**Abbreviations and Acronyms**
EQ-5D-5L: 5-Level EuroQol 5-Dimension
IPG: Implantable pulse generator
LBP: Low back pain
NRS: Numeric rating scale
ODI: Oswestry Disability Index

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of the back muscles, including fat and connective tissue infiltration, atrophy, and muscle fiber changes resulting in reduced strength and endurance. These changes persist through a self-sustaining cycle of injury, inhibition, inflammation, degeneration, disuse, and injury. Ultimately, neuroplastic changes occur as an adaptive mechanism to attempt to disrupt this degenerative cascade by recruiting alternative, less well-suited structures for postural stability and motor function. This altered motor control subsequently underpins the recurrence and ultimate chronification of LBP.

One key structure that is significantly affected by both acute and chronic LBP is the multifidus muscle. Anatomically the multifidus is the most medial of the paraspinal muscles and inserts between the spinous and mammillary processes. It is innervated segmentally via the medial branch of the dorsal ramus and consists of both deep fascicles spanning a single segment and longer, more superficial fascicles that can span the entire lumbar spine. Functionally, this muscle provides segmental stability through the combination of short and long fibers providing compressive forces and acting across single and multiple segments.

Biomechanical studies have shown the relative contribution of the paraspinal musculature to maintaining stability and motor control by preventing deviations from normal range of motion[6] and providing proprioceptive feedback to the control loop. In particular, the lumbar multifidus provides dynamic stability by tonically activating in a carefully choreographed response to spinal perturbations, such as moving, lifting, and changes to the center of gravity. At the same time, the high density of muscle spindles in the multifidus provides lumbosacral position sense. The lumbar multifidus appears to be particularly sensitive to the onset of acute LBP and undergoes rapid atrophy and functional inhibition.[7,8] The intervertebral disc and zygapophyseal joint have been shown to have a direct neurological influence on the activation and inhibition[9,10] of the multifidus, and the divergence of this dysfunction is thought to manifest in loose versus tight motor control strategies.[11]

Nociception arising from these structures activates protective reflexes, which may result over time in a cycle of instability, thereby inducing pain and maintaining further motor dysfunction and chronic nociceptive input.[12] Overcoming multifidus inhibition is believed to disrupt this cycle and restore motor control to the spine, thereby improving dynamic function. This restoration facilitates durable improvements in pain, disability, and quality of life.[13-15]

As the multifidus is uniquely vulnerable to neurological inhibition and degenerative changes, this muscle has been the target of restorative motor control strategies using physical and exercise therapies for several decades. As a frontline conservative approach, this is both clinically rational and often effective, but a significant proportion of patients derive no benefit. After failing physical therapy the remaining options are usually palliative, including medical management with opioids, anesthetic injections, and neurotomies.

An emerging approach for patients with mechanical LBP that has been refractory to conservative management is restorative neurostimulation (ReActiv8; Mainstay Medical, Dublin Ireland). This therapy involves direct stimulation of the medial branch of the dorsal ramus nerve via implanted leads and a pulse generator. This stimulation modality elicits smooth tetanic contractions of the multifidus and is intended to restore function through a mechanism involving restoration of motor control.

The efficacy of restorative neurostimulation has been demonstrated in a randomized controlled trial with a 2-year published follow-up[16] and multicenter cohort studies with 2-year[17] and 4-year[18] published data showing a consistent durable effect. The experience in a real-world setting has not yet been documented in the literature; thus we present here the results from a single surgeon recruiting patients directly from the community. These data were obtained from the ReActiv8 Post Market Surveillance Registry (ReActiv8-C) in consecutive patients with untreated back pain from a single center with 1 year of clinical follow-up.

## MATERIALS AND METHODS

### Ethics Approval

This study was conducted with the approval of the Schleswig-Holstein Ethics Committee endorsing the decision of the North Rhine Medical Association Ethics Committee and performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendment. All patients were required to provide written informed consent before participation. The trial was registered on ClinicalTrials.gov (ClinicalTrials.gov Identifier: NCT03255200).

### Patient Selection and Inclusion Criteria

Patients were selected based on a history of refractory, chronic mechanical LBP with minimal leg pain that was refractory to conservative treatment. The definition of chronicity was consistent with current literature as "chronic when it persists for 12 weeks or more."[19] Patients were considered refractory to conservative treatment if they had attempted and failed a combination of physiotherapy, cognitive-behavioral therapy, and/or pharmacological management. In practice, to meet these criteria meant patients generally had a considerably longer pain duration than the minimum 12-week definition. Additionally, patients were enrolled only if they reported a back pain numeric rating scale (NRS) score >6 and no report of leg pain radiating below the knee. Patients with a history of prior lumbar spine surgery such as decompression or fusion were excluded; patients with current pathologies, such as foraminal stenosis and high-grade spondylolistheses, indicated to be amenable to surgical treatment were also excluded. Other degenerative changes not treatable with surgery but visible on magnetic resonance imaging, such as Modic changes, facet arthropathy, annular tears, and low-grade spondylolisthesis, were not considered to be cause for exclusion. In this study, rhizotomy was not considered to be spine surgery, and patients with a previous rhizotomy were enrolled provided that the patient reported pain intensity meeting the inclusion criteria (i.e., they had not had a durable response to the rhizotomy) and that their most recent ablation was performed >10 months prior, so that any damaged peripheral neural structures had sufficient time to regenerate.

Multifidus dysfunction was identified on magnetic resonance imaging as substantial (>10%)[20] replacement of muscle by high-intensity signal in the multifidus at L4 and/or L5. This threshold has been shown to be associated with chronic LBP,[20] and

mechanistic studies of chronic LBP with motor control dysfunction have identified this as a hallmark sign of dysfunction.[21] The mechanical nature of the patient's LBP was determined through a physical assessment that included observations of aberrant movement patterns[22,23] to identify functional lumbar segmental instability and motor control impairment. Ultimately, a 44 consecutive patients were recruited at a single center (Klinikum Itzehoe, Itzehoe, Germany) between November 2018 and September 2020 and underwent implantation of the restorative neurostimulation device by a single surgeon (AA).

### Device Description

The ReActiv8 system consists of 2 leads connected to a programmable implanted pulse generator (IPG). Located at the distal ends of each lead are 4 stimulating electrodes and 2 sets of passive fixation tines. The IPG can be programmed to deliver stimulation between any pair of electrodes on each lead. The device and its anatomical location is illustrated in Figure 1.

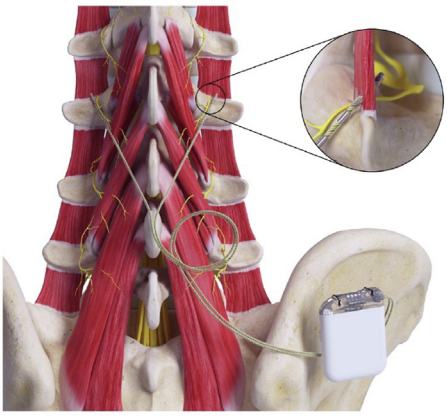

**Figure 1.** Reactiv8 device and implantation location.

### Surgical Technique

The system was implanted with patients under general anesthesia. Leads were implanted bilaterally from a small midline incision over the L4 spinous process under fluoroscopic guidance through 7F introducers that were placed using a modified Seldinger technique. The leads were advanced through the introducers, and the tines were deployed on either side of the intertransversarii to secure the electrodes in position adjacent to the L2 medial branch of the dorsal ramus in the junction of the root of the L3 transverse process with the root of the superior articular process, similar to the positioning of a radiofrequency ablation electrode. After on-table multifidus contraction testing, leads were tunneled to the subcutaneous IPG pocket, and excess lead was looped behind the IPG. The IPG was positioned under the skin in the lower lumbar or upper gluteal area through a 3- to 4-cm incision. The surgical incisions were closed, final testing was completed, and anteroposterior and lateral images of the implanted system were obtained.

### Device Activation and Programming

Devices were programmed 14 days after implantation to elicit strong, smooth multifidus contractions with a stimulation frequency of 20 Hz, a pulse width of 214 μs, and a pulse amplitude and electrode configuration programmed on an individual basis to ensure that the muscle contractions were comfortable and pain-free. Stimulation parameters were reviewed and adjusted when needed at each follow-up or between scheduled visits if required. Patients were instructed to perform two 30-minute stimulation sessions per day while remaining at rest in either a supine or a lateral position. Stimulation induced muscle contractions that lasted 10 seconds alternating with 20 seconds of rest.

### Data Collection and Statistical Analysis

Patients were assessed during clinic visits preoperatively and at 90, 180, and 365 days after device activation. Assessments of LBP (NRS), disability (Oswestry Disability Index [ODI]), and quality of life (5-level EuroQol 5-Dimension [EQ-5D-5L]) were collected directly from the patient by trained research staff not involved in their clinical care.

Patients were divided into therapy response groups for pain (NRS: $\geq$30% moderate improvement, $\geq$50% substantial improvement, remitters [NRS score$\leq$3]) and disability (ODI: $\geq$10 points minimal clinically important change, $\geq$20 points clinically substantial improvement) according to the guidelines recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials.[24] This was presented as proportion of patients per response group at each assessment time point. The 1-year data are presented as completed cases and imputed for the 2 patients who withdrew from the study using last observation carried forward.

Continuous variables such as patient-reported outcomes were compared with baseline values using repeated-measures analysis of variance, with post hoc pairwise testing performed using Bonferroni adjustments. We used an $\alpha$ level of 0.05 for all statistical tests. All statistical analysis was conducted using R Version 3.6.1 (https://www.R-project.org).

## RESULTS

### Demographics

The cohort included in this analysis comprised 44 consecutive patients. Demographic data are presented in Table 1. Median age of patients was 54 years, and median duration of chronic LBP was 5.8 years. Three patients with a previous rhizotomy (6.8%) were included because the rhizotomy was performed >10 months before enrollment and pain had persisted or returned despite this intervention. At the time of inclusion, 44.7% of patients were smokers. Of 44 patients, 40 (91%) completed follow-up after 1 year of therapy; 2 patients withdrew from the study before completing 1 year of therapy, and 2 patients were unable to attend follow-up appointments due to the COVID-19 pandemic (Figure 2). Two patients did not complete baseline ODI and EQ-5D-5L questionnaires, and hence they were included only in the analysis of NRS and demographics data.

### Patient-Reported Outcomes

Patient-reported outcomes at baseline and at 90, 180, and 365 days after device activation are summarized in Table 2. Statistically significant improvements in pain (NRS), disability (ODI), and quality of life (EQ-5D-5L) were seen at all assessment time points compared with baseline (Figure 3). A completer analysis showing the proportion of patients reaching specific thresholds of pain relief is shown in Figure 4A. After 1 year of therapy, 68% of patients had moderate (≥30%) reductions in pain, 52% had substantial (≥50%) reductions in pain, and 48% were remitters and had a pain score ≤3, which is considered to be mild pain to pain-free. There were 38 patients in the cohort who had baseline and 1-year data, and the ODI responder rates were 74% and 55% for minimal clinically important change (10 points) and substantial (20 points) response, respectively (Figure 4B). Health-related quality of life measured by EQ-5D-5L index increased from a baseline value of 0.466 ± 0.04 to 0.770 ± 0005 after 12 months of treatment, which demonstrates a change from severely impacted quality of life to a measure approaching the estimated German population norms for health-related quality of life of 0.908 and 0.881 in 45–54 and 55–65 age ranges, respectively.[25]

### Safety Outcomes

No lead migrations were observed. One patient required revision for a lead fracture. One patient presented with isolated sacroiliac joint pain that resolved after anesthetic injections. Two patients were withdrawn from the study due to lack of efficacy and elected to have the device removed. One of these patients did so after presenting with new-onset radicular pain in an L4-5 distribution attributed to a disc herniation diagnosed on computed tomography. This patient opted for explant 4 months after discectomy surgery for the herniation. No serious procedure- or device-related adverse events were reported.

## DISCUSSION

The translation of clinical trial outcomes to routine clinical practice is an important phase in the adoption of new technologies to ensure the generalizability of the therapy. As such, this cohort represents a single-surgeon, real-world cohort of severely affected patients with long-standing chronic LBP with a poor prognosis for improvement. Patients were recruited from the community and selected based on recommendations from the clinical trials rather than strict inclusion/exclusion criteria. This approach ensures a deeper understanding of therapy impact that is generalizable to the chronic LBP patient population. We present the collective experience of 44 consecutive patients who completed 12 months of ReActiv8 therapy. Patients with chronic LBP experiencing severe symptoms and pain duration of many years as included in this study rarely have spontaneous remission of symptoms.[26] Despite many available treatments for LBP, the prognosis for these patients with chronic pain remains poor.[27]

### Therapy Response

Restorative neurostimulation for the treatment of mechanical chronic LBP was shown to be effective in 2 clinical trials, and durability of effect was demonstrated at 1, 2, and 4 years after implantation in different studies.[16-18] In the ReActiv8-B clinical trial, 74% of the patients reported moderate and 64% reported substantial reductions in LBP at 1 year; 78% and 57% reported

**Table 1.** Baseline Patient Characteristics of Consecutive Cohort ($N = 44$)

| Characteristic | Value |
|---|---|
| Age, years, median (IQR) | 54 (11.5) |
| Sex, female (%) | 61 |
| Body mass index, mean (SD) | 28.2 (5.2) |
| Pain duration, years, median (IQR) | 5.8 (8.45) |
| Previous rhizotomy (%) | 6.8 |
| Smokers (%) | 44.7 |
| Physiotherapy sessions, median (IQR) | 68 (52) |
| Diagnosed or treated depression (%) | 12 |

IQR, interquartile range; SD, standard deviation.

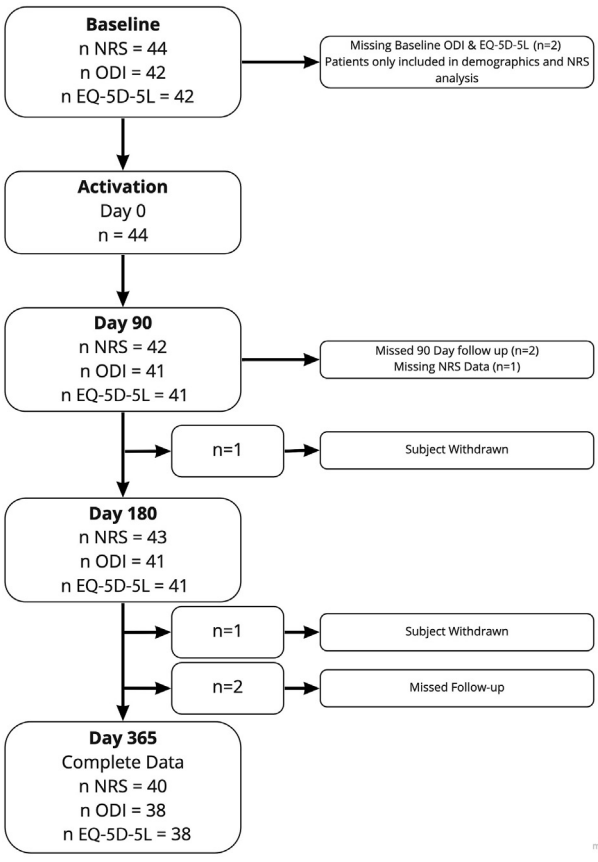


**Figure 2.** Patient disposition. NRS, numeric rating scale; ODI, Oswestry Disability Index; EQ-5D-5L, 5-level EuroQol 5-Dimension.

**Table 2.** Patient-Reported Outcomes for Patients Completing 1 Year of Therapy

| Outcome Measure | Baseline ($N = 44$) | 12 Months ($n = 40$) | *P* Value* | 12-Month LOCF ($N = 44$) | *P* Value* |
|---|---|---|---|---|---|
| NRS | 7.6 ± 0.2 | 3.9 ± 0.4 | <0.001 | 3.95 ± 0.5 | <0.001 |
| ODI | 43.0 ± 2.8† | 25.8 ± 3.9† | <0.001 | 26.9 ± 4.4† | <0.001 |
| EQ-5D-5L | 0.504 ± 0.034† | 0.755 ± 0.039† | <0.001 | 0.742 ± 0.045† | <0.001 |

All values are mean ± standard error of the mean.
LOCF, Last observation carried forward; NRS, numeric rating scale; ODI, Oswestry Disability Index; EQ-5D-5L, 5-level EuroQol 5-Dimension.
*Repeated-measures analysis of variance with Bonferroni adjustment for multiplicity compared with baseline.
†2 patients with missing baseline ODI and EQ-5D data were excluded from this completer analysis.

minimal clinically important and substantial reductions in ODI, respectively. In the single-center consecutive cohort reported here, 73% of patients reported a moderate and 53% reported a substantial reduction in LBP at 1 year; 75% and 61% reported minimal clinically important and substantial reductions in ODI, respectively. Moreover, data from the clinical trials[16,18] and postmarket studies[17] demonstrate not only that the response to this therapy is durable, but also that the benefits accumulate over time consistent with the restorative mechanism of action. These observations are consistent with the results from this cohort. Thus, the results of this postmarket cohort study demonstrate that the positive clinical trial outcomes may also apply to a real-world patient population, and patients should be expected to maintain or further improve the benefits gained.

## Limitations

As this study presents early open-label experience in routine clinical practice, it is limited by its small sample size, lack of a sham or untreated control arm, lack of blinding, and relatively short follow-up. Nevertheless, the results of this real-world experience are consistent with the published data from the earlier ReActiv8-A[18,28] and ReActiv8-B[29] studies.

Two patients were missing baseline ODI and EQ-5D-5L data, and these data could therefore not be included in the aggregate analysis of these outcome measures; however, they reported 12-month ODI scores of 8/100 and 10/100 points and 12-month EQ-5D-5L scores of 0.910 and 0.828, suggesting that their current state was equivalent to age-adjusted German population norms for quality of life and they were experiencing very low levels of disability. These values are compatible with the observed improvements in NRS scores from 8 to 3 and 6 to 3, respectively. Four other patients had data imputed in the 12-month analysis; 2 had not experienced clinical benefit and had the system explanted and 2 had not returned for follow-up due to the COVID-19 pandemic. The clinical benefit of restorative neurostimulation accrues over time, and patients opting for early explantation may have preempted the onset of therapeutic benefit. Longitudinal follow-up of morphological and functional changes in the multifidus muscle could potentially show some interesting adaptive changes; however the current device label does not currently

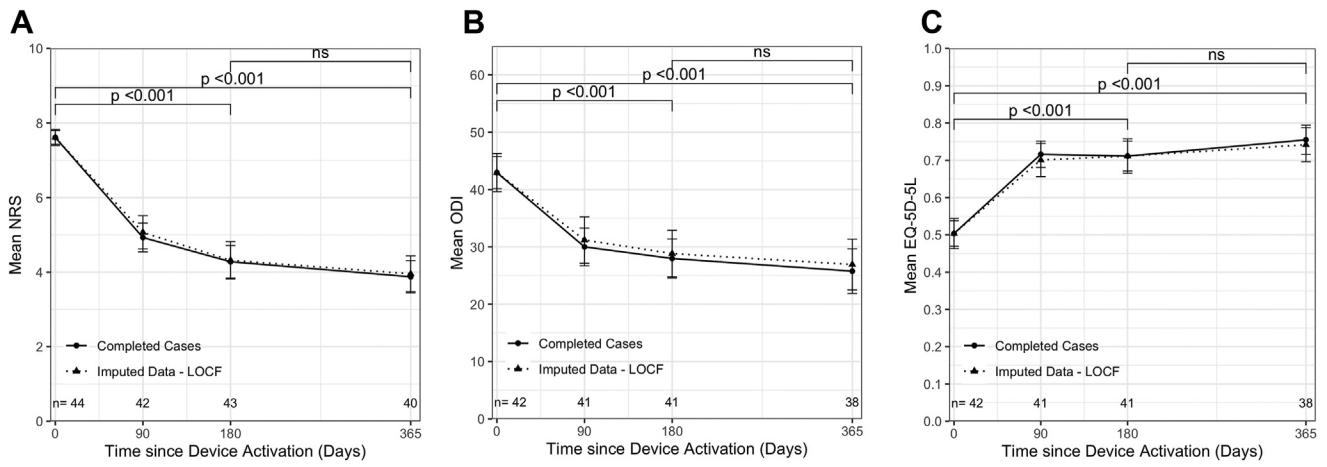


**Figure 3.** Mean patient-reported outcomes according to (**A**) numeric rating scale, (**B**) Oswestry Disability Index, and (**C**) 5-level EuroQol 5-Dimension showing statistically significant improvements over baseline at all time points (repeated measures analysis of variance with Bonferroni adjustment for multiplicity). NRS, numeric rating scale; ODI, Oswestry Disability Index; EQ-5D-5L, 5-level EuroQol 5-Dimension; ns, not significant; LOCF, last observation carried forward.

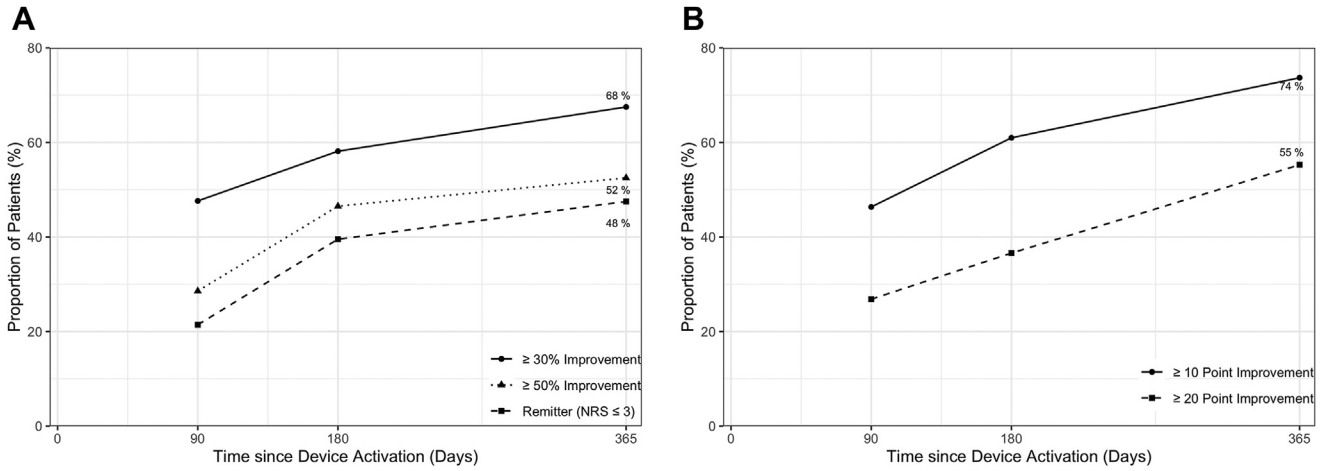


**Figure 4.** Proportion of patients by different responder thresholds for (**A**) numeric rating scale ($n = 40$) and (**B**) Oswestry Disability Index ($n = 38$). NRS, numeric rating scale.

permit postimplantation scans. This is a topic for further studies when magnetic resonance imaging compatibility has been established.

## CONCLUSIONS

Based on published evidence from multiple clinical trials, restorative neurostimulation has become established as an effective treatment for patients with refractory, mechanical chronic LBP. The meaningful clinical improvements achieved in pain, disability, and quality of life in our real-world cohort suggest that these published outcomes achieved in the clinical trial setting can also be achieved in routine clinical practice.

## CRediT AUTHORSHIP CONTRIBUTION STATEMENT

**Ardeshir Ardeshiri:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Writing — original draft, Writing — review & editing. **Christopher Shaffrey:** Formal analysis, Writing — original draft, Writing — review & editing. **Klaus-Peter Stein:** Writing — original draft, Writing — review & editing. **Ibrahim Erol Sandalcioglu:** Writing — original draft, Writing — review & editing.

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## REFERENCES

1. Vos T, Abajobir AA, Abbafati C, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the global burden of disease study 2016. *Lancet*. 2017;390:1211-1259.

2. Airaksinen O, Brox JI, Cedraschi C, et al. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. *Eur Spine J*. 2006;15 Suppl 2(Suppl 2):S192-S300.

3. Manchikanti L, Boswell MV, Singh V, et al. Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain. *Pain Physician*. 2009;12:699-802.

4. North American Spine Society. *Evidence-Based Clinical Guidelines for Multidisciplinary Spine Care: Diagnosis and Treatment of Low Back Pain*. Burr Ridge, IL: North American Spine Society; 2020:217. https://www.spine.org/Portals/o/assets/downloads/ResearchClinicalCare/Guidelines/LowBackPain.pdf.

5. Hartvigsen J, Hancock MJ, Kongsted A, et al. What low back pain is and why we need to pay attention. *Lancet*. 2018;391:2356-2367.

6. Panjabi MM. A hypothesis of chronic back pain: Ligament subfailure injuries lead to muscle control dysfunction. *Eur Spine J*. 2006;15:668-676.

7. Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine*. 2006;31:2926-2933.

8. Hodges PW, Danneels L. Changes in structure and function of the back muscles in low back pain: different time points, observations, and mechanisms. *J Orthop Sports Phys Ther*. 2019;49:464-476.

9. Indahl A, Kaigle AM, Reikerås O, Holm SH. Interaction between the porcine lumbar intervertebral disc, zygapophysial joints and paraspinal muscles. *Spine*. 1997;22:2834-2840.

10. Indahl A, Kaigle A, Holm S, Reikerss O. Electromyographic response of the porcine multifidus

musculature after nerve stimulation. *Spine*. 1995; 20:2652-2658.

11. Van Dieën JH, Peter Reeves N, Kawchuk G, Van Dillen LR, Hodges PW. Motor control changes in low back pain: divergence in presentations and mechanisms. *J Orthop Sports Phys Ther*. 2019;49: 370-379.

12. MacDonald D, Moseley GL, Hodges PW. Why do some patients keep hurting their back? Evidence of ongoing back muscle dysfunction during remission from recurrent back pain. *Pain*. 2009; 142:183-188.

13. Verbunt JA, Seelen HA, Vlaeyen JW, et al. Pain-related factors contributing to muscle inhibition in patients with chronic low back pain: an experimental investigation based on superimposed electrical stimulation. *Clin J Pain*. 2005;21:232-240.

14. Thunberg J, Ljubisavljevic M, Djupsjöbacka M, Johansson H. Effects on the fusimotor-muscle spindle system induced by intramuscular injections of hypertonic saline. *Exp Brain Res*. 2002; 142:319-326.

15. Freeman MD, Woodham MA, Woodham AW. The role of the lumbar multifidus in chronic low back pain: a review. *PM&R*. 2010;2:142-146.

16. Gilligan CJ, Volschenk W, Russo M, et al. Long-term outcomes of restorative neurostimulation in patients with refractory chronic low back pain secondary to multifidus dysfunction : 2-year results of the ReActiv8-B pivotal trial. *Neuromodulation*. 2021. https://doi.org/10.1016/j.neurom.2021.10.011.

17. Thomson S, Chawla R, Love-Jones S, et al. Restorative neurostimulation for chronic mechanical low back pain: results from a prospective multi-centre longitudinal cohort. *Pain Ther*. 2021; 10:1451-1465.

18. Mitchell B, Deckers K, De Smedt K, et al. Durability of the therapeutic effect of restorative neurostimulation for refractory chronic low back pain. *Neuromodulation*. 2021;24:1024-1032.

19. Chou R. Clinical evidence handbook. *Am Fam Physician*. 2011;84:437-438.

20. Kjaer P, Bendix T, Sorensen JS, Korsholm L, Leboeuf-Yde C. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? *BMC Med*. 2007;5:1-10.

21. James G, Sluka KA, Blomster L, et al. Macrophage polarization contributes to local inflammation and structural change in the multifidus muscle after intervertebral disc injury. *Eur Spine J*. 2018;27: 1744-1756.

22. Wattananon P, Ebaugh D, Biely SA, Smith SS, Hicks GE, Silfies SP. Kinematic characterization of clinically observed aberrant movement patterns in patients with non-specific low back pain: A cross-sectional study. *BMC Musculoskelet Disord*. 2017;18:1-12.

23. Denteneer L, Stassijns G, De Hertogh W, Truijen S, Van Daele U. Inter- and Intrarater reliability of clinical tests associated with functional lumbar segmental instability and motor control impairment in patients with low back pain: a systematic review. *Arch Phys Med Rehabil*. 2017;98: 151-164.e6.

24. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain*. 2005;113:9-19.

25. Szende A, Janssen B, Cabasés J. *Self-Reported Population Health: An International Perspective Based on EQ-5D*. 2014:1-196.

26. Kongsted A, Hestbæk L, Kent P. How can latent trajectories of back pain be translated into defined subgroups? *BMC Musculoskelet Disord*. 2017;18:1-13.

27. Pengel LHM, Herbert RD, Maher CG, Refshauge KM. Acute low back pain: systematic review of its prognosis. *BMJ*. 2003;327:323-325.

28. Deckers K, De Smedt K, Mitchell B, et al. New therapy for refractory chronic mechanical low back pain—restorative neurostimulation to activate the lumbar multifidus: one year results of a prospective multicenter clinical trial. *Neuromodulation*. 2018;21:48-55.

29. Gilligan C, Volschenk W, Russo M, et al. An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. *Pain*. 2021;162:2486-2498.

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