

International Society for the Advancement of Spine Surgery Statement: Restorative Neurostimulation for Chronic Mechanical Low Back Pain Resulting From Neuromuscular Instability

Morgan Lorio, Kai-Uwe Lewandrowski, Domagoj Coric, Frank Phillips and Christopher I. Shaffrey

Int J Spine Surg 2023, 17 (5) 728-750

doi: <https://doi.org/10.14444/8525>

<https://www.ijssurgery.com/content/17/5/728>

This information is current as of May 2, 2025.

Email Alerts Receive free email-alerts when new articles cite this article. Sign up at:
<http://ijssurgery.com/alerts>

International Society for the Advancement of Spine Surgery Statement: Restorative Neurostimulation for Chronic Mechanical Low Back Pain Resulting From Neuromuscular Instability

MORGAN LORIO, MD¹; KAI-UWE LEWANDROWSKI, MD^{2,3,4}; DOMAGOJ CORIC, MD⁵; FRANK PHILLIPS, MD⁶; AND CHRISTOPHER I. SHAFFREY, MD⁷

¹Advanced Orthopedics, Altamonte Springs, FL, USA; ²Center for Advanced Spine Care of Southern Arizona, The Surgical Institute of Tucson, Tucson, AZ, USA;

³Department of Orthopedics, Fundación Universitaria Sanitas, Bogotá, DC, Colombia; ⁴Department of Orthopedics Hospital Universitário Gaffre e Guinle, Universidade Federal do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil; ⁵Neuroscience Institute, Carolinas Healthcare System and Carolina Neurosurgery & Spine Associates, Charlotte, NC, USA; ⁶Department of Orthopedic Surgery, Rush University Medical Center, Chicago, IL, USA; ⁷Spine Division, Duke Neurosurgery, Durham, NC, USA

ABSTRACT

This International Society for the Advancement of Spine Surgery statement has been generated to respond to growing requests for background, supporting literature and evidence, and proper coding for restorative neurostimulation for chronic low back pain. Chronic low back pain describes the diverse experience of a significant proportion of the population. Conservative management of these patients remains the predominant care pathway, but for many patients, symptom relief is poor. The application of new techniques in patients who have exhausted traditional care paradigms should be undertaken with a detailed understanding of the pathology being treated, the mechanisms involved, and the data supporting efficacy. This statement on restorative neurostimulation places this technology in the context of the current understanding of the etiology of mechanical low back pain and the currently available evidence for this technique. In an appropriately selected cohort with a specific subset of chronic low back pain symptoms, this technique may provide benefit to payers and patients.

Testing & Regulatory Affairs

Keywords: low back pain, lumbar spine, restorative neurostimulation, peripheral nerve, multifidus

MECHANICAL CHRONIC LOW BACK PAIN CLINICAL PRESENTATION

The Problem of Low Back Pain

As clinicians, we often recite, “low back pain is a symptom, not a diagnosis.” Still, despite this, the conflation of symptoms and diagnosis has led to the persistence of what we know as nonspecific low back pain (LBP), a term that arguably underserves our patients. The biopsychosocial model of LBP attributes the problem to a complex interplay of biological, psychological, and social factors.^{1,2}

In most cases of LBP persisting past 8 weeks, clinical investigation fails to diagnose a clear pathology other than common degenerative changes.³ These changes range from asymptomatic to painful, but the reliable identification of pain generators remains challenging.⁴ In many cases, more than 1 location may be suspected, but the complexity of the degenerative cascade overlaid with the biopsychosocial nature of chronic low back

pain (CLBP) complicates focal diagnosis and moderates the efficacy of focal therapies.⁵ Our understanding of the biological mechanisms of LBP involving the generation and maintenance of pain signals has dramatically improved, as has the distinction between nociceptive, neuropathic, and nociplastic pain.⁶ Furthermore, the biological processes responsible for structural changes in the spine are now profoundly understood.^{7,8} Still, in many cases of persistent LBP, there needs to be more clarity between what can be observed diagnostically and what can be reliably targeted for treatment. In the absence of infection, inflammatory disease, malignancy, fracture, or neurological compression with concordant radiculopathy, identifying specific pain generators in the lumbar spine is difficult. It generally arises from the disc, the vertebral body, the zygapophysial joint (including the articular surface or capsule), ligaments, or the sacral iliac joint. Imaging such as magnetic resonance imaging (MRI) can easily visualize degenerative changes to these structures, but the sensitivity and specificity in predicting the effect of treatment could be

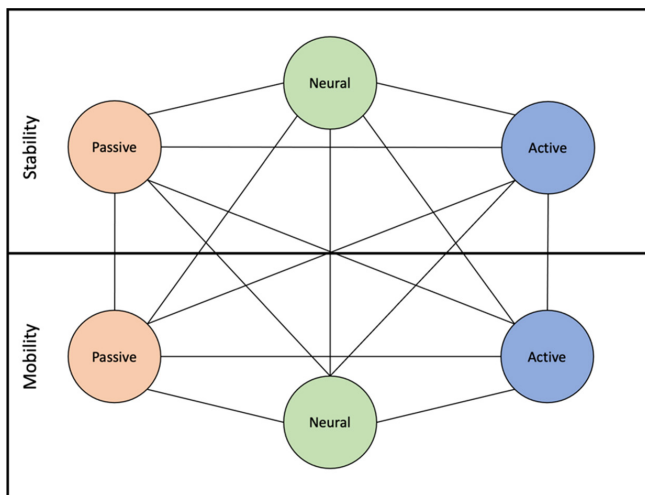


Figure 1. Panjabi's model of spinal stability.⁹

better. In most cases, there are multiple potential pain generators and limited therapeutic options that can universally address them all concurrently. In the absence of effective and durable interventions targeting the underlying pathomechanisms of CLBP, psychosocial interventions have become practically the only clinical practice guideline–recommended treatments.

One pathomechanism of particular interest is neuromuscular instability or a loss in the fidelity of the motor control system proposed by Panjabi.^{9,10} In this model, normal function of spinal stability is an interactive

process between the passive structures of the spine, the actuators (i.e., the muscles), and their neurological control (Figure 1). He predicted that dysfunction in these subsystems could lead to dysfunctional movement exceeding the normal range of motion, deviating from the neutral zone, and putting healthy and damaged tissues at further risk.

This dynamic approach to understanding the problem of LBP explains several clinical features that are not satisfactorily addressed by identifying and treating focal pain generators. It predicts that treatments with a multimodal action mechanism are more likely to be effective. Specifically, this includes the pattern of remission and recurrence observed early in the course of the disease, the lack of specificity and sensitivity of diagnostic imaging, and the lack of efficacy and durability in many treatments.

Scope of the Problem

LBP is the leading cause of years lived with disability worldwide and is often a determinant for chronic opioid use.^{1,11,12} In the United States, low back and neck pain are the most expensive health conditions, estimated at \$134.5 billion, with 58.7% of this spending in ambulatory care and 26.3% as an inpatient or in the emergency department. Compared with other expensive health conditions such as diabetes or ischemic heart disease

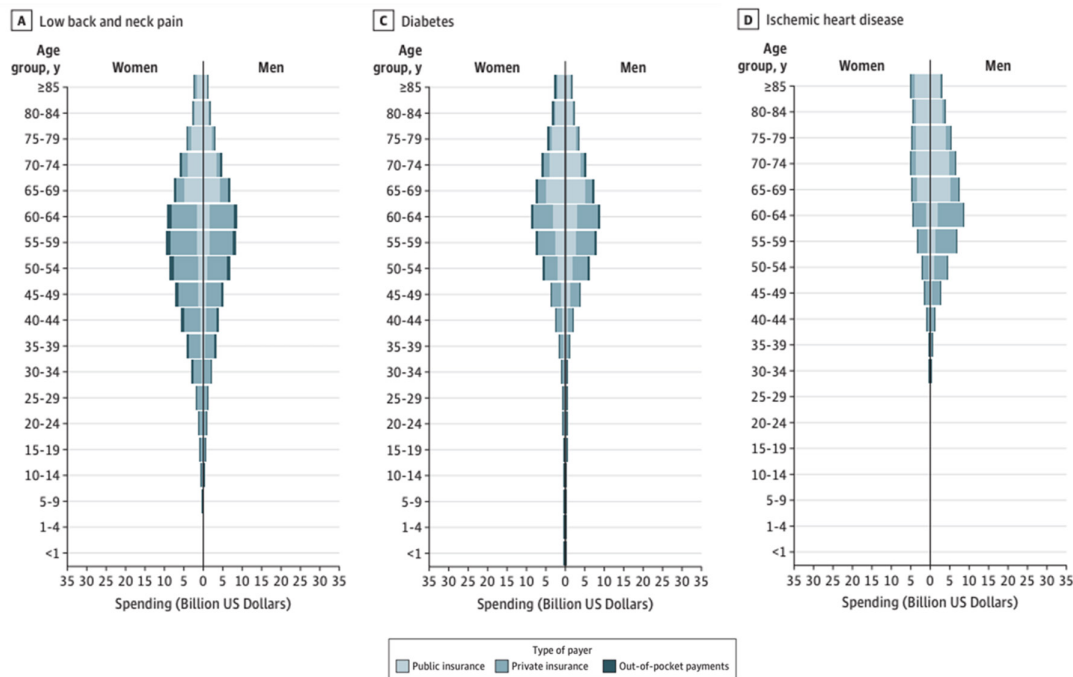


Figure 2. The US health care spending by payer for low back and neck pain totals \$134.5 billion, compared with total diabetes spending of \$111.2 billion and ischemic heart disease spending of \$89.3 billion¹⁴ Reproduced with permission from Dieleman, J. L., et al., Journal of the American Medical Association, 2020, 323 (9) 863-884. Copyright © 2020. American Medical Association. All rights reserved.

(Figure 2), the prevalence is higher in a younger demographic, and the burden is more likely to be placed on private insurance. As this condition often occurs in the working-age population, the indirect costs, including disability benefits and days of work missed, are estimated to be as high as \$624.8 billion.¹³

PREVALENCE

The prevalence of all CLBP in the adult population is estimated to be between 5% and 10%.^{15–17} Herman et al¹⁵ used Medical Expenditure Panel Survey survey data to conclude that 6.0% of US adults suffer from chronic spinal pain, and 2.2% of US adults suffer from high-impact chronic spinal pain. Johannes et al¹⁷ found in an internet survey of US adults that 8.1% reported having CLBP, with 5.5% reporting having this pain most of the time and 1.8% saying their LBP intensity was severe, consistent with high-impact CLBP. Yu et al¹⁸ analyzed 2016/2017 economic health records and found that among patients aged 35 years or older who recently visited their primary care physician for LBP, an estimated 26.0% of them had moderate to severe CLBP defined as LBP present on most or all days in the previous 6 months and an average intensity ≥ 5 on a 0–10 numerical rating scale (NRS). This finding is consistent with the proportion of roughly one-third of patients having CLBP found by Herman et al¹⁵ and Johannes et al.¹⁷

CLBP resulting from motor control dysfunction and neuromuscular instability is a subset of this population. This phenotype can be segmented from the general low-back population by the application of several filters:

- No prior surgery and no indication for surgery: >87% of patients.¹⁸
- Predominantly nociceptive pain: >85% of patients.¹⁹
- Positive physical findings consistent with impaired neuromuscular control of the deep multifidus muscles: 65% of all CLBP patients.²⁰
- No widespread musculoskeletal pain.
 - Three main categories of pain that co-occur with persistent or CLBP are (1) axial pain (18%–58%), (2) extremity pain (6%–50%), and (3) multisite musculoskeletal pain (10%–89%).²¹

Even after applying these criteria, the prevalence of patients meeting mechanical LBP from neuromuscular instability is estimated to be a significant proportion of the adult population.

Cost Drivers

In the United States, 40% of chronic pain patients have high-impact chronic pain (ie, chronic pain with high symptom severity that frequently limits life or work activities for more than >6 months).²² These patients are more likely to be frequent health care users for pain, reported substantially higher average pain intensity, and described higher pain-related interference with life- and work-related activities and lower quality of life.^{23,24} Longitudinal studies of CLBP patients suggest that the level of pain interference with daily activities (ie, disability) is a stronger predictor of health-related quality of life and costs than pain intensity.^{23–27} The National Pain Strategy has recommended operationalizing this relationship to focus health care resources on chronic patients with high-impact chronic pain, that is, significant levels of life interference with work, social, and self-care activities.^{24,28}

Due to the limited effectiveness and durability of available treatments prognosis for this group remains poor.^{15,27,29–31} Inception cohort studies and latent class analyses demonstrate that patients with a declared high CLBP burden will likely remain severely affected.^{30,32–39} Patients in this group tend to follow a pain trajectory with very few fluctuations over long periods and have a high probability of still reporting persistent severe pain after 7 years.^{33,35,40–43} Although less than 28% of LBP cases fall in the “severe” categories, they are responsible for 77% of all years lived with disabilities.³² A 2010 US chronic pain prevalence survey showed that 32% of CLBP patients reported severe pain, and 47% had daily pain.¹⁷

In patients seeking multidisciplinary spine care for CLBP, quality of life and workability are poor, and health care-related costs are twice as high as costs for those seeking primary care.³¹ In a published analysis of a moderate-sized US commercial insurer of enrollees with CLBP, mean health care costs reached almost double that of the population mean (\$11,932 vs \$6034).²⁷ A recent claims analysis study found that after a diagnosis of nonspecific CLBP, median total annual health care cost almost doubled from \$3732 (Q1 \$1292 and Q3 \$9072) to \$6590 (Q1 \$2710 and Q3 \$13,922) with the highest increases. The total cost among patients with Medicare supplemental insurance was \$10,156 (Q1 \$5481 and Q3 \$18,570).⁴⁴ Review of the interquartile ranges revealed that approximately half of the patients generate three-quarters, and a quarter of the patients are responsible for half of the total incremental expenditure related to CLBP. The most significant opportunity to reduce disease burden and associated costs lies with

treatments potent enough to reduce activity limitations in patients with high-impact CLBP sustainably.

Impact on Work Performance

CLBP and the accompanying psychological and sociological problems commonly associated with it are the second most common pain condition contributing to lost productive time at work,⁴⁵ experienced as either diminished work capacity, paid absenteeism, or permanent exit from the workforce.⁴⁶ Many episodes of acute back pain resolve with time and may result in a short duration of absenteeism or reduced employment capacity during the recuperation period. However, in many patients, pain recurs, inter-episode span shrinks, and occupational performance diminishes as pain transitions to a chronic, intractable phenotype.⁴⁷ This is especially so for those with activity-limiting LBP, most of whom experience episodes that are likely to be progressively worse, with increasing disability and little, if any, remission from symptoms.⁴⁸

Significant factors associated with poor work outcomes include previous work absence, activity limitation, worsening of pain, and disability.⁴⁹ A strong predictor of future CLBP is a history of LBP; therefore, one might presume workplace absence due to LBP impacts future work for many patients.^{48,50} When a worker exits paid employment due to CLBP, the pathway to return to work is often unsuccessful.¹³

The occupational impact of pain is manifested in three main domains listed in order of economic implications to employers:

Presenteeism: A decrease in the capacity to perform the designated job or a reduction in the employer's expectation of performance (i.e. reduced duties).

Absenteeism: Increase in the number of days of work missed for health-related reasons.

Health-Related Exit: Inability to participate in the workforce.

Presenteeism is the concept of attending work despite health issues or complaints that should prompt rest and sickness absence.⁵¹ For those living with chronic pain, sickness absence or delaying re-entry into the workforce are not always an option, particularly so in the United States, where many workers do not have paid sick leave in their jobs, and most disability insurance coverage comes with limits on length and amount of income covered.⁵² Chronic pain patients already face an

increased financial burden associated with health care costs for their condition and are more likely to be socio-economically disadvantaged.⁵³

This dynamic presents as an issue of “pain presenteeism,” defined as the capacity to remain at work less productively despite the continued experience of pain.⁵² Presenteeism is a largely overlooked factor contributing to the economic burden of chronic pain despite the increasing evidence that lost productivity in the workforce is primarily a result of reduced work effectiveness rather than absenteeism.^{18,54} In a large, cross-sectional study of workers in the United States that captured both absenteeism and presenteeism, over 75% of the lost productive time due to common pain conditions was found to occur due to reduced work performance.⁴⁵

LBP and other musculoskeletal disorders are among the most common causes of absenteeism.⁵⁵ The evidence for CLBP and absenteeism, however, is much less clear but possibly more visible in workers with more physically demanding jobs and where there is a greater risk of CLBP-related disability.⁵⁶ In a systematic review and meta-analysis of work absence and return-to-work data from 45 studies across different countries, it was reported that while a high proportion (68%) of workers with LBP return to work by the 1 month mark, the remainder are at a significantly increased risk of frequent or long-term work absences without any intervention.⁵⁷ Population studies have shown that the transition from work to sickness absence, and then to disability pension, is increased in workers with chronic disease.⁵⁸

Health-related work exit significantly contributes to the socioeconomic burden of CLBP.⁵⁹ This includes exit accompanied by receiving health-related benefits or disability pension, involuntary transition to unemployment, and early retirement.⁶⁰ In an extensive 28-year follow-up of workers with back pain, recurrent pain was associated with health-related exit, whereas occasional, single reports of pain were not.⁴⁶

While a consistent body of evidence supports physical activity and exercise programs in improving LBP, there are limited data regarding work-related outcomes such as presenteeism and absenteeism.⁶¹ There is some evidence of reduced work absence in nonspecific LBP patients who undergo formal physical therapy (ie, physical conditioning and graded-activity interventions).^{62,63} Similarly, for spinal cord stimulation (SCS) therapy, evidence of effectiveness mainly focuses on reductions in pain intensity, while work-related outcomes are often overlooked or neglected. A few studies of conventional SCS for failed back surgery syndrome patients have reported a poor return to work outcomes.^{64,65}

ROLE OF MUSCLES IN LBP

Natural History of the Aging Spine

Both genetics and environmental factors predispose patients to the onset of degenerative changes in the spine. While not all degenerative changes induce pain, they can be closely aligned to mechanisms by which nociception or neuropathy can occur.^{3,66,67} Early proteoglycan loss in the nucleus pulposus has been studied in depth. It is often considered an index event leading to observable disc degeneration, loss of disc height, and annular tears. These changes, in turn, have mechanical consequences that tend to result in segmental instability, which both offload and overload the facet joints.⁶⁸ The degenerative cascade continues as these altered mechanics at the articular joint surface result in osteoarthritic changes and cartilage degeneration.⁶⁹ Facet osteoarthritis and hypertrophy may lead to foraminal and central stenosis. Direct nociception due to poor disc and facet biomechanics or neurological impingement from hypertrophic tissues are the more commonly recognized sources of spinal disorders.

The inherent complexity of the spine, overlaid with concurrent multiple degenerative processes often means that attempting to identify a single pain generator can be futile. The degeneration of various structures may result in pain at the same segment or different motion segments, or it may refer pain to other regions. CLBP without precise pain generators is a frustratingly common presentation that is poorly understood and often managed palliatively. These patients are generally not considered surgical candidates; thus, the current treatment guidelines include therapies that are temporary at best and ineffective at worst. It has been argued

that some of these patients have apparent pathology—motor control dysfunction secondary to degenerative spine changes.

Sensory Motor Control of the Spine

Motor control of the lumbopelvic region serves to both move and stabilize the trunk. Without muscles, the spine is inherently unstable. Thus, the muscles of the trunk must have not only capacity and endurance but the fidelity of timing and activation to choreograph the complex responses required to move, maintain stability, and anticipate external perturbations.⁷⁰ The controller of this feedback/feedforward network is the central nervous system (CNS). The CNS compiles sensory input from diverse sources, including visual and vestibular systems and peripheral mechanoreceptors in spinal muscle and discoligamentous tissues.^{71–73} This network ensures that the appropriate postural responses are generated at the proper time and magnitude. The complexity of truncal motion to maintain spinal stability throughout daily activity requires multiple interdependent muscle actions to control multiplanar movement (rotation, translation, and flexion-extension) over single segments that combine to achieve the desired functional goal.

Functional goals, whether they are simple like flexion or complex like sitting or locomotion, require multiple inputs from the various aspects of the motor control “matrix” (Figure 3).⁷⁴ Planning originates in the motor cortex, and execution to the plan relies on input from mechanoreceptors, found in muscle (muscle spindles) and tendon (Golgi tendon organs), facet capsules (Ruffini corpuscles) to regulate paraspinal muscle load and reflex responses.

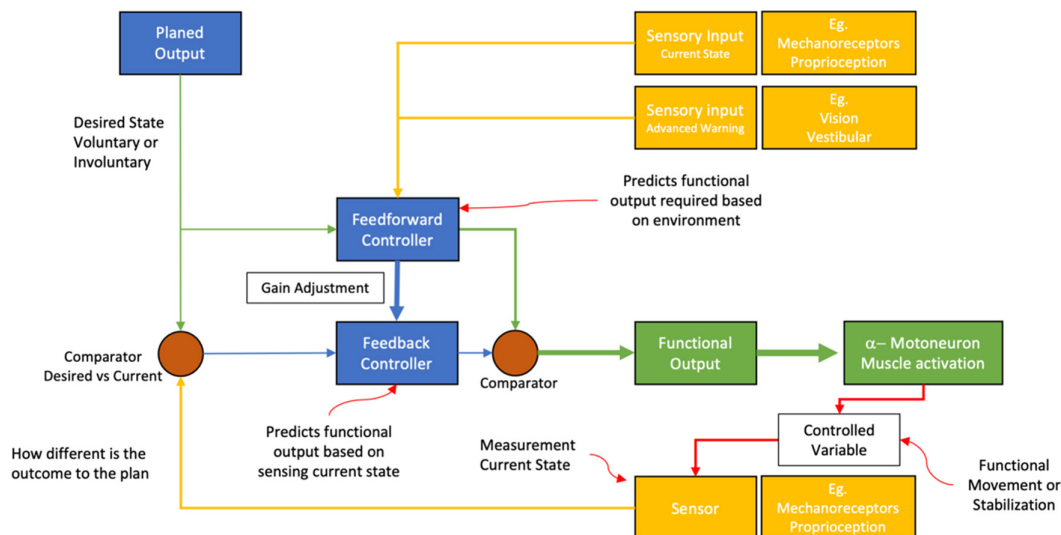


Figure 3. Motor control feedforward and feedback loops. Source: Adapted from Holm et al.⁷⁴

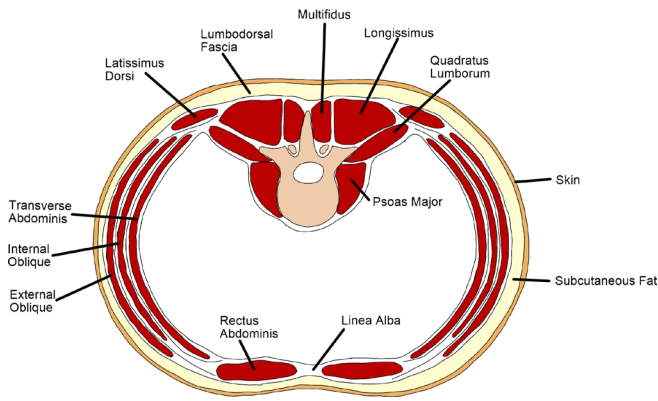


Figure 4. Key muscles of the lumbar trunk.

Each lumbar paraspinal muscle (Figure 4) generates moments, compressive and shear forces dependent on its relative location and insertions.⁷⁵ The more superficial muscles tend to span multiple segments and have a mechanical advantage to generate movement rather than stability. The mechanical advantage of deeper, shorter, more medial muscles is to provide compressive stabilizing forces over individual motion segments. The multifidus is of particular interest in understanding the motion and stability of the lumbar spine as the most medial and, therefore, most important for intersegmental stabilization.⁷⁶ Morphologically, the multifidus spans the entire lumbar spine from the laminae and the spinous processes cranially, and inserting at the caudal mammillary process, arranged in deep intermediate and superficial fascicles. The deep multifidus spans 2 motion segments, the intermediate 3 motion segments, and the superficial 4 motion segments. All of the fascicles originating at a single level are innervated by the medial branch of the dorsal ramus immediately caudal to that level.^{77,78}

The proper functioning of the back muscles, particularly the multifidus, is essential for motor control of the trunk. There is a deficiency in back muscle function in many cases of CLBP. In a vicious cycle, pain and injury affect muscle structure and function, and muscle dysfunction and structural changes can elicit pain or injury. Injury and degeneration of spinal tissues result in lesions and inflammation that alter spinal mechanoreceptors' proprioceptive and reflex function.⁷ The sensitization of these nerve endings elicit either reflex activation or inhibition of various paraspinal muscles, which may directly or indirectly induce pain by altering biomechanical function.

Structural and Functional Changes in the Spinal Muscles During LBP

Some paraspinal muscles respond to painful stimuli and unstable biomechanics via a reflex activation intended to provide stability to the spine. In contrast, others, particularly the deep multifidus, respond with compromised activation.⁷⁹ This underactivation of the multifidus is related to inhibitory reflexes originating from stretch receptors in the facet capsule and intervertebral disc and initiates a cascade of degenerative processes resulting in structurally and functionally compromised spinal function.⁸⁰ Changes in the muscle correspond with multiple underlying mechanisms that have been described over 3 temporal phases (Figure 5).⁷

Acute/Inhibitory

The index event in an acute episode of LBP is generally thought to be an excursion of spinal tissues outside the safe range of motion, which may occur due to high-strain trauma or a low-strain injury in the presence of

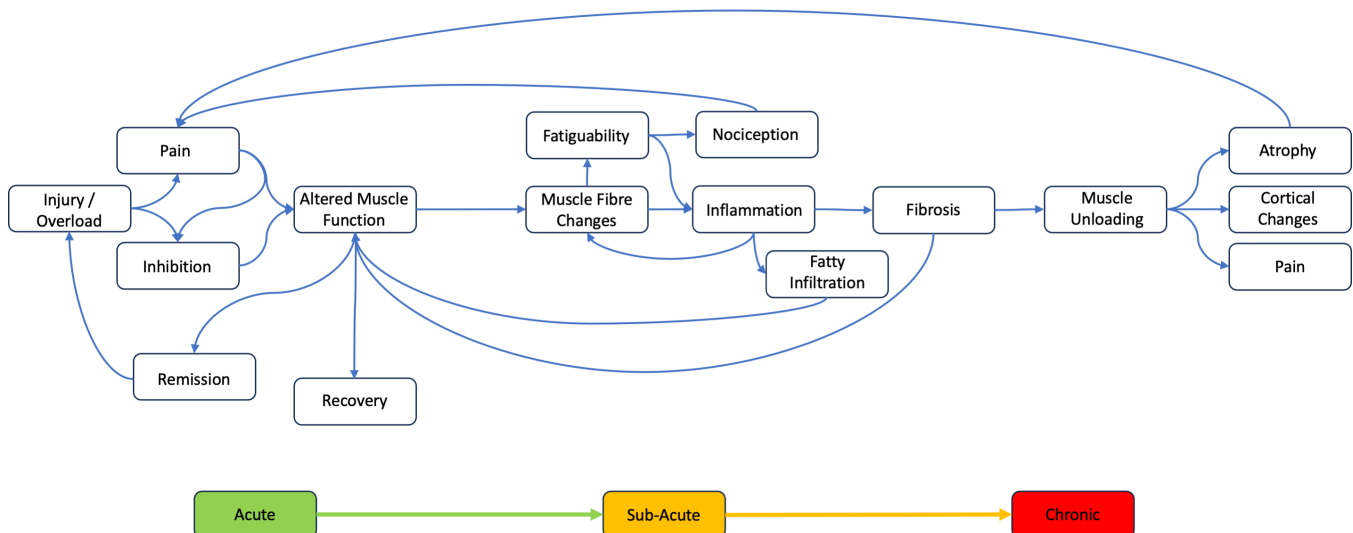


Figure 5. Progression of acute to chronic low back pain. Source: Adapted from Hodges et al.⁷

altered biomechanics resulting from ongoing degenerative processes. Irrespectively, the mechanical deviation initiates pain and sensory neural processes, including spinal reflex inhibition and altered descending drive that reduces multifidus activation. This process is rapid and initially functionally reversible, but there is strong evidence that persistent pain and inflammation result in changes to muscle structure over multiple episodes. During the acute phase, the multifidus undergoes significant atrophy, though these structural changes are not hypotrophic and are likely a result of sympathetic vasoconstriction or other mechanism.⁸¹

The reversibility of these changes in the early disease state suggests that targeted therapies to alleviate pain, overcome inhibition, and downregulate inflammatory processes can be beneficial in the resolution of muscle dysfunction. General activity and targeted motor control exercise have both demonstrated some benefit for these patients.⁸²

Subacute/Inflammatory

Acute LBP commonly improves spontaneously or with limited intervention in many cases; however, the consensus increasingly is that this is a long-lasting condition with a variable course rather than unrelated episodes. This consensus is mechanistically consistent with the alteration of biomechanics resulting from the ongoing degenerative processes predisposing to multiple acute episodes. Each episode results in further structural and functional compromise of the paraspinal muscles. In turn, this dysfunction results in a propensity for further injury and perpetuation of the cycle of pain, inhibition, and dysfunction.³⁹ Many people presenting to primary care with LBP have either persistent and severe pain or are in a cycle of symptom and remission. Over time, the symptomatic phase becomes more disabling and the remission phase shorter.³⁴

The structural changes to the multifidus are believed to result from a dysregulated inflammatory process resulting in adaptive changes to muscle tissue, including fibrosis, fat infiltration, and transition in the proportion of muscle fiber types.^{83–85} Inhibition and inflammation of the deep multifidus lead to a protective strategy of superficial muscle activation, relying on less well-adapted structures like the erector spinae for stability and control. In many other disease states, exercise has been shown to rebalance the inflammatory milieu, reverse fibrosis, and change muscle fiber type distribution. Still, the deep muscle inhibition and overarching protective strategy of the superficial muscles make this a challenging functional task for rehabilitation.^{86,87} This

suggests that specific activation of the multifidus by alternative methods, such as electrical stimulation, may address inhibition and degenerative changes.

Chronic/Disuse

The progression from the subacute to the chronic phase is accompanied by a proliferation of structural changes to the muscle as function is adapted to compensate for the loss of motor control. The altered movement patterns preferentially recruit superficial muscles, and the dysfunctional deep stabilizers are offloaded.⁸⁸ These altered movement patterns are perpetuated by both pain and fear avoidance behaviors and are associated with the loss of discrete cortical organization of inputs to back muscles.⁸⁹ The disuse of the deep stabilizing muscles results in a bilateral reduction in cross-sectional area and further fat tissue deposition.

Therapies applied to this LBP process stage have not been broadly successful. Similarly to the inflammatory phase, the neural and structural changes to the muscle are difficult to overcome with traditional exercise and physical medicine. Numerous well-constructed exercise trials have failed to produce compelling outcomes for these patients, not because activating the multifidus in CLBP patients is incorrect but because the reduction to practice is challenging.⁹⁰ Specific strategies that target full physiological contractions of the multifidus are necessary to reverse physiological processes of inhibition, inflammation, and disuse.

CURRENT TREATMENTS FOR CLBP

Early Treatment Options

Physical Medicine and Rehabilitation

The most recent Cochrane review⁹¹ concludes that there is moderate certainty that exercise-based physical therapy is effective for the treatment of CLBP compared with no treatment, usual care, or placebo, though the treatment effect size is smaller than the threshold for a minimally clinically important difference. Due to the heterogeneity of the patient presentation, a generalizable understanding of the efficacy of physical therapy is limited.

Physical medicine approaches remain guideline-recommended treatments for LBP, though there is a variable quality of evidence for the timing and nature of the intervention. The North American Spine Society guidelines⁹² gave detailed recommendations based on specific trial results. They proposed a consensus statement:

In the absence of reliable evidence for patients with nonspecific back pain, based on abundant data for other spinal disorders that result in back pain, it is the work group's opinion that remaining active is preferred and likely results in better short-term outcomes than does bed rest. This advice is consistent with guidelines from other societies.⁹³

Despite the small effect, physical therapy is a safe and relatively inexpensive intervention and remains at the forefront of the treatment and triage of CLBP patients.

Pharmacological Management

Various drugs are routinely prescribed to manage CLBP, and the efficacy has been the subject of multiple systematic reviews and society guidelines. Reviewing pharmacological options in detail is well beyond the scope of the present article; however, guidelines from the relevant US and European Societies require more evidence for their general application. We recommend that interested readers consult the appropriate guidelines and reviews.^{92–97}

Psychological Therapies

Psychological therapies consistently receive the most robust recommendations from multiple society guidelines due to the emphasis on the biopsychosocial nature of CLBP. Guidelines developed under the European Cooperation in Science and Technology Framework⁹⁵ make strong recommendations for behavioral treatments compared with placebo, waiting list control, and usual care. However, they also cite strong evidence that there is no difference between the treatment modalities. The North American Spine Surgery (NASS) guidelines⁹² make strong recommendations for applying cognitive behavioral therapy to augment physical therapy outcomes. A Cochrane systematic review by Henschke et al⁹⁸ concluded that these behavioral interventions were more effective than usual care over the short term. However, over the longer term, there was no incremental benefit. Table 1 summarizes the relative benefits of some psychological treatments.

Interventional Treatment Options

Epidural Steroid Injections

The European⁹⁵ or NASS⁹² guidelines do not support epidural steroid injection for treating mechanical LBP. Several high-quality systematic reviews assess the evidence for radicular pain but provide limited evidence for mechanical pain. The latest Cochrane review⁹⁹ supports these findings, concluding that there is “insufficient evidence to support or refute the use of injection therapy, regardless of type and dosage, for patients with subacute and [CLBP] without radicular pain.” The UK’s National Institute of Clinical Excellence (NICE) only recommends epidural injections of local anesthetic and steroid in people with acute and severe sciatica.¹⁰⁰

Intra-articular Facet Injection

In appropriately selected patients, intra-articular facet injections have moderate quality evidence for no effect in the medium term (6 months), according to the NASS and European guidelines. A recent systematic review¹⁰¹ assessed 42 studies for eligibility and provided qualitative evidence based on 6 studies based on heterogeneity of treatment, outcome, and follow-up period preventing a formal meta-analysis. By way of example, a randomized controlled trial conducted by Lakemeier et al¹⁰² compared intra-articular injection with radiofrequency ablation (RFA) and concluded that both techniques provided limited relief over the short term but were similar. The injection cohort in this study showed improvements in visual analog scale (VAS) from 7.0 ± 1.7 to 5.4 ± 2.1 and improvement in Oswestry Disability Index (ODI) from 38.7 ± 18.4 to 33.0 ± 17.4 , consistent with a clinically insignificant treatment effect.

Facet Joint RFA

RFA remains at the forefront of clinical interventions for CLBP. It is well tolerated by patients and has few complications. Despite being in clinical practice for decades, this procedure still has concerns regarding efficacy and durability. The most recent Cochrane review¹⁰³ summarized the published evidence through 2015 and suggested that there was moderate quality evidence that

Table 1. Representative comparisons for behavioral therapies.

Treatment Comparison and Timeframe	Pain	Depression	Functional Status
Cognitive behavioral therapy vs waiting list control			
Short term	−0.6 (−0.97, −0.22)	−1.92 (−6.16, 2.32)	−0.37 (−0.87, 0.13)
Behavioral treatment vs group exercise			
Short term	−2.31 (−6.33, 1.7)	0.25 (−0.07, 0.58)	−
Intermediate term	1.18 (3.16, 5.53)	0.02 (−0.32, 0.35)	−
Long term	0.14 (−4.4, 4.67)	0.07 (−0.27, 0.41)	−

suggests that RFA might better relieve facet joint pain and improve function over the short term when compared with placebo. Not included in this review was the minimal interventional treatments for participants with chronic low back pain (MINT) trials report,¹⁰⁴ a high-quality prospective randomized control trial comparing a standardized exercise program to RFA. Of the patients being treated for facet-related problems, there was no difference in outcomes between denervation and exercise. Some criticism has been leveled at the trial design and interpretation,^{105–107} including a lack of standardization of patient selection and diagnostic blocks.

The durability of the effect of RFA is often questioned. There is conflicting low-quality evidence (Grade II and III) of the long-term effect, for example, including a study by McCormick et al,¹⁰⁸ which included a wide range of follow-up times (median 39 months [IQR 21]) and which reported that a greater than 50% improvement in pain and function was maintained in 58% of patients. Alternatively, in a retrospective review of 500 patients at 1 year, Yadav et al¹⁰⁹ showed responder rates of $\leq 30\%$ reduction in VAS of 60%, 44%, and 24% at 3, 6, and 12 months, respectively.

The conflicting evidence for durability and efficacy has resulted in society guidelines recommending this procedure for temporary relief in chronic mechanical LBP patients with only strict diagnostic protocols.^{92,95}

Late Treatment Options

Surgical Interventions

The Spine Patient Outcomes Research Trial¹¹⁰ comparing surgical and nonsurgical treatments for patients with degenerative spondylolisthesis with CLBP with or without leg pain demonstrated that spinal fusion outcomes (pain and disability) were better compared with outcomes of patients who received nonsurgical treatments in an as-treated analysis. This finding was also compared with a nonrandomized observational cohort to overcome the methodological challenges of surgical trials and demonstrated similar results. Patients in this study had neurological claudication or radicular leg pain and back pain and thus are not a direct comparison to the CLBP alone phenotype discussed here. Still, the results show significant improvements in outcome and demonstrate the benefit of fusion in a well-selected patient. Other studies from the early 2000s, such as the Swedish Lumbar Spine Study¹¹¹ and the Maine Lumbar Spine Study,^{112,113} employed open surgical techniques and compared spinal fusion to nonsurgical treatments for CLBP alone. Neither were able to identify significant differences in patient-reported outcomes and

showed higher complication rates in the surgical cohort. Modern minimally invasive surgical techniques may improve these outcomes, but that has yet to be effectively demonstrated.

More recently, ISASS has taken a pragmatic stance on the role of fusion and disc arthroplasty for degenerative disc disease with back and leg pain based on the results of several RCTs and systematic reviews. Long-term fusion outcomes have been assessed from the control arms of arthroplasty investigational device exemption (IDE) studies. The Charité Food and Drug Administration (FDA) IDE trial¹¹⁴ has published 5-year outcomes on 43 anterior lumbar interbody fusion control patients and reported a 17-point improvement in ODI and a success rate per the IDE protocol of 51%. Similarly, the Pro-Disc FDA IDE trial has published the 2-year outcomes on 2-level circumferential fusion patients.¹¹⁵ A minimum 15-point improvement in ODI was seen in 60% of the fusion patients, and the mean VAS pain score dropped from 75 mm at pre-op to 38 mm at 2 years. In the fusion arm from a prospective study by Berg et al,¹¹⁶ 72 patients with degenerative disc disease received posterior fusion (posterior lumbar fusion or posterior lumbar interbody fusion), and mean VAS back pain decreased from 59/100 at before the operation to 29/100 at 2 years, while ODI decreased from 41 to 23. This study shows that good clinical outcomes can be achieved in many patients. Brox et al¹¹⁷ compared fusion to nonsurgical therapy and showed that the fusion cohort improved by 4 years from 44.1 to 29.7. However, this was not significantly different from the cognitive and exercise-based interventions (43.4–27.0).

NASS,⁹² NICE,¹⁰⁰ and the European Guidelines⁹⁵ do not suggest spinal fusion for LBP without radicular symptoms, except in extraordinary circumstances.

REVIEW OF RESTORATIVE NEUROSTIMULATION

Target Anatomy; Medial Branch Motor Nerve Stimulation

The dorsal ramus nerve is a mixed sensory and motor nerve formed from the nerve roots and gives rise to the lateral and the medial branches on the superior border of the transverse process (Figure 6). The medial branch runs in the groove at the junction of the transverse and the superior articular process. Then it descends caudally and posteriorly, accompanying the vessels arising from the lumbar artery and vein. The medial branch innervates the capsules of the facet joints, skin, muscles, and

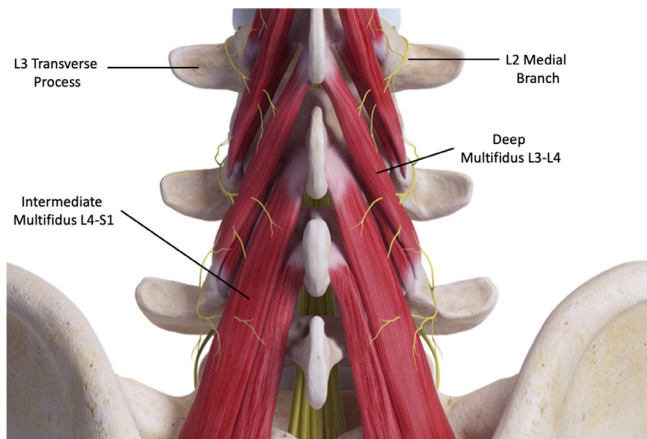


Figure 6. Anatomical orientation of the lumbar dorsal ramus.

ligaments medial to the facet joint line. The paraspinal multifidus muscles are critical for lumbosacral stability and are innervated solely by the medial branch of the dorsal ramus, which is of particular clinical significance.

Device, Procedure, and Therapy Description

The system consists of an Implantable Pulse Generator, two stimulation leads, an radio frequency telemetry programmer, and a patient-controlled activator (Figure 7).

The stimulator and leads are implanted in a minimally invasive, single-stage procedure involving 2 skin incisions in the posterior lumbosacral region down through the adipose tissue. The patient is positioned in a prone position on a pillow to flatten out lordosis. A 1- to 2-cm incision for lead placement is made midsagittal, approximately at the level of the L4 vertebral body. From this incision, leads are percutaneously placed bilaterally, with the electrodes positioned adjacent to the medial branch of the dorsal ramus as it crosses the transverse process at L3 (Figure 8). Under fluoroscopic visualization, the leads are introduced percutaneously and advanced through the L2/3 intertransversarii using a needle, guide wire, and delivery sheath with a dilator (modified Seldinger approach). Withdrawal of the

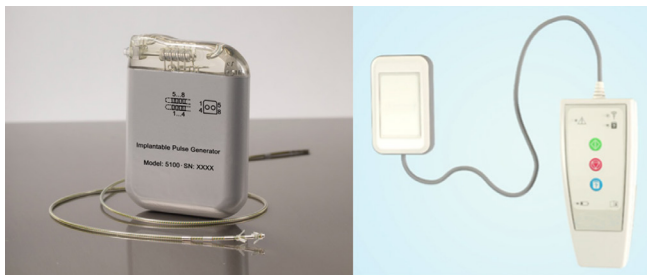


Figure 7. A restorative neurostimulation system.

sheath deploys 2 opposing sets of flexible tines, which bracket either side of the intertransversarii for distal anchoring. A 4- to 5-cm incision is made near the iliac crest, and a pocket is created to implant the IPG. After confirming the placement of the leads through fluoroscopy, the IPG is attached to the leads to test for multifidus response through a trial (Figure 9). Response is confirmed through trial stimulation of the nerve and observation or palpation of the contractions of the multifidus.

Leads are tunneled subcutaneously between the lead implant incision and the IPG pocket, and once tunneled, the lead terminals are cleaned, dried, and inserted into the IPG header. Like other implantable neurostimulation systems, the IPG is implanted in a subcutaneous pocket, either in the low back or high buttock region. The IPG is placed in a location deemed appropriate by the implanting physician and considering the patient's ability to reach the IPG location with the activator to initiate stimulation sessions.

The patient initiates stimulation sessions via the application of the activator. During stimulation sessions, the system repetitively delivers 10-second trains of electrical stimulation twice per minute for 30 minutes. During programming, the parameters stored in the IPG control the precise timing and stimulation intensity. Amplitude, pulse width, and rate may be adjusted in the clinic to control the energy (charge) and stimulation rate. Stimulation sessions are recorded within the IPG and can be accessed by the health care professional to assess compliance and use of the system.

In contrast to SCS, leads are placed outside the spinal canal, avoiding the risk of spinal cord injuries. And the risk of lead migration, which represents the most common adverse event reported in neurostimulation clinical trials, has been effectively mitigated with the lead design incorporating flexible fixation tines.

Mechanisms of Action

The mechanism of the reversibility of motor control dysfunction of the multifidus by the activation of muscles is achieved by a combination of changes to the muscle architecture and neurological control. Changes in muscle composition function have mainly been observed in animal and human models of targeted exercise rather than direct electrophysiological stimulation. However, at face value, electrical stimulation is a more robust and consistent way of achieving specific activation.

Muscle activation has demonstrated changes in hypertrophy, muscle fiber type distribution, inflammation, mechanoreceptor function, adipogenesis, and

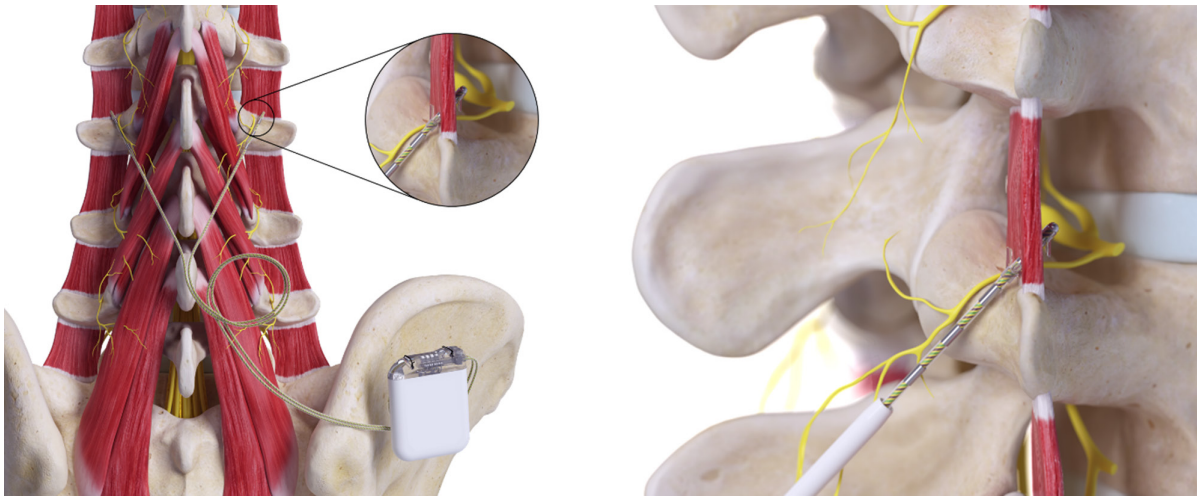


Figure 8. Implanted restorative neurostimulation system with lead fixation to the L2/3 intertransversarii.

fibrosis. The role of the central and peripheral nervous system is also mechanistically relevant as patients commonly develop potentially reversible changes in proprioception, motor cortex representations, excitation of the pain matrix, and peripheral and central hypersensitivity.

Danneels et al¹¹⁸ measured significant changes in the multifidus muscle area following stabilization training combined with progressive dynamic-static resistance training. Berglund et al¹¹⁹ demonstrated that specific motor control exercise reduced multifidus asymmetry in patients with nociceptive mechanical LBP. The severity of the disease in these patients was relatively mild (VAS 4–4.8/10). As such, the methodology may not be applicable, but these studies highlight that functional activation of the paraspinal muscles can elicit hypertrophy.

While the reversibility of back pain-induced loss of type I (slow twitch) muscle fibers¹²⁰ in the multifidus has yet to be proven, studies in other muscles clarify the physiology involved. Muscle biopsy studies of

endurance training, that is, multiple low-load contractions, demonstrated an increased proportion of type I fibers relative to type II/Ix. In human and animal studies, different muscles have shown variable propensities for fiber-type transition in various muscles and locations within those muscles¹²¹ and highlighted the role of appropriate neural input to maintain the fiber population.¹²²

Increased muscle fatigability stems from altered motor control, and changes in the muscle architecture induce a persistent and dysregulated inflammatory process.⁸³ These inflammatory processes drive further degenerative changes, including fibrosis and adipogenesis, and impact the function of tissue mechanoreceptors.^{123,124} The current hypothesis based on animal experiments is that improving muscle activity down-regulates this inflammatory process and attenuates or reverses these changes.^{83,125,126}

Neurological inhibition and alterations to motor planning can develop from changes to the central and peripheral nervous system. Studies have shown an absence in the differentiation of motor cortex regions representing the erector spinae and multifidus, suggesting a central homogenization of control strategies.^{89,127} With appropriate simulation/muscle activation, the distinction between these regions can be reestablished,¹²⁸ at least over short timeframes, but it is suspected that long-term patterning associated with cortical plasticity may reestablish fidelity in descending control strategies.¹²⁹ The adverse effect that degenerative changes and persistent inflammation have on peripheral input into motor control via muscle spindles is also believed to be a reversible phenomenon when properly timed sensory neuron-intrafusal muscle fiber interaction is present.¹³⁰

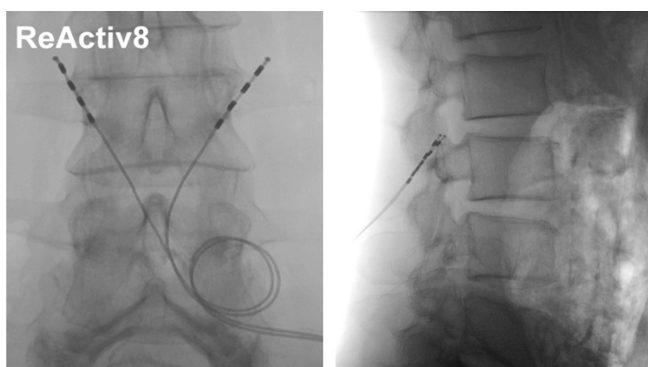


Figure 9. Anteroposterior and lateral view of the implanted leads. The leads are placed outside the spinal canal, adjacent to the peripheral nerve that innervates the multifidus muscle.

Ultimately improvements at the cellular- and structural-level result in functional improvements in the motor control system. Restoration of appropriate motor planning at the cortical level, accurate proprioceptive input, and functional activation, both timing and durability of contractions, improve dynamic spinal stability. This stability restores the interactions between the active, passive, and control subsystems described by Panjabi and allows for the complicated tradeoff between spinal movement and spinal stability required for pain-free activities of daily living.

Role of Trialing in Restorative Neurostimulation

Although the economic cost and clinical benefit remain questionable, trialing is common in many neuromodulation procedures.^{131,132} The objective of a trial is to enrich the clinical success rate by determining whether an appropriate response relative to the mechanism of action can be elicited. Thus a trial must replicate the mechanism of action or demonstrate that the mechanism by which the permanent implant elicits efficacy can be achieved in a specific individual. In palliative approaches such as SCS, where the outcome of interest is pain, a trial should elicit a clinically meaningful treatment effect within the trial period. Where the mechanism is restorative and an accumulation of therapy is needed to elicit a treatment effect, it is not feasible for a trial to establish a measurable effect during a short-term trial period. In this case, the trial should show that the mechanism of action (MOA) is viable (or not). For example, a demonstration that stimulation of the medial branch during on-table intraprocedure testing does or does not evoke a contraction of the multifidus would be 1 way of excluding people unlikely to respond to restorative neurostimulation. In restorative neurostimulation, on-table testing is a predictor of outcomes outside of robust identification of the patient with appropriate physical examination and clinical workup.

PATIENT SELECTION CHARACTERISTICS

Clinical Consultation

Diagnosing mechanical CLBP resulting from neuromuscular instability begins by developing a complete clinical history of the patient's pain presentation. The evaluation of neuropathic LBP has been detailed by Freynhagen et al,¹³³ and Cook et al¹³⁴ proposed several patient-reported signs related to clinical instability and mechanical LBP that, when combined, provide insight into the underlying pathophysiology for the treating

Table 2. Subjective factors for chronic low back resulting from clinical lumbar spine instability.

Consultation Considerations

Neuropathic origin

- Does the pain present in a dermatomal pattern?
- Is the pain unilateral leg pain?
- Is the leg pain greater than the low back pain?
- Are there sensory disturbances, such as allodynia or paresthesia?
- Is there a lower limb motor disturbance?
- Is there a positive Lasègue's sign or straight leg raise?

Mechanical origin

- Does your back giving way or giving out cause feelings of instability?
- Do you need to frequently crack or pop the back to reduce symptoms?
- Do you experience painful catching or locking during trunk motions?
- Do you experience pain during transitional activities (sit to stand, etc)?
- Does returning to an erect position from flexion cause greater pain?
- Do you find it more difficult to sit unsupported than with a backrest?
- Do sudden, trivial, or mild movements such as brushing teeth or low load task while flexed cause pain?
- Is pain worse with sustained postures (driving, extended standing, etc)?
- Are you fearful of moving?

physician. After ruling out red flags suggestive of a potentially serious cause for pain such as malignancy, fracture, infection, and cauda equina syndrome, Table 2 highlights some essential factors that should be investigated.

High-Impact Pain

High-impact pain refers to pain experienced by a specific subset of patients that has significant negative consequences on activities of daily living. Work is ongoing on reaching a consensus and validating the categorization of pain impact states. Several approaches have been proposed and studied, including responses to various patient-reported outcomes score items. Regardless of categorization methodology, high-impact pain is classified based on the duration and severity of symptoms and the impact those symptoms have on the ability to work, perform usual activities, perform self-care activities, and find overall enjoyment of life. High-impact LBP is associated with a poor prognosis for recovery and a tendency for high health care resource utilization. A subanalysis of the ReActiv8 B population¹³⁵ demonstrated that at baseline, 71% of patients presented with high-impact LBP, and by 2 years, 85% of patients reported little or no impact.

Physical Examination for Multifidus Motor Control Dysfunction

Prone Instability Test

The Prone Instability Test (PIT) has adequate interrater reliability (reported as $\kappa = 0.87$) and good face validity.^{136,137} A positive PIT was 1 of the 4 variables shown to predict success with a stabilization exercise

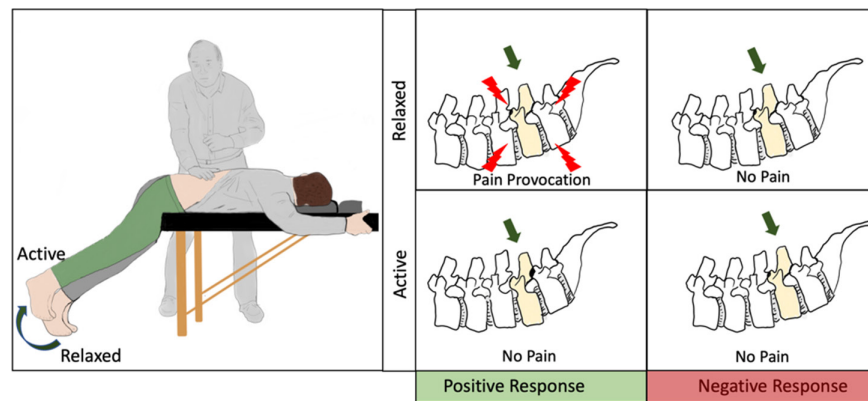


Figure 10. Prone Instability Test. Source: Reprinted from Chakravarthy et al. Restorative neurostimulation: a clinical guide for therapy adoption. *J Pain Res.* 2022;15:1759–1774 under the Creative Commons Attribution Non-commercial license.

program for patients with subacute LBP (a sample of 40 subjects with an average duration of 75 days) that included exercises designed to reactivate the lumbar multifidus.²⁰ In another study, of 105 patients with an average duration of 65 days, positive PITs and aberrant movement patterns were shown to have reduced disability and pain following a course of motor control retraining exercises when compared with patients who did not have these clinical findings.¹³⁸

The PIT is performed with the patient prone in a relaxed and neutral spine posture. The tester applies posterior to anterior glides (pressure) over each lumbar segment. If 1 or more glides produce pain, the glides are repeated when the subject's posterior spinal muscles are activated, extending the hips by lifting the feet off the floor. If the pain is significantly diminished when the glides are performed during muscle activation, the test is considered positive and suggestive of a motor control deficit, including multifidus dysfunction (Figure 10).

Multifidus Lift Test

Hebert et al reported the reliability of the multifidus lift test (MLT), a palpation technique designed to test for multifidus function (Figure 11). Herbert et al used the MLT procedure and compared the results of palpation to determine diminished multifidus response compared with normal multifidus contraction to measure multifidus muscle thickness change via sonography.¹³⁹ Intertester reliability of the MLT at the L4–L5 was reported to be $\kappa = 0.75$ with 86% agreement and at the L5–S1 level demonstrated a $\kappa = 0.81$ with 91% agreement. To establish the validity of the test, they assessed the correlation between the outcome of the MLT and the ultrasound measure of thickness change. The correlation coefficients demonstrated a consistent relationship (0.59–0.73, $P < 0.01$) between the MLT findings and the ultrasound measures of lumbar multifidus function at L4–L5 and L5–S1.

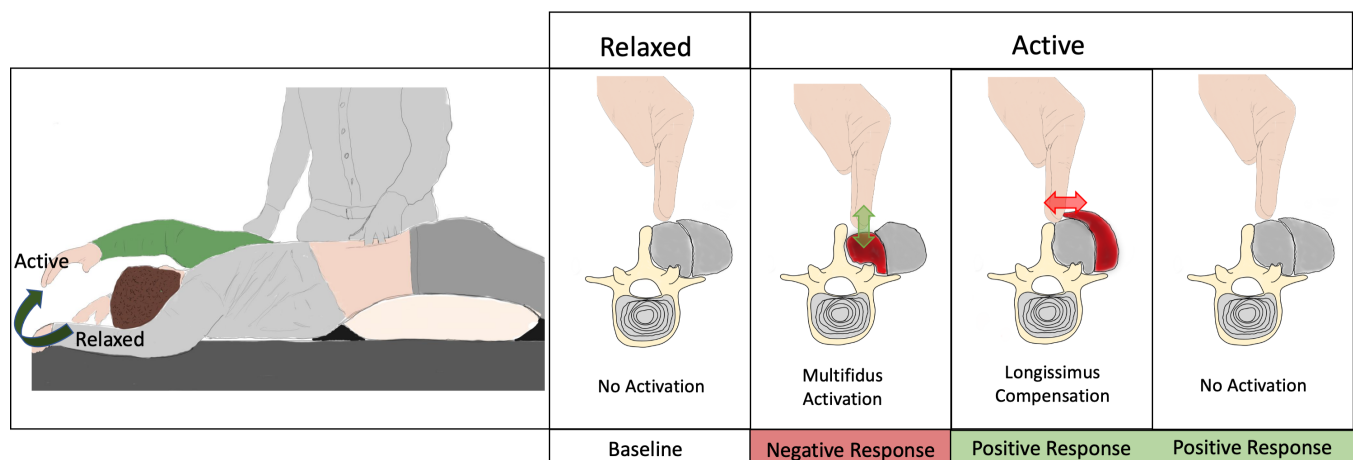


Figure 11. Multifidus lift test. Source: Reprinted from Chakravarthy et al. Restorative neurostimulation: a clinical guide for therapy adoption. *J Pain Res.* 2022;15:1759–1774 under the Creative Commons Attribution Non-commercial license. The negative and positive responses have been reversed from the published version.

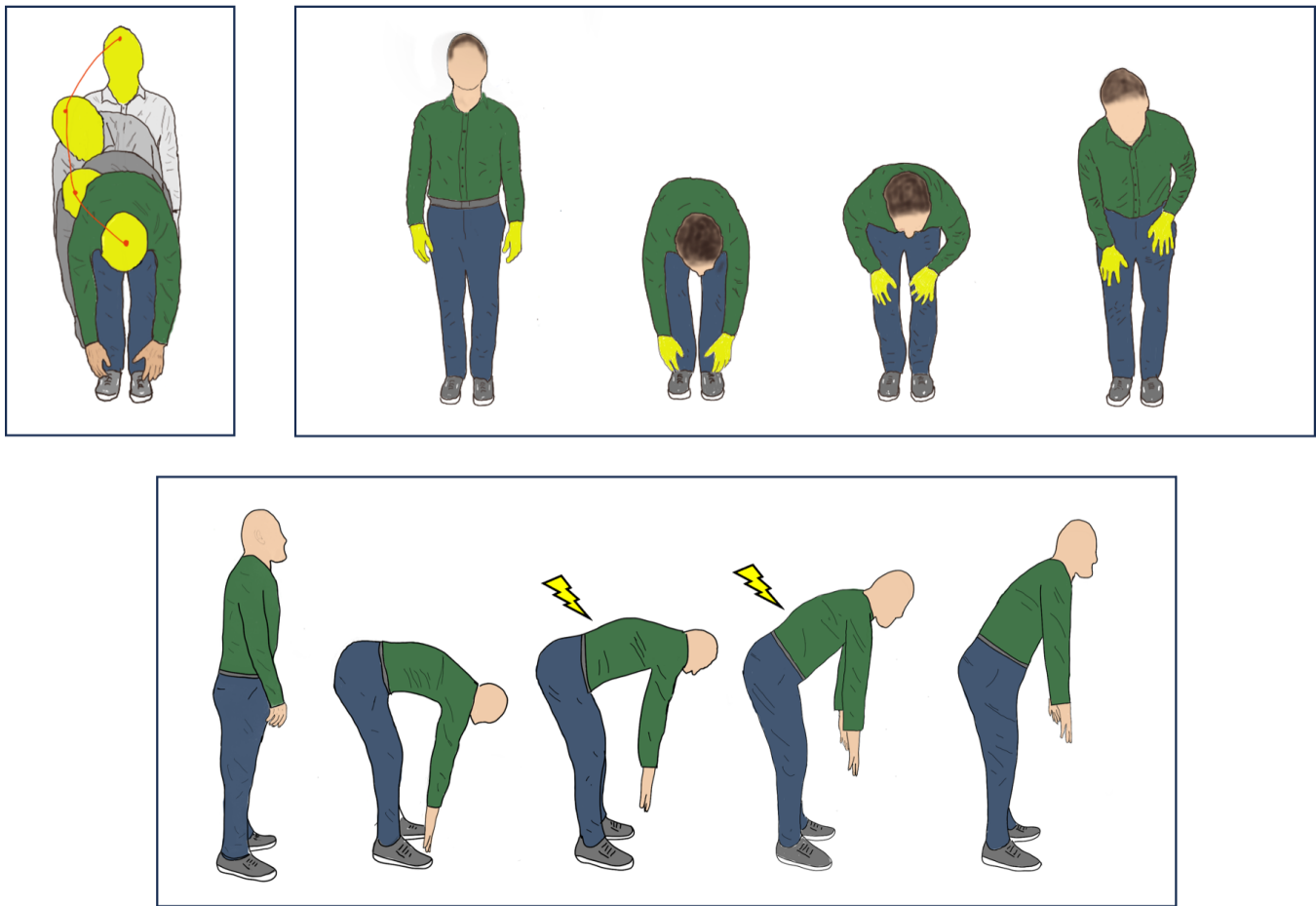


Figure 12. Aberrant movement patterns/multifidus toe touch test.

Aberrant Movements

Observing the quality of truncal motion is essential to a spinal physical examination and can highlight deficits in motor control and multifidus function (Figure 12). Five specific movement patterns are relevant; altered lumbopelvic rhythm, Gower's sign, sagittal plane deviation, instability catch, and painful arc of motion.¹⁴⁰ The observation by trained clinicians has a high interobserver reliability ($\kappa = 0.35\text{--}0.89$) and was associated with patients with CLBP compared with healthy controls or patients with remission of symptoms.

Imaging Characteristics

Changes to the multifidus muscle apparent with MRI are strongly associated with back pain. However, since back pain of any cause can lead to changes in the multifidus cross-sectional area and amount of fat infiltration, the diagnostic value of such muscle changes alone is limited in individual patients.¹⁴¹ There appears to be no relationship between multifidus function and the amount of fat infiltration.¹⁴² There is some evidence that

the severity of fat infiltration correlates with decreased range of motion in flexion¹⁴³ and that the amount of fat infiltration may be a predictor for continued CLBP, but the diagnostic utility of imaging alone is unclear.¹⁴⁴ Figure 13 highlights the MRI classifications of fatty infiltration.

CLINICAL EVIDENCE SUMMARY

Current Publications

The evidence supporting the clinical effect of restorative neurostimulation comes from several multicenter and 1 single-center study (Table 3).

The key points of these studies include the following:

- Studies consistently show that most patients report substantial and durable improvements in pain, disability, and quality of life.
- Clinical benefits accrue over time, consistent with the restorative mechanism of action.
- 71% of the patients (36 of 51) had voluntarily discontinued (49%) or reduced (22%) opioid

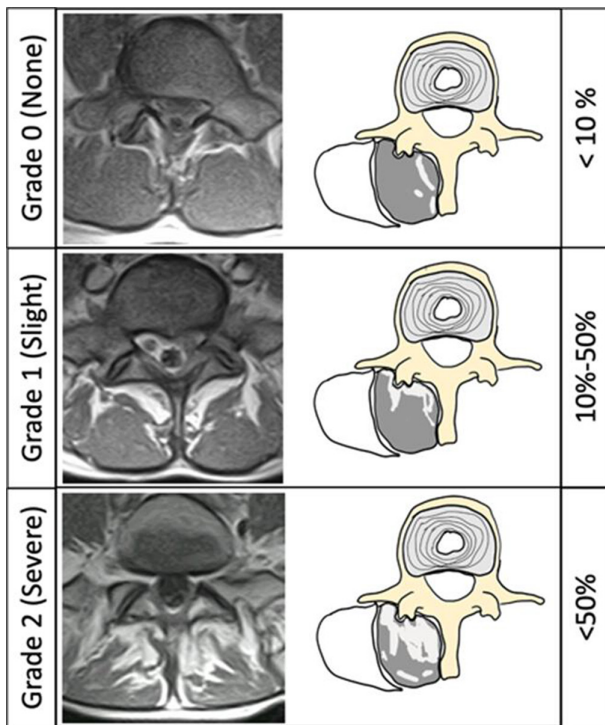


Figure 13. Magnetic resonance imaging classification of fatty infiltration. Source: Reprinted from Chakravarthy et al. Restorative neurostimulation: a clinical guide for therapy adoption. *J Pain Res.* 2022;15:1759–1774 under the Creative Commons Attribution Non-commercial license.

intake at 3-year follow-up in the ReActiv8-B study.

ReActiv8-B Pivotal Trial

The ReActiv8-B Pivotal trial is a recent randomized, sham-controlled, double-blinded clinical trial (clinicaltrials.gov NCT02577354) that included 204 patients, and outcomes provided safety and effectiveness evidence that supported FDA approval restorative neurostimulation using the ReActiv8 Device.³⁵

Participants had a mean age of 47 ± 9 years, and 54% were women. The mean duration of CLBP was 14 ± 11 years (7 months to 50 years) from the onset of the first

occurrence, and the mean percentage of days with LBP in the previous year was $97\% \pm 8\%$. The mean VAS was 7.3 ± 0.7 cm, the mean ODI was 39 ± 10 , and the mean EQ-5D-5L index was 0.585 ± 0.174 . All participants had undergone physical therapy with an average of 31 ± 52 sessions. Of all participants, 12% had undergone medial branch rhizotomy (>1 year before enrollment), 49% had received spinal injections (>30 days before enrollment), and 37% were taking opioid analgesics for LBP. Although the primary endpoint was inconclusive, overall data from this trial's (successfully) blinded phase are consistent with a clinically meaningful benefit at 120 days. After unblinding and switching from sham to therapeutic stimulation in the sham-control group, improvements increased to the 1 year mark in the combined cohort. At 1 year, 64% of patients reported an improvement in VAS of $\geq 50\%$, 52% of patients reported LBP resolution (VAS ≤ 2.5), and 69% reported an improvement of ≥ 15 points in ODI. No lead migrations were reported, and the overall safety profile was favorable compared with other implantable neurostimulator therapies for chronic pain.

Three-Year Outcomes

Three-year peer reviewed evidence from the ReActiv8-B¹⁵² study suggests that the clinical benefits are maintained and show durable, statistically significant, and clinically substantial help in this cohort. Consistent with the restorative mechanism and improvements in neuromuscular control, participants derived benefits that increased with treatment duration. To date, 4-year outcomes have been presented at national meetings. Although these outcomes have not been peer reviewed yet, they are included here for completeness.¹⁵³

ReActiv8-PMCF Study

The ReActiv8-PMCF is a postmarket clinical follow-up of 37 patients from 5 sites in the United

Table 3. Current published evidence for restorative neurostimulation for CLBP.

Clinical Study	Number of Participants	LOF	Evidence Level	Publication
Feasibility study	26	3 mo	II-1	Deckers et al 2015 ¹⁴⁵
ReActiv8-A	53	12 mo	II-1	Deckers et al 2018 ¹⁴⁶
		48 mo	II-1	Mitchell et al 2021 ¹⁴⁷
		24 mo	II-1	Thomson et al 2021 ¹⁴⁸
ReActiv8- PMCF	37	36 mo	II-1	Thomson et al 2023 ¹⁴⁹
ReActiv8-B	204	120 d/12 mo	I/II	Gilligan et al 2021 ¹⁵⁰
		24 mo	II-1	Gilligan et al 2022 ¹⁵¹
		36 mo	II-1	Gilligan et al 2022 ¹⁵²
		48 mo	N/A	Gilligan et al ¹⁵³
ReActiv8-C	41	Subanalysis	II-1	Shaffrey et al 2022 ¹³⁵
		12 mo	II-1	Ardeschiri et al 2022 ¹⁵⁴

Abbreviation: LOF, length of follow-up.

Kingdom.¹⁴⁸ This study represents real-world clinical outcomes as the inclusion/exclusion criteria aligned with the device instructions for use at the treating physician's discretion. These criteria resulted in demographically very similar patients to the pivotal trial, with an average age of 47.2 ± 11 years and an LBP history of 13.7 ± 10.2 years. However, at baseline, the mean NRS pain score was 7.0 ± 0.2 , mean ODI score was 46.6 ± 2.2 , and mean quality-of-life index (EQ-5D-5L) was 0.426 ± 0.035 , indicating there was worse disability and HRQoL than the ReActiv8-B cohort. After 2 years of therapy, average NRS scores had reduced to 3.5 ± 0.3 ($P < 0.001$), ODI scores decreased to 29.2 ± 3.1 ($P < 0.001$), and the EQ5D-5L index improved to 0.680 ± 0.030 ($P < 0.001$). The improvement in mean NRS between 1 and 2 years also met the threshold for statistical significance ($P < 0.001$). The recent publication of the 3-year outcomes shows continued durable and meaningful benefit in this patient group.¹⁴⁹

ReActiv8-C Registry

The ReActiv8 C Registry is a postmarket study undertaken in Germany. One publication has arisen from this, a single center consecutive cohort, although more results will likely be forthcoming.

Single Center Interim Analysis

Ardeshiri et al¹⁵⁴ published 12-month outcomes from 44 consecutive patients. Patients in this cohort were, on average, slightly older than in previous studies (54 years) and had a shorter reported history of CLBP (5.8 years). While baseline outcome measures were worse than other reports, the magnitude of improvement and responder rates were comparable to those seen in other publications. Pain scores (NRS) improved from a baseline of 7.6 ± 0.2 to 3.9 ± 0.4 at 1 year. Disability at baseline improved from 43.0 ± 2.8 to 25.8 ± 3.9 and HRQoL (EQ-5D) from 0.504 ± 0.034 to 0.755 ± 0.039 .

COMBINED OUTCOMES OF REACTIV8-A, REACTIV8-B, REACTIV8-C, AND REACTIV8-A-PMCF — 1- TO 4-YEAR COMPLETERS

The cumulative data supporting restorative neurostimulation from several well-constructed prospective studies and real-world data through 4 years suggest the durability of the treatment effect in these patients. Figure 14 compares the published outcomes across studies in (a) pain, (b) disability, and (c) HRQoL,

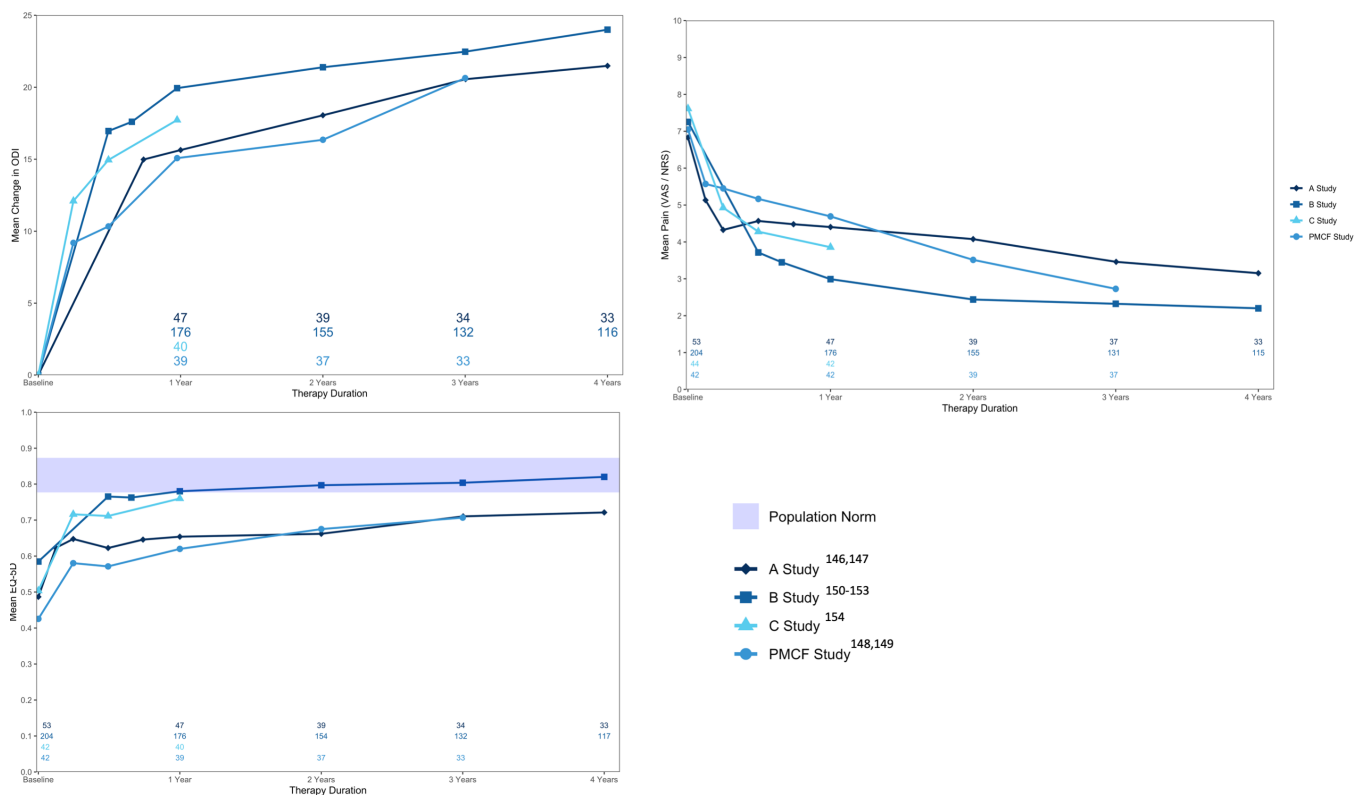


Figure 14. Aggregated clinical data from published studies on restorative neurostimulation (ReActiv8-A Study,^{146,147} ReActiv8-B Study,¹⁵⁰⁻¹⁵³ ReActiv8-C Study,¹⁵⁴ and ReActiv8-A-PMCF Study^{148,149}).

showing that the magnitude of benefit is sustained and that real-world outcomes are similar to those achieved in the regulated clinical trials.

GUIDANCE ON APPROPRIATE COVERAGE CRITERIA

Patients who have documented evidence of the following clinical indications may be eligible for coverage:

- Patient has severe, disabling, CLBP that has persisted for more than 12 months with pain on more than 50% of the days.
- Patient has failed all conservative medical management, including a minimum of both:
 - Physical therapy
 - Medication (nonsteroidal anti-inflammatory drugs, muscle relaxants, and other).
- Documented multifidus dysfunction through physical examination (PIT/MLT or aberrant movement patterns) or imagery (MRI)
- Pain is consistent with a predominant mechanical/nociceptive origin.

Patients who are candidates for spine surgery are excluded.

CURRENT COSTS ASSOCIATED WITH THE TREATMENT OF CLBP

LBP accounts for 7.6% or 42.5 million years lived with disability, and a recent study estimated that the United States spent US\$134.5 billion on health care for low back and neck pain in 2016, leading the top 154 conditions.¹⁵⁵ The data on the economic impact such as this is often stratified across the severity of the disease spectrum. However, the actual consumption of health care resources is disproportionately skewed toward those with more severe disease states. Patients with high-impact chronic pain were demonstrated to use more than double the overall and spine-related health care costs compared with patients less severely affected.¹⁵

Using data from the Medicare Expenditure Panel Survey, Herman et al¹⁵ estimated overall and spine-related annual health care costs for individuals with high-impact chronic pain to be \$14,661 and \$5979, respectively. These were significantly greater than other chronic pain patients that did not have a high impact of their pain on work, self-care, and activities of daily living (\$6371 overall and \$2300 spinal).

Spears et al⁴⁴ attempted to differentiate the cost of care for CLBP patients who were not candidates for spine surgery using a claims analysis from the IBM Marketscan Database. Of the approximately 56,000 patients identified with chronic refractory LBP, the upper quartile (14,000 patients) all experience costs greater than \$14,000 in the first- and second-year postindex diagnosis, with the majority of costs coming from outpatient services.

To estimate the economic impact of restorative neurostimulation, Shaffrey and Gilligan¹³⁵ stratified patients to pain impact status as a predictor of health care resource utilization. In a complete analysis of 146 patients, 103 (71%) were in a high-impact pain state at baseline. By the second year of therapy, 15 (10%) remained high impact and 124 (85%) reported no or low impact pain only. The previous studies suggest that utilization and costs are directly proportional to chronic pain impact; in combination with these data, these findings provide some evidence for cost efficacy.

CODING FOR RESTORATIVE NEUROSTIMULATION

ICD-10-CM Codes for Coverage

Restorative neurostimulation is a new approach to managing mechanical LBP specific to patients who suffer from neuromuscular instability from multifidus dysfunction. The resulting characteristics often appear as atrophy and wasting of the lower back muscles. Atrophy and weakening of muscles can result in weakness, decreased range of motion, and other functional impairments that are causal for LBP.^{156,157}

Typical International Classification of Diseases, 10 Revision, diagnosis codes that indicate medical necessity are as follows:

- Primary diagnosis: M62.5A2 (atrophy and wasting of muscles, not elsewhere classified, back, lumbosacral)
- Secondary diagnosis: M54.59 (low back pain, other)

Current Procedural Terminology

The procedures invoking restorative neurostimulation may include the use of a peripheral nerve stimulator and placement of percutaneous neurostimulator electrodes for which category 1 Current Procedural Terminology (CPT) codes are available to report. These codes include:

- CPT1 - 64555—Percutaneous implantation of neurostimulator electrode array, peripheral nerve.
- CPT1 - 64590—Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling.

CONCLUSION

Restorative neurostimulation for chronic mechanical LBP is supported by several clinical studies that show robust and durable clinical effects over the pretreatment condition. The totality of evidence suggests that in a well-selected patient population who have exhausted conventional care paradigms, the potential benefits outweigh the risks and costs. These patients tend to be exposed to multiple therapies with limited durability, resulting in a continuous cycle of high-cost health care utilization. Restorative neurostimulation should be considered for clinically appropriate patients who have exhausted reasonable conservative approaches.

LIMITATIONS

1. Industry funding is a potential source of study bias for the available data reviewed.
2. A limited number of studies is available.

REFERENCES

1. Hartvigsen J, Hancock MJ, Kongsted A, et al. What low back pain is and why we need to pay attention. *Lancet*. 2018;391(10137):2356–2367. doi:10.1016/S0140-6736(18)30480-X
2. Maher C, Underwood M, Buchbinder R. Non-specific low back pain. *Lancet*. 2017;389(10070):736–747. doi:10.1016/S0140-6736(16)30970-9
3. Korff MV. Studying the natural history of back pain. *Spine*. 1994;19(Supplement):2041S–2046S. doi:10.1097/00007632-199409151-00005
4. Carragee EJ, Hannibal M. Diagnostic evaluation of low back pain. *Orthop Clin North Am*. 2004;35(1):7–16. doi:10.1016/S0030-5898(03)00099-3
5. Andersson GBJ. Epidemiological features of chronic low-back pain. *Lancet*. 1999;354(9178):581–585. doi:10.1016/S0140-6736(99)01312-4
6. Fitzcharles M-A, Cohen SP, Clauw DJ, Littlejohn G, Usui C, Häuser W. Nociceptive pain: towards an understanding of prevalent pain conditions. *Lancet*. 2021;397(10289):2098–2110. doi:10.1016/S0140-6736(21)00392-5
7. 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(6):464–476. doi:10.2519/jospt.2019.8827
8. Kregel J, Meeus M, Malfliet A, et al. Structural and functional brain abnormalities in chronic low back pain: a systematic review. *Semin Arthritis Rheum*. 2015;45(2):229–237. doi:10.1016/j.semarthrit.2015.05.002
9. Panjabi MM. The stabilizing system of the spine. Part I function, dysfunction, adaptation and enhancement. *J Spinal Disord*. 1992;5(4):383–389. doi:10.1097/00002517-199212000-00001
10. Panjabi MM. The stabilizing system of the spine. Part II. Neutral zone and instability hypothesis. *J Spinal Disord*. 1992;5(4):390–396. doi:10.1097/00002517-199212000-00002
11. Hoy D, March L, Brooks P, et al. The global burden of low back pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis*. 2014;73(6):968–974. doi:10.1136/annrheum-dis-2013-204428
12. Reuben DB, Alvanzo AAH, Ashikaga T, et al. National Institutes of health pathways to prevention workshop: the role of opioids in the treatment of chronic pain. *Ann Intern Med*. 2015;162(4):295–300. doi:10.7326/M14-2775
13. Dagenais S, Caro J, Haldeman S. A systematic review of low back pain cost of illness studies in the United States and internationally. *The Spine Journal*. 2008;8(1):8–20. doi:10.1016/j.spinee.2007.10.005
14. Dieleman JL, Cao J, Chapin A, et al. US health care spending by payer and health condition, 1996–2016. *JAMA*. 2020;323(9):863–884. doi:10.1001/jama.2020.0734
15. Herman PM, Broten N, Lavelle TA, Sorbero ME, Coulter ID. Health care costs and opioid use associated with high-impact chronic spinal pain in the United States. *Spine (Phila Pa 1976)*. 2019;44(16):1154–1161. doi:10.1097/BRS.0000000000003033
16. Meucci RD, Fassa AG, Faria NM. Prevalence of chronic low back pain: systematic review. *Rev Saude Publica*. 2015;49:1. doi:10.1590/S0034-8910.2015049005874
17. Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH. The prevalence of chronic pain in United States adults: results of an internet-based survey. *J Pain*. 2010;11(11):1230–1239. doi:10.1016/j.jpain.2010.07.002
18. Yu D, Peat G, Jordan KP, et al. Estimating the population health burden of musculoskeletal conditions using primary care electronic health records. *Rheumatology (Oxford)*. 2021;60(10):4832–4843. doi:10.1093/rheumatology/keab109
19. Deyo RA, Weinstein JN. Low back pain. *N Engl J Med*. 2001;344(5):363–370. doi:10.1056/NEJM200102013440508
20. Hebert JJ, Koppenhaver SL, Magel JS, Fritz JM. The relationship of transversus abdominis and lumbar multifidus activation and prognostic factors for clinical success with a stabilization exercise program: a cross-sectional study. *Arch Phys Med Rehabil*. 2010;91(1):78–85. doi:10.1016/j.apmr.2009.08.146
21. Øverås CK, Johansson MS, de Campos TF, et al. Distribution and prevalence of musculoskeletal pain Co-occurring with persistent low back pain: a systematic review. *BMC Musculoskeletal Disord*. 2021;22(1):91. doi:10.1186/s12891-020-03893-z
22. Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of chronic pain and high-impact chronic pain among adults - United States, 2016. *MMWR Morb Mortal Wkly Rep*. 2018;67(36):1001–1006. doi:10.15585/mmwr.mm6736a2
23. Pitcher MH, Von Korff M, Bushnell MC, Porter L. Prevalence and profile of high-impact chronic pain in the United States. *J Pain*. 2019;20(2):146–160. doi:10.1016/j.jpain.2018.07.006
24. Von Korff M, DeBar LL, Krebs EE, Kerns RD, Deyo RA, Keefe FJ. Graded chronic pain scale revised: mild, bothersome, and high-impact chronic pain. *Pain*. 2020;161(3):651–661. doi:10.1097/j.pain.0000000000001758

25. Mutubuki EN, Luitjens MA, Maas ET, et al. Predictive factors of high societal costs among chronic low back pain patients. *Eur J Pain*. 2020;24(2):325–337. doi:10.1002/ejp.1488
26. Nahin RL. Estimates of pain prevalence and severity in adults: United States, 2012. *The Journal of Pain*. 2015;16(8):769–780. doi:10.1016/j.jpain.2015.05.002
27. Von Korff M, Scher AI, Helmick C, et al. United States national pain strategy for population research: concepts, definitions, and pilot data. *The Journal of Pain*. 2016;17(10):1068–1080. doi:10.1016/j.jpain.2016.06.009
28. Mackey SC. *National Pain Strategy: A Comprehensive Population Health-Level Strategy for Pain*. National Institutes of Health; 2017. https://iprcc.nih.gov/sites/default/files/HHSNational_Pain_Strategy_508C.pdf.
29. Deyo RA, Dworkin SF, Amtmann D, et al. Report of the NIH task force on research standards for chronic low back pain. *Int J Ther Massage Bodywork*. 2015;8(3):16–33. doi:10.3822/ijtm.v8i3.295
30. Hayden JA, Dunn KM, van der Windt DA, Shaw WS. What is the prognosis of back pain? *Best Pract Res Clin Rheumatol*. 2010;24(2):167–179. doi:10.1016/j.berh.2009.12.005
31. Dutmer AL, Schiphorst Preuper HR, Soer R, et al. Personal and societal impact of low back pain: the Groningen spine cohort. *Spine (Phila Pa 1976)*. 2019;44(24):E1443–E1451. doi:10.1097/BRS.00000000000003174
32. da Silva T, Mills K, Brown BT, Herbert RD, Maher CG, Hancock MJ. Risk of recurrence of low back pain: a systematic review. *J Orthop Sports Phys Ther*. 2017;47(5):305–313. doi:10.2519/jospt.2017.7415
33. Chen Y, Campbell P, Strauss VY, Foster NE, Jordan KP, Dunn KM. Trajectories and predictors of the long-term course of low back pain: cohort study with 5-year follow-up. *Pain*. 2018;159(2):252–260. doi:10.1097/j.pain.0000000000001097
34. Kongsted A, Kent P, Axen I, Downie AS, Dunn KM. What have we learned from ten years of trajectory research in low back pain *BMC Musculoskelet Disord*. 2016;17:220. doi:10.1186/s12891-016-1071-2
35. Dunn KM, Campbell P, Jordan KP. Long-term trajectories of back pain: cohort study with 7-year follow-up. *BMJ Open*. 2013;3(12):e003838. doi:10.1136/bmjopen-2013-003838
36. Itz CJ, Geurts JW, van Kleef M, Nelemans P. Clinical course of non-specific low back pain: a systematic review of prospective cohort studies set in primary care. *Eur J Pain*. 2013;17(1):5–15. doi:10.1002/j.1532-2149.2012.00170.x
37. Hallegraeff JM, Krijnen WP, van der Schans CP, de Greef MHG. Expectations about recovery from acute non-specific low back pain predict absence from usual work due to chronic low back pain: a systematic review. *J Physiother*. 2012;58(3):165–172. doi:10.1016/S1836-9553(12)70107-8
38. Menezes Costa L da C, Maher CG, Hancock MJ, McAuley JH, Herbert RD, Costa LOP. The prognosis of acute and persistent low-back pain: a meta-analysis. *CMAJ*. 2012;184(11):E613–E624. doi:10.1503/cmaj.111271
39. da Silva T, Mills K, Brown BT, et al. Recurrence of low back pain is common: a prospective inception cohort study. *J Physiother*. 2019;65(3):159–165. doi:10.1016/j.jphys.2019.04.010
40. Macedo LG, Maher CG, Latimer J, McAuley JH, Hodges PW, Rogers WT. Nature and determinants of the course of chronic low back pain over a 12-month period: a cluster analysis. *Phys Ther*. 2014;94(2):210–221. doi:10.2522/ptj.20120416
41. Norton G, McDonough CM, Cabral HJ, Shwartz M, Burgess JF. Classification of patients with incident non-specific low back pain: implications for research. *Spine J*. 2016;16(5):567–576. doi:10.1016/j.spinee.2015.08.015
42. Kongsted A, Leboeuf-Yde C. The Nordic back pain sub-population program: course patterns established through weekly follow-UPS in patients treated for low back pain. *Chiropr Osteopat*. 2010;18:2. doi:10.1186/1746-1340-18-2
43. Stewart WF, Yan X, Boscarino JA, et al. Patterns of health care utilization for low back pain. *J Pain Res*. 2015;8:523–535. doi:10.2147/JPR.S83599
44. Spears CA, Hodges SE, Kiyani M, et al. Health care resource utilization and management of chronic, refractory low back pain in the United States. *Spine (Phila Pa 1976)*. 2020;45(20):E1333–E1341. doi:10.1097/BRS.0000000000003572
45. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA*. 2003;290(18):2443. doi:10.1001/jama.290.18.2443
46. Lallukka T, Mänty M, Cooper C, et al. Recurrent back pain during working life and exit from paid employment: a 28-year follow-up of the Whitehall II study. *Occup Environ Med*. 2018;75(11):786–791. doi:10.1136/oemed-2018-105202
47. Steenstra IA, Munhall C, Irvin E, et al. Systematic review of prognostic factors for return to work in workers with sub acute and chronic low back pain. *J Occup Rehabil*. 2017;27(3):369–381. doi:10.1007/s10926-016-9666-x
48. Hoy DG, Protani M, De R, Buchbinder R. The epidemiology of low back pain. *Best Pract Res Clin Rheumatol*. 2010;24(6):783–792. doi:10.1016/j.berh.2011.01.019
49. Cancelliere C, Donovan J, Stochkendahl MJ, et al. Factors affecting return to work after injury or illness: best evidence synthesis of systematic reviews. *Chiropr Man Therap*. 2016;24(1):32. doi:10.1186/s12998-016-0113-z
50. Côté P, Baldwin ML, Johnson WG, Frank JW, Butler RJ. Patterns of sick-leave and health outcomes in injured workers with back pain. *Eur Spine J*. 2008;17(4):484–493. doi:10.1007/s00586-007-0577-6
51. Aronsson G, Gustafsson K, Dallner M. Sick but yet at work. An empirical study of sickness presenteeism. *J Epidemiol Community Health*. 2000;54(7):502–509. doi:10.1136/jech.54.7.502
52. Karoly P, Ruehlman LS, Okun MA. Psychosocial and demographic correlates of employment vs disability status in a national community sample of adults with chronic pain: toward a psychology of pain presenteeism. *Pain Med*. 2013;14(11):1698–1707. doi:10.1111/pme.12234
53. Shmagel A, Foley R, Ibrahim H. Epidemiology of chronic low back pain in US adults: data from the 2009-2010 national health and nutrition examination survey. *Arthritis Care Res (Hoboken)*. 2016;68(11):1688–1694. doi:10.1002/acr.22890
54. van Leeuwen MT, Blyth FM, March LM, Nicholas MK, Cousins MJ. Chronic pain and reduced work effectiveness: the hidden cost to Australian employers. *Eur J Pain*. 2006;10(2):161–166. doi:10.1016/j.ejpain.2005.02.007
55. Virtanen M, Ervasti J, Head J, et al. Lifestyle factors and risk of sickness absence from work: a multicohort study. *Lancet Public Health*. 2018;3(11):e545–e554. doi:10.1016/S2468-2667(18)30201-9
56. Serranheira F, Sousa-Uva M, Heranz F, Kovacs F, Sousa-Uva A. Low back pain (LBP), work and absenteeism. *Work*. 2020;65(2):463–469. doi:10.3233/WOR-203073

57. Wynne-Jones G, Cowen J, Jordan JL, et al. Absence from work and return to work in people with back pain: a systematic review and meta-analysis. *Occup Environ Med.* 2014;71(6):448–456. doi:10.1136/oemed-2013-101571
58. Pedersen J, Bjorner JB, Burr H, Christensen KB. Transitions between sickness absence, work, unemployment, and disability in Denmark 2004–2008. *Scand J Work Environ Health.* 2012;38(6):3293:516–526. doi:10.5271/sjweh.3293
59. Gustavsson A, Bjorkman J, Ljungcrantz C, et al. Socio-economic burden of patients with a diagnosis related to chronic pain—register data of 840,000 Swedish patients. *Eur J Pain.* 2012;16(2):289–299. doi:10.1016/j.ejpain.2011.07.006
60. van Rijn RM, Robroek SJW, Brouwer S, Burdorf A. Influence of poor health on exit from paid employment: a systematic review. *Occup Environ Med.* 2014;71(4):295–301. doi:10.1136/oemed-2013-101591
61. Becker BA, Childress MA. Nonspecific low back pain and return to work. *Am Fam Physician.* 2019;100(11):697–703.
62. Kool J, de Bie R, Oesch P, Knüsel O, van den Brandt P, Bachmann S. Exercise reduces sick leave in patients with non-acute non-specific low back pain: a meta-analysis. *J Rehabil Med.* 2004;36(2):49–62. doi:10.1080/16501970310020104
63. Schaafsma FG, Whelan K, van der Beek AJ, van der Es-Lambeck LC, Ojajärvi A, Verbeek JH. Physical conditioning as part of a return to work strategy to reduce sickness absence for workers with back pain. *Cochrane Database Syst Rev.* 2013;2013(8):CD001822. doi:10.1002/14651858.CD001822.pub3
64. Szmuda T, Słoniewski P, Ali S, Aleksandrowicz K. Does spinal cord stimulation due to failed back surgery syndrome lead to permanent occupational disability? *Neuromodulation.* 2020;23(5):653–659. doi:10.1111/ner.13014
65. Turner JA, Hollingworth W, Comstock BA, Deyo RA. Spinal cord stimulation for failed back surgery syndrome: outcomes in a workers' compensation setting. *Pain.* 2010;148(1):14–25. doi:10.1016/j.pain.2009.08.014
66. Aebi M, Gunzburg R, Szpalski M, eds. *The Aging Spine.* Berlin Heidelberg: Springer; 2001.
67. Benoist M. Natural history of the aging spine. *Eur Spine J.* 2003;12 Suppl 2(Suppl 2):S86–9. doi:10.1007/s00586-003-0593-0
68. Adams MA, Roughley PJ. What is intervertebral disc degeneration, and what causes it *Spine (Phila Pa 1976).* 2006;31(18):2151–2161. doi:10.1097/01.brs.00000231761.73859.2c
69. Gellhorn AC, Katz JN, Suri P. Osteoarthritis of the spine: the facet joints. *Nat Rev Rheumatol.* 2013;9(4):216–224. doi:10.1038/nrrheum.2012.199
70. Goossens N, Rummens S, Janssens L, Caeyenberghs K, Brumagne S. Association between sensorimotor impairments and functional brain changes in patients with low back pain: a critical review. *Am J Phys Med Rehabil.* 2018;97(3):200–211. doi:10.1097/PHM.0000000000000859
71. Massé-Alarie H, Flamand VH, Moffet H, Schneider C. Corticomotor control of deep abdominal muscles in chronic low back pain and anticipatory postural adjustments. *Exp Brain Res.* 2012;218(1):99–109. doi:10.1007/s00221-012-3008-9
72. Massé-Alarie H, Beaulieu L-D, Preuss R, Schneider C. Influence of paravertebral muscles training on brain plasticity and postural control in chronic low back pain. *Scand J Pain.* 2016;12:74–83. doi:10.1016/j.sjpain.2016.03.005
73. Seidler RD, Noll DC, Thiers G. Feedforward and feedback processes in motor control. *Neuroimage.* 2004;22(4):1775–1783. doi:10.1016/j.neuroimage.2004.05.003
74. Holm S, Indahl A, Solomonow M. Sensorimotor control of the spine. *J Electromyogr Kinesiol.* 2002;12(3):219–234. doi:10.1016/s1050-6411(02)00028-7
75. Quint U, Wilke HJ, Shirazi-Adl A, Parnianpour M, Löer F, Claes LE. Importance of the intersegmental trunk muscles for the stability of the lumbar spine. A biomechanical study in vitro. *Spine (Phila Pa 1976).* 1998;23(18):1937–1945. doi:10.1097/00007632-199809150-00003
76. Rosatelli AL, Ravichandiran K, Agur AM. Three-dimensional study of the musculotendinous architecture of lumbar multifidus and its functional implications. *Clin Anat.* 2008;21(6):539–546. doi:10.1002/ca.20659
77. Bogduk N. A reappraisal of the anatomy of the human lumbar erector spinae. *J Anat.* 1980;131(Pt 3):525–540.
78. Bogduk N, Wilson AS, Tynan W. The human lumbar dorsal rami. *J Anat.* 1982;134(Pt 2):383–397.
79. Hodges PW, Coppieters MW, MacDonald D, Cholewicki J. New insight into motor adaptation to pain revealed by a combination of modelling and empirical approaches. *Eur J Pain.* 2013;17(8):1138–1146. doi:10.1002/j.1532-2149.2013.00286.x
80. Indahl A, Kaigle AM, Reikerås O, Holm SH. Interaction between the porcine lumbar Intervertebral disc. *Zygapophyseal Joints and Paraspinal Muscles Spine.* 1997;22:2834–2840. doi:10.1097/00007632-199712150-00006
81. Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine (Phila Pa 1976).* 2006;31(25):2926–2933. doi:10.1097/01.brs.0000248453.51165.0b
82. Tsao H, Druitt TR, Schollum TM, Hodges PW. Motor training of the lumbar paraspinal muscles induces immediate changes in motor coordination in patients with recurrent low back pain. *J Pain.* 2010;11(11):1120–1128. doi:10.1016/j.jpain.2010.02.004
83. 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(8):1744–1756. doi:10.1007/s00586-018-5652-7
84. James G, Chen X, Diwan A, Hodges PW. Fat infiltration in the multifidus muscle is related to inflammatory cytokine expression in the muscle and epidural Adipose tissue in individuals undergoing surgery for intervertebral disc herniation. *Eur Spine J.* 2021;30(4):837–845. doi:10.1007/s00586-020-06514-4
85. Ward SR, Kim CW, Eng CM, et al. Architectural analysis and intraoperative measurements demonstrate the unique design of the multifidus muscle for lumbar spine stability. *J Bone Joint Surg Am.* 2009;91(1):176–185. doi:10.2106/JBJS.G.01311
86. MacDonald D, Moseley LG, 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(3):183–188. doi:10.1016/j.pain.2008.12.002
87. van Dieën JH, Flor H, Hodges PW. Low-back pain patients learn to adapt motor behavior with adverse secondary consequences. *Exerc Sport Sci Rev.* 2017;45(4):223–229. doi:10.1249/JES.0000000000000121
88. van Dieën JH, Reeves NP, 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(6):370–379. doi:10.2519/jospt.2019.7917
89. Schabrun SM, Elgueta-Cancino EL, Hodges PW. Smudging of the motor cortex is related to the severity of low back pain. *Spine (Phila Pa 1976).* 2017;42(15):1172–1178. doi:10.1097/BRS.0000000000000938

90. Grooten WJA, Boström C, Dederer Å, et al. Summarizing the effects of different exercise types in chronic low back pain - a systematic review of systematic reviews. *BMC Musculoskelet Disord.* 2022;23(1):801. doi:10.1186/s12891-022-05722-x
91. Hayden JA, Ellis J, Ogilvie R, Malmivaara A, van Tulder MW. Exercise therapy for chronic low back pain. *Cochrane Database Syst Rev.* 2021;9(9):CD009790. doi:10.1002/14651858.CD009790.pub2
92. Kreiner DS, Matz P, Bono CM, et al. Guideline summary review: an evidence-based clinical guideline for the diagnosis and treatment of low back pain. *Spine J.* 2020;20(7):998–1024. doi:10.1016/j.spinee.2020.04.006
93. Corp N, Mansell G, Stynes S, et al. Evidence-based treatment recommendations for neck and low back pain across Europe: a systematic review of guidelines. *Eur J Pain.* 2021;25(2):275–295. doi:10.1002/ejp.1679
94. Schreijenberg M, Koes BW, Lin C-WC. Guideline recommendations on the pharmacological management of non-specific low back pain in primary care-is there a need to change? *Expert Rev Clin Pharmacol.* 2019;12(2):145–157. doi:10.1080/17512433.2019.1565992
95. Airaksinen O, Brox JJ, 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):S192–300. doi:10.1007/s00586-006-1072-1
96. Chaparro LE, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared to placebo or other treatments for chronic low-back pain. *Cochrane Database Syst Rev.* 2013;CD004959(8):CD004959. doi:10.1002/14651858.CD004959.pub4
97. Cashin AG, Wand BM, O'Connell NE, et al. Pharmacological treatments for low back pain in adults: an overview of Cochrane reviews. *Cochrane Database Syst Rev.* 2020. doi:10.1002/14651858.CD013815
98. Henschke N, Ostelo RW, van Tulder MW, et al. Behavioural treatment for chronic low-back pain. *Cochrane Database Syst Rev.* 2010;2010(7):CD002014. doi:10.1002/14651858.CD002014.pub3
99. Staal JB, de Bie R, de Vet HC, Hildebrandt J, Nelemans P. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev.* 2008;2008(3):CD001824. doi:10.1002/14651858.CD001824.pub3
100. National Institute for Health and Care Excellence. *Low Back Pain and Sciatica in over 16s: Assessment and Management (NICE Guideline 59). Preprint At.* 2016. <https://www.nice.org.uk/guidance/ng59>.
101. Vekaria R, Bhatt R, Ellard DR, Henschke N, Underwood M, Sandhu H. Intra-articular facet joint injections for low back pain: a systematic review. *Eur Spine J.* 2016;25(4):1266–1281. doi:10.1007/s00586-016-4455-y
102. Lakemeier S, Lind M, Schultz W, et al. A comparison of Intraarticular lumbar facet joint steroid injections and lumbar facet joint radiofrequency denervation in the treatment of low back pain: a randomized, controlled, double-blind trial. *Anesth Analg.* 2013;117(1):228–235. doi:10.1213/ANE.0b013e3182910c4d
103. Maas ET, Ostelo RWJG, Niemisto L, et al. Radiofrequency denervation for chronic low back pain. *Cochrane Database Syst Rev.* 2015;2015(10):CD008572. doi:10.1002/14651858.CD008572.pub2
104. Juch JNS, Maas ET, Ostelo RWJG, et al. Effect of radiofrequency denervation on pain intensity among patients with chronic low back pain: the MINT randomized clinical trials. *JAMA.* 2017;318(1):68–81. doi:10.1001/jama.2017.7918
105. van Kuijk SMJ, Van Zundert J, Hans G, et al. Flawed study design and incorrect presentation of data negatively impact potentially useful interventional treatments for patients with low back pain: a critical review of JAMA's mint study. *Pain Pract.* 2018;18(3):292–295. doi:10.1111/papr.12673
106. McCormick ZL, Vorobeychik Y, Gill JS, et al. Guidelines for composing and assessing a paper on the treatment of pain: a practical application of evidence-based medicine principles to the mint randomized clinical trials. *Pain Med.* 2018;19(11):2127–2137. doi:10.1093/pm/pny046
107. Ehsanian R, Malone DC, Hambræus J, et al. Guidelines for composing and assessing a paper on the treatment of pain: a practical application of evidence-based medicine principles to a cost-effectiveness analysis of the MINT randomized clinical trials. *Interventional Pain Medicine.* 2022;1(1):100010. doi:10.1016/j.inpm.2022.100010
108. McCormick ZL, Marshall B, Walker J, McCarthy R, Walega DR. Long-term function, pain and medication use outcomes of radiofrequency ablation for lumbar facet syndrome. *Int J Anesth.* 2015;2(2):028. doi:10.23937/2377-4630/2/21028
109. Yadav A, Hagedorn JM, D'Souza RS, Engle AM, Deer TR. Effect of patient characteristics on reported outcomes over 12 months following lumbar radiofrequency ablation: a retrospective review of 500 patients. *Pain Pract.* 2021;21(2):152–159. doi:10.1111/papr.12938
110. Weinstein JN, Lurie JD, Tosteson TD, et al. Surgical compared with nonoperative treatment for lumbar degenerative spondylolisthesis: four-year results in the spine patient outcomes research trial (SPORT) randomized and observational cohorts. *J Bone Joint Surg Am.* 2009;91(6):1295–1304. doi:10.2106/JBJS.H.00913
111. Fritzell P, Hägg O, Wessberg P, Nordwall A, Swedish Lumbar Spine Study Group. 2001 Volvo award winner in clinical studies: lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish lumbar spine study group. *Spine (Phila Pa 1976).* 2001;26(23):2521–2532. doi:10.1097/00007632-200112010-00002
112. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study. *Spine (Phila Pa 1976).* 2005;30(8):927–935. doi:10.1097/01.brs.0000158954.68522.2a
113. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of lumbar spinal stenosis: 8 to 10 year results from the maine lumbar spine study. *Spine (Phila Pa 1976).* 2005;30(8):936–943. doi:10.1097/01.brs.0000158953.57966.c0
114. Guyer RD, McAfee PC, Banco RJ, et al. Prospective, randomized, multicenter food and drug administration investigational device exemption study of lumbar total disc replacement with the CHARITE artificial disc versus lumbar fusion: five-year follow-up. *Spine J.* 2009;9(5):374–386. doi:10.1016/j.spinee.2008.08.007
115. Delamarter R, Zigler JE, Balderston RA, Cammisa FP, Goldstein JA, Spivak JM. Prospective, randomized, multicenter food and drug administration investigational device exemption study of the prodisc-L total disc replacement compared with circumferential arthrodesis for the treatment of two-level lumbar degenerative disc disease: results at twenty-four months. *J Bone Joint Surg Am.* 2011;93(8):705–715. doi:10.2106/JBJS.I.00680

116. Berg S, Tullberg T, Branth B, Olerud C, Tropp H. Total disc replacement compared to lumbar fusion: a randomised controlled trial with 2-year follow-up. *Eur Spine J*. 2009;18(10):1512–1519. doi:10.1007/s00586-009-1047-0
117. Brox JI, Nygaard ØP, Holm I, Keller A, Ingebrigtsen T, Reikerås O. Four-year follow-up of surgical versus non-surgical therapy for chronic low back pain. *Ann Rheum Dis*. 2010;69(9):1643–1648. doi:10.1136/ard.2009.108902
118. Danneels LA, Vanderstraeten GG, Cambier DC, et al. Effects of three different training modalities on the cross sectional area of the lumbar multifidus muscle in patients with chronic low back pain. *Br J Sports Med*. 2001;35(3):186–191. doi:10.1136/bjsm.35.3.186
119. Berglund L, Aasa B, Michaelson P, Aasa U. Effects of low-load motor control exercises and a high-load lifting exercise on lumbar multifidus thickness: a randomized controlled trial. *Spine (Phila Pa 1976)*. 2017;42(15):E876–E882. doi:10.1097/BRS.0000000000001989
120. Mannion AF. Fibre type characteristics and function of the human paraspinal muscles: normal values and changes in association with low back pain. *J Electromyogr Kinesiol*. 1999;9(6):363–377. doi:10.1016/s1050-6411(99)00010-3
121. Cagnie B, Dhooge F, Schumacher C, et al. Fiber typing of the erector spinae and multifidus muscles in healthy controls and back pain patients: a systematic literature review. *J Manipulative Physiol Ther*. 2015;38(9):653–663. doi:10.1016/j.jmpt.2015.10.004
122. Buller AJ, Eccles JC, Eccles RM. Interactions between Motoneurons and muscles in respect of the characteristic speeds of their responses. *The Journal of Physiology*. 1960;150(2):417–439. doi:10.1113/jphysiol.1960.sp006395
123. Delliaux S, Brerro-Saby C, Steinberg JG, Jammes Y. Reactive oxygen species and inflammatory mediators enhance muscle spindles mechanosensitivity in rats. *Pflugers Arch*. 2009;457(4):877–884. doi:10.1007/s00424-008-0554-x
124. James G, Stecco C, Blomster L, et al. Muscle spindles of the multifidus muscle undergo structural change after intervertebral disc degeneration. *Eur Spine J*. 2022;31(7):1879–1888. doi:10.1007/s00586-022-07235-6
125. James G, Klyne DM, Millecamps M, Stone LS, Hodges PW. ISSLS prize in basic science 2019: physical activity attenuates fibrotic alterations to the multifidus muscle associated with intervertebral disc degeneration. *Eur Spine J*. 2019;28(5):893–904. doi:10.1007/s00586-019-05902-9
126. Kharraz Y, Guerra J, Mann CJ, Serrano AL, Muñoz-Cánoves P. Macrophage plasticity and the role of inflammation in skeletal muscle repair. *Mediators Inflamm*. 2013;2013:491497. doi:10.1155/2013/491497
127. Tsao H, Danneels LA, Hodges PW. ISSLS prize winner: smudging the motor brain in young adults with recurrent low back pain. *Spine (Phila Pa 1976)*. 2011;36(21):1721–1727. doi:10.1097/BRS.0b013e31821c4267
128. Schabrun SM, Jones E, Elgueta Cancino EL, Hodges PW. Targeting chronic recurrent low back pain from the top-down and the bottom-up: a combined transcranial direct current stimulation and peripheral electrical stimulation intervention. *Brain Stimul*. 2014;7(3):451–459. doi:10.1016/j.brs.2014.01.058
129. Adkins DL, Boychuk J, Remple MS, Kleim JA. Motor training induces experience-specific patterns of plasticity across motor cortex and spinal cord. *J Appl Physiol (1985)*. 2006;101(6):1776–1782. doi:10.1152/japplphysiol.00515.2006
130. Rogers SL. Muscle spindle formation and differentiation in regenerating rat muscle grafts. *Dev Biol*. 1982;94(2):265–283. doi:10.1016/0012-1606(82)90347-5
131. Eldabe S, Duarte RV, Gulve A, et al. Does a screening trial for spinal cord stimulation in patients with chronic pain of neuropathic origin have clinical utility and cost-effectiveness (TRIAL-STIM)? A randomised controlled trial. *Pain*. 2020;161(12):2820–2829. doi:10.1097/j.pain.0000000000001977
132. Chadwick R, McNaughton R, Eldabe S, et al. To trial or not to trial before spinal cord stimulation for chronic neuropathic pain: the patients' view from the TRIAL-STIM randomized controlled trial. *Neuromodulation*. 2021;24(3):459–470. doi:10.1111/ner.13316
133. Freynhagen R, Baron R. The evaluation of neuropathic components in low back pain. *Curr Pain Headache Rep*. 2009;13(3):185–190. doi:10.1007/s11916-009-0032-y
134. Cook C, Brismée JM, Sizer PS. Subjective and objective descriptors of clinical lumbar spine instability: a delphi study. *Man Ther*. 2006;11(1):11–21. doi:10.1016/j.math.2005.01.002
135. Shaffrey C, Gilligan C. Effect of restorative neuromodulation on major drivers of chronic low back pain economic impact. *Neurosurgery*. 2023;92(4):716–724. doi:10.1227/neu.0000000000002305
136. 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(1):151–164. doi:10.1016/j.apmr.2016.07.020
137. Hicks GE, Fritz JM, Delitto A, Mishock J. Interrater reliability of clinical examination measures for identification of lumbar segmental instability. *Arch Phys Med Rehabil*. 2003;84(12):1858–1864. doi:10.1016/s0003-9993(03)00365-4
138. Rabin A, Shashua A, Pizem K, Dickstein R, Dar G. A clinical prediction rule to identify patients with low back pain who are likely to experience short-term success following lumbar stabilization exercises: a randomized controlled validation study. *J Orthop Sports Phys Ther*. 2014;44(1):6–B13. doi:10.2519/jospt.2014.4888
139. Hebert JJ, Koppenhaver SL, Teyhen DS, Walker BF, Fritz JM. The evaluation of lumbar multifidus muscle function via palpation: reliability and validity of a new clinical test. *Spine J*. 2015;15(6):1196–1202. doi:10.1016/j.spinee.2013.08.056
140. Biely SA, Silfies SP, Smith SS, Hicks GE. Clinical observation of standing trunk movements: what do the aberrant movement patterns tell us? *J Orthop Sports Phys Ther*. 2014;44(4):262–272. doi:10.2519/jospt.2014.4988
141. Kalichman L, Hodges P, Li L, Guermazi A, Hunter DJ. Changes in paraspinal muscles and their association with low back pain and spinal degeneration: CT study. *Eur Spine J*. 2010;19(7):1136–1144. doi:10.1007/s00586-009-1257-5
142. Le Cara EC, Marcus RL, Dempsey AR, Hoffman MD, Hebert JJ. Morphology versus function: the relationship between lumbar multifidus intramuscular adipose tissue and muscle function among patients with low back pain. *Arch Phys Med Rehabil*. 2014;95(10):1846–1852. doi:10.1016/j.apmr.2014.04.019
143. Hildebrandt M, Fankhauser G, Meichtry A, Luomajoki H. Correlation between lumbar dysfunction and fat infiltration in lumbar multifidus muscles in patients with low back pain. *BMC Musculoskelet Disord*. 2017;18(1):1–9. doi:10.1186/s12891-016-1376-1

144. Fortin M, Gibbons LE, Videman T, Battié MC. Do variations in paraspinal muscle morphology and composition predict low back pain in men *Scand J Med Sci Sports*. 2015;25(6):880–887. doi:10.1111/sms.12301
145. Deckers K, De Smedt K, van Buyten J-P, et al. Chronic low back pain: restoration of dynamic stability. *Neuromodulation: Technology at the Neural Interface*. 2015;18(6):478–486. doi:10.1111/ner.12275
146. 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(1):48–55. doi:10.1111/ner.12741
147. 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(6):1024–1032. doi:10.1111/ner.13477
148. 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(2):1451–1465. doi:10.1007/s40122-021-00307-3
149. Thomson S, Williams A, Vajramani G. Restorative neurostimulation for chronic mechanical low back pain – three year results from the United Kingdom post market clinical follow-up registry. *Br J Pain*. 2021. doi:10.1177/20494637231181498
150. 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(10):2486–2498. doi:10.1097/j.pain.0000000000002258
151. Gilligan C, Volschenk W, Russo M, et al. Long-term outcomes of restorative neurostimulation in patients with refractory chronic low back pain secondary to multifidus dysfunction: two-year results of the reactiv8-B pivotal trial. *Neuromodulation*. 2023;26(1):87–97. doi:10.1016/j.neurom.2021.10.011
152. Gilligan C, Volschenk W, Russo M, et al. Three-year durability of restorative neurostimulation effectiveness in patients with chronic low back pain and multifidus muscle dysfunction. *Neuromodulation*. 2023;26(1):98–108. doi:10.1016/j.neurom.2022.08.457
153. Gilligan C. Four-year durability of restorative neurostimulation effectiveness in patients with refractory chronic low back pain. *Neuromodulation: Technology at the Neural Interface*. 2023;26(4):S148. doi:10.1016/j.neurom.2023.04.260
154. Ardeshiri A, Shaffrey C, Stein K-P, Sandalcioğlu IE. Real-world evidence for restorative neurostimulation in chronic low back pain—a consecutive cohort study. *World Neurosurg*. 2022;168:e253–e259. doi:10.1016/j.wneu.2022.09.104
155. Buchbinder R, Underwood M, Hartvigsen J, Maher CG. The Lancet series call to action to reduce low value care for low back pain: an update. *Pain*. 2020;161 Suppl 1(1):S57–S64. doi:10.1097/j.pain.0000000000001869
156. Hodges PW, Tucker K. Moving differently in pain: a new theory to explain the adaptation to pain. *Pain*. 2011;152(3 Suppl):S90–S98. doi:10.1016/j.pain.2010.10.020
157. World Health Organization. *International Statistical Classification of Diseases and Related Health Problems*. 11th edn. World Health Organization; 2019. <https://icd.who.int/>.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests: The authors report no conflicts of interest in this work.

Corresponding Author: Morgan Lorio, Advanced Orthopedics, 499 E. Central Pkwy, Ste. 130, Altamonte Springs, FL 32701, USA; mloriomd@gmail.com

Published 09 August 2023

This manuscript is generously published free of charge by ISASS, the International Society for the Advancement of Spine Surgery. Copyright © 2023 ISASS. To see more or order reprints or permissions, see <http://ijssurgery.com>.