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CLINICAL TRIAL REPORT

Comparing Conventional Medical Management to Spinal Cord Stimulation for the Treatment of Low Back Pain in a Cohort of DISTINCT RCT Patients

Timothy Deer[1,*], Robert Heros[2,*], Edward Tavel[3], Sayed Wahezi[4], Robert Funk[5], Patrick Buchanan[6], Anne Christopher[7], Jacqueline Weisbein[8], Christopher Gilligan[9], Denis Patterson[10], Ajay Antony[11], Mohab Ibrahim[12], Nathan Miller[13], Keith Scarfo[14], Gayle Johnson[15], Thadchaigeni Panchalingam[15], Udoka Okaro[15], James Yue[16]

[1]Pain Management, The Spine and Nerve Center of the Virginias, Charleston, WV, USA; [2]Pain Management, Spinal Diagnostics, Tualatin, OR, USA; [3]Pain Management, Clinical Trials of South Carolina, Charleston, SC, USA; [4]Pain Management, Montefiore Medical Center, Bronx, NY, USA; [5]Pain Management, Indiana Spine Group, Indianapolis, IN, USA; [6]Pain Management, Spanish Hills Interventional Pain Specialists, Camarillo, CA, USA; [7]Pain Management, Saint Louis Pain Consultants, Chesterfield, MO, USA; [8]Pain Management, Napa Valley Orthopedic Medical Group, Napa, CA, USA; [9]Pain Management, Robert Wood Johnson University Hospital, New Brunswick, NJ, USA; [10]Pain Management, Nevada Advanced Pain Specialists, Reno, NV, USA; [11]Pain Management, the Orthopedic Institute, Gainesville, FL, USA; [12]Pain Management, Coastal Pain & Spinal Diagnostics Medical Group, Carlsbad, CA, USA; [13]Pain Management, Banner University Medical Center, Tucson, AZ, USA; [14]Pain Management, Rhode Island Hospital, Providence, RI, USA; [15]Neuromodulation, Abbott Labs, Austin, TX, USA; [16]Orthopaedic spine Surgery, Connecticut Orthopedics, Hamden, CT, USA

*These authors contributed equally to this work

Correspondence: Timothy Deer, Pain Management, The Spine and Nerve Center of the Virginias, 400 Court Street, Suite 100, Charleston, WV, 25301, USA, Tel +1 304 347 – 6120, Fax +1 304 347 – 6126, Email doctdeer@aol.com

Aim: Low Back Pain (LBP) is a prevalent condition. Spinal cord stimulation (SCS) has emerged as a more effective, long-term treatment compared to conventional medical management (CMM). The DISTINCT study enrolled and randomized chronic LBP patients with no indication of traditional spine surgery. This analysis focuses comparing study outcomes on patients initially randomized to receive CMM treatment and subsequently crossed over to SCS after 6 months.

Purpose: To compare the therapeutic effectiveness and cost-efficiency of passive recharge burst SCS to CMM.

Patients and Methods: A total of 269 patients were enrolled with 162 randomly assigned to SCS and 107 to CMM. The DISTINCT study design allowed a crossover to the alternative treatment arm after 6 months. Patients underwent a trial and received a permanent implant if they reported ≥50% pain reduction. Outcome analysis included pain (NRS), disability (ODI), catastrophizing (PCS), quality of life (PROMIS-29) and health care utilization.

Results: Seventy out of eighty-one patients opted to cross over to trial SCS at 6M with 94% (66/70) undergoing a trial. Among those, 88% (58/66) reported a ≥50% or more pain relief and 55 received a permanent implant. At 12M visit, 71.4% reported a ≥50% pain improvement sustained at the 18M visit, with 24.5% (12/49) indicating a ≥80% improvement. Disability reductions (79% meeting the minimally important difference of a 13-point decrease), decreased catastrophizing, and significant improvements in all PROMIS-29 domains were noted. Furthermore, 42% of the patients reported decreased or discontinued opioid usage. Clinical benefits at the 12M visit were sustained through the 18M visit accompanied by a significant reduction in healthcare utilization and a $1214 cost savings.

Conclusion: SCS demonstrates superior, long-term performance and safety outcomes compared to CMM therapy in LBP patients who received both CMM and SCS therapy. Additionally, SCS patients experienced reduced healthcare resource utilization and lower costs compared to those receiving CMM.

Keywords: DISTINCT, low back pain, BurstDR, spinal cord stimulation, healthcare utilization, persistent spinal pain syndrome, neuromodulation

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Introduction

DISTINCT was a multicenter, prospective randomized controlled trial comparing the efficacy of Spinal Cord Stimulation (SCS) to Comprehensive Medical Management (CMM) in treating chronic, refractory axial low back pain in patients with no prior lumbar spine surgery and for whom surgery was not indicated. Patients whose primary diagnosis was chronic low back pain were included, and those randomized to CMM could cross over to SCS after primary endpoint analysis at 6 months.

In the clinical evidence hierarchy, randomized controlled trials (RCTs) are considered the gold standard study design for minimizing bias and confounding factors. Their aim is to provide credible, unbiased evidence of a cause-and-effect relationship between treatment and outcome within a target population. While RCTs offer high internal validity, their external validity may be restricted by stringent patient selection, limited duration, and strict clinical protocols.[1–3] A crossover design compares treatment effects within individual patients, as each patient acts as both treatment and control minimizing inter-patient variability in group comparisons while reducing bias and the impact of covariates during outcome analysis.[4]

Pain produces an unpleasant sensory experience imposing significant physiological and financial burdens.[5] Conventional treatment options for pain include pharmacological, interventional and/or surgical approaches.[6] Spinal cord stimulation (SCS) is a long-accepted treatment for managing intractable pain in the trunk and/or limbs associated with conditions such as Complex Regional Pain Syndrome, diabetic peripheral neuropathy of the lower extremities, and failed back surgery syndrome (now commonly referred to as Persistent Spinal Pain Syndrome - PSPS). PSPS-type 1 refers to patients with chronic pain without previous spinal surgery and PSPS-type 2 is chronic pain, persisting after spine surgery. More recently, SCS has also emerged as a potential option for non-surgical low back pain patients.[7–11] The majority of SCS patients experience satisfactory pain relief.[12,13] Over 70% of SCS patients report at least a 50% pain improvement in addition to improvements in disability and psychosocial symptoms.[10,14,15]

Advances in neuromodulation technology such as the introduction of new waveforms and hardware have further enhanced clinical outcomes for patients.[15–20] Due to the overall cost of treating chronic pain and specifically spinal pain, SCS (like all back pain treatments) has been the subject of economic evaluations.[21] Decision trees and Markov models have been utilized to report evidence on the cost analysis of SCS compared to nonsurgical CMM.[22,23] Clinical evidence supports the assertion that SCS is more effective and cost efficient than CMM, over the lifetime of a patient.[16,24,25] SCS therapy not only reduces medical costs but also decreases the demand for medical care among PSPS-2 patients by improving their ongoing symptom burden and quality of life.[21,26]

The crossover nature of the DISTINCT study represents an opportunity for patients to have the CMM therapies optimized and carefully consider the SCS treatment, allowing us to garner further insights on SCS therapy. Additionally, it compares the healthcare utilization and associated costs of the DISTINCT CMM crossover patients under both therapies.

Methods

Two hundred and seventy (270) patients were included in the study and randomized in a 2:3 ratio to receive either conventional medical management (CMM) or passive burst recharge SCS (Abbott, TX) +CMM. One patient was enrolled and not randomized. The data presented here does not include non-randomized patients. Patient inclusion criteria was previously discussed in Deer et al.[10] All study documents received institutional review board (IRB) approval prior to patient enrollment. The study is registered on ClinicalTrials.gov (NCT04479787). Consent was obtained from all potential patients prior to enrollment. The study is conducted in accordance with the US Code of Federal Regulations and the World Medical Association Declaration of Helsinki.

Patients randomized to the CMM arm received supervised medical care, including physical modalities, medication optimization, and interventional therapies as decided by the investigator depending on the diagnosis. Medication optimization included nonsteroidal anti-inflammatories, anticonvulsants, muscle relaxants, opioids, and other analgesics as appropriate. Supervised noninterventional therapy could include physical therapy, chiropractic care, cognitive-behavioral therapy, massage, and acupuncture. Interventional therapies, such as injections and radiofrequency therapy, were also allowed. The primary endpoint was evaluated at 6 months after which patients had the option to cross over to the other treatment arm. Patients crossing over from CMM to the SCS arm followed the standard trial procedure for 4–7 days and underwent implant procedures only if they experienced at least a 50% pain relief during the trial phase. The study endpoints incorporated outcome measures and associated clinically meaningful improvements per the IMMPACT guidelines.[27] Responders were defined by at least a 50% reduction in low back pain (LBP) as measured by the Numeric Rating Scale (NRS). Other endpoints assessed included back pain-related physical

disability (Oswestry Disability Index [ODI]), pain-related emotional distress (Pain Catastrophizing Scale [PCS]), quality of life (Patient-Reported Outcome Measure Information System [PROMIS-29] domains, the patient impression (Patient Global Impression of Change [PGIC] and satisfaction), pain-related medication usage, and healthcare utilization.

All endpoints are summarized at baseline and follow-up visits up at 6, 12, and 18 months. Continuous variables are presented as means, standard deviations (SD), and 95% confidence intervals of the mean. Categorial variables are summarized as percentages, and where applicable, with exact 95% Clopper–Pearson confidence intervals. *T*-tests were used for statistical analysis.

The primary healthcare utilization (HCU) analyses focused on the proportion of patients using each therapy and therapy-associated costs, including physical therapy, chiropractic therapy, injection treatments, and ablation procedures. Costs of therapies and medication were imputed using data from the Optum Market Clarity multi-payer claims database from 2016 to 2022. Procedures were identified using Current Procedural Terminology (CPT), Healthcare Common Procedure Coding System (HCPCS), and ICD-10 Procedure Coding System (PCS) codes. The differences in average costs, along with their 95% CIs, were calculated using the BCA bootstrap method with 10,000 replications. All costs were reported in 2021 US dollars (US $).

Results

Patient Demographics

Of the 270 enrolled patients, 107 patients were randomized to receive optimized CMM therapy for 6 months. Twenty-six patients withdrew from the CMM arm (mostly citing lack of efficacy) before the primary endpoint analysis. A total of 81 patients reported for the primary endpoint follow-up at 6M. Seventy patients (86%) originally randomized to the CMM group elected to crossover to the SCS arm. Of the 70 patients, 66/70 received a trial system for 4–7 days and the 4 patients withdrew from the study before the trial implant. Eighty-eight percent (58/66) were considered trial responders (reported ≥50% pain relief). Ninety-five percent (55/58) of SCS trial responders received a permanent implant. Three patients withdrew consent and were not implanted. The demographic and performance analysis are based on 55 patients who reported for follow-up at 12M (6 months after SCS implant) - Figure 1. The mean age ± SD (n) of patients was 59.5 ± 11.8 (55) with females accounting for 47.3% (26/55) of the study population. Patients reported mean ± SD of 13.25 ± 12.76 for average years with pain. About 98.1% (52/53) and 92.0% (46/50) indicated they had received physical therapy and injections treatment before study enrollment. Percutaneous leads were implanted in 58.2% (32/55) of patients and 41.8% (23/55) received a paddle lead implant. Leads were implanted at spinal levels T6 5.5% (3/55), T7 43.6% (24/55), T8 43.6% (24/55), and T9 10.9% (6/55) with one patient each implanted at spinal levels T5 and T10- Table 1.

Pain, Function and Catastrophizing Scores

At the 6M primary endpoint analysis, 6.2% of the CMM group reported ≥50% pain relief with no statistical change in average pain score (p = 0.2282). Citing therapy dissatisfaction, 86% (70/81) of the CMM patients elected to cross over (Table S1). At the 12M follow-up, after 6 months of passive recharge burst therapy, patients pain scores reduced by an average of 60% from 7.9 ± 0.9 at the 6M visit to 3.1 ± 2.2 at the 12M visit, representing an average decrease of 4.9 ± 2.4 in pain score- (Figure 2 and Table S2). A ≥50% improvement was reported in 71.4% of the crossover patients at the 12M visit and sustained at the 18M visit. Substantial pain improvement (≥80% pain relief) was reported by 24.5% (12/49) of patients. About 22% of the patients did not meet the 12M 50% reduction but reported a ≥30% reduction in pain (when compared to the 6M /baseline data) which is considered MCID per the IMMPACT guidelines.[28]

Patients reported an insignificant ODI baseline change of 0.4 ± 13.5 after 6M of CMM (Baseline score-54.5 ± 13.7; 6M score – 54.0 ± 15.5, p = 0.8581). Post permanent implant, patients reported an average baseline improvement of 25.5 ± 20.4 representing a responder rate of 64.6% (31/48) at 12M, and 79.6% (39/49) at 18M for a ≥13-point minimal clinically important difference (MCID) improvement – Figure 3.[29] Additionally, 56.3% (27/48) of patients reported a ≥20 point substantial improvement in disability.

Pain-related catastrophizing related to lower back pain was assessed using the PCS questionnaire.[30] Patients originally reported nominal improvement at 6M from a baseline score of 26.3 ± 11.8 to a 6M score of 24.9 ± 13.2, p = 0.5588 – Figure 4. The scores improved at after 6 months of SCS therapy to 11.7 ± 11.0 (50), p <0.000001, which is

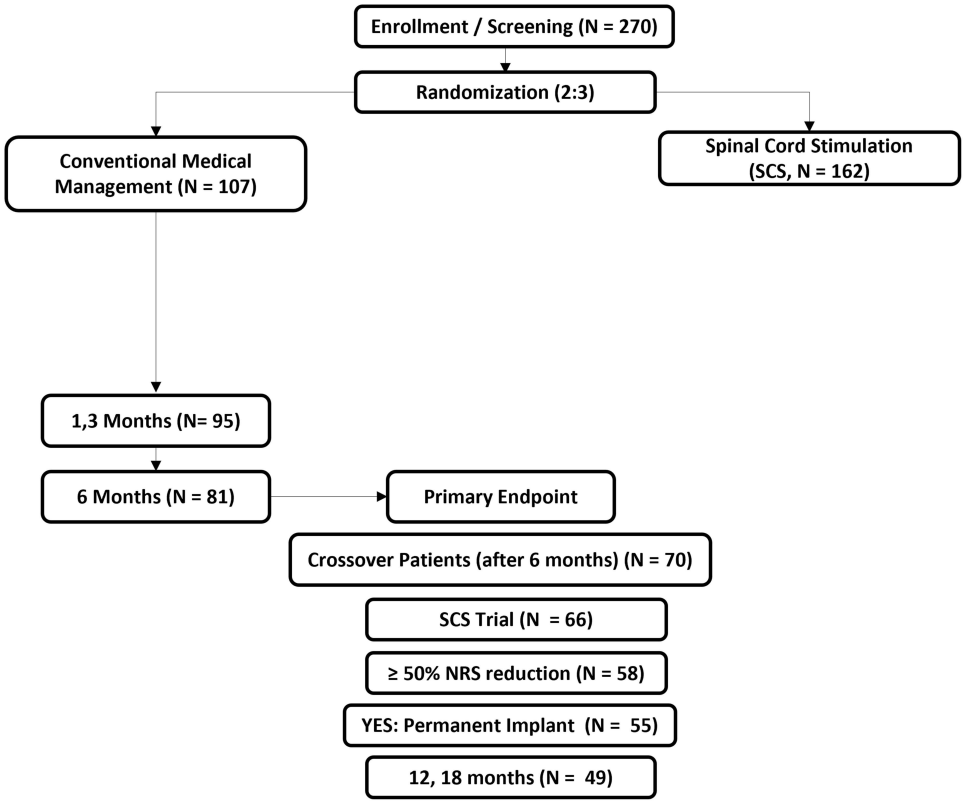

Figure 1 70 of CMM elected to cross over to SCS. 69 patients cross over within months 6–9 and 1 patient crossed over after 9 months. Of all 70 patients, 66 completed the trial period with 58 reporting ≥50% pain relief at 6M. 79% of the crossover patients elected received a permanent implant with 49 patients reporting at the 12M and 18M F/U.

below the average (13.9) presented as the population norm for a non-chronic pain population.[30] The responder rate for the patients post crossover was 77.1% (responder rate after CMM- 23.6%). All pain, disability and catastrophizing improvements were sustained through the 18M follow-up.

Table 1 Patient Baseline Information

	CMM (N=55)
Age (year)	
Mean ± SD (n)	59.5 ± 11.8 (55)
Median (Q1, Q3)	58.0 (50.0, 69.0)
Gender, n(%)	
Female	47.3% (26/55)
Male	52.7% (29/55)
Duration of patient's pain on patient's life (year)	
Mean ± SD (n)	13.25 ± 12.76 (55)
Median (Q1, Q3)	10.00 (4.00, 15.00)
Treatment for current condition	
Physical Therapy	94.5% (52/55)
Occupational Therapy	16.4% (9/55)
Massage Therapy	34.5% (19/55)
Chiropractic Therapy	52.7% (29/55)
Injection	83.6% (46/55)

(*Continued*)

Table 1 (Continued).

	CMM (N=55)
Acupuncture	18.2% (10/55)
Radiofrequency Ablation/Rhizotomy	49.1% (27/55)
Pain Numeric Rating Scale (NRS)	
Mean ± SD (n)	7.9 ± 0.9 (55)
Median (Q1, Q3)	8.0 (7.0, 8.0)
Duration of patient's pain on patient's life (year)	
Mean ± SD (n)	13.25 ± 12.76 (55)
Median (Q1, Q3)	10.00 (4.00, 15.00)
Pain Diagnosis*	
Chronic, non-specific, low back pain	58.2% (32/55)
Discogenic pain	5.5% (3/55)
Degenerative disc disease	34.5% (19/55)
Lumbar disc herniation	1.8% (1/55)
Lumbar facet arthropathy	25.5% (14/55)
Lumbar radiculopathy	45.5% (25/55)
Lumbar spinal stenosis	20.0% (11/55)
Lumbar spondylosis	52.7% (29/55)
Mechanical low back pain	1.8% (1/55)
Spondylolisthesis	1.8% (1/55)
Scoliosis	3.6% (2/55)
IPG Model	
3660	98.2% (54/55)
3662	1.8% (1/55)
3772	0.0% (0/55)
Lead Model	
3186 (Percutaneous)	58.2% (32/55)
3228 (Paddle)	41.8% (23/55)
Lead Level Implanted	
T5	1.8% (1/55)
T6	5.5% (3/55)
T7	43.6% (24/55)
T8	43.6% (24/55)
T9	10.9% (6/55)
T10	1.8% (1/55)

Notes: *Patients may have more than one diagnosis.

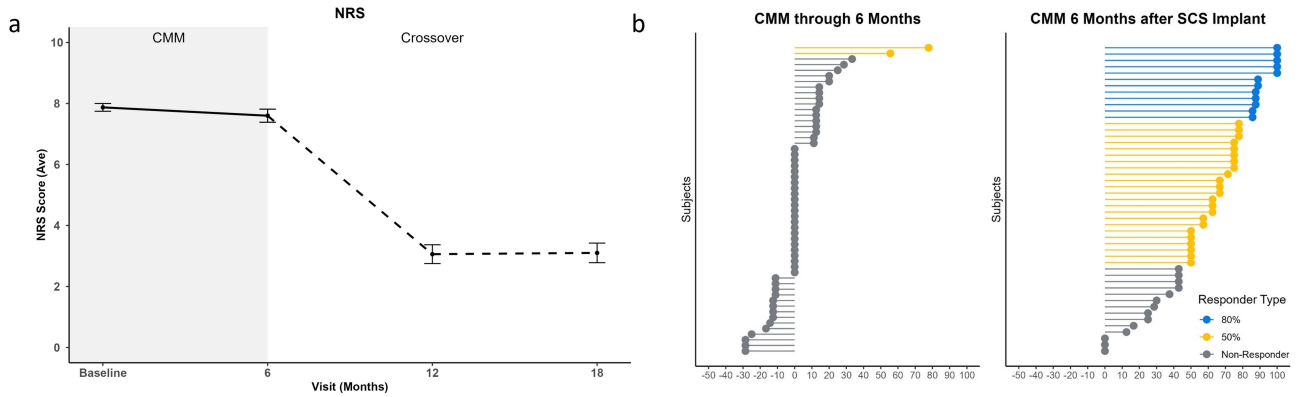

Figure 2 6.2% of CMM group reported ≥50% pain relief at 6M. 86% of the patients elected to cross over. At the 12M F/U, (after 6 months of passive recharge burst therapy **a**) Pain reduced by an average of 60% from 7.9 ± 0.9 to 3.1 ± 2.2, p <0.000001. **b**) 71.4% of crossover patients reported ≥50% pain relief. 24.5% of patients reported substantial pain improvement (≥80% pain relief).

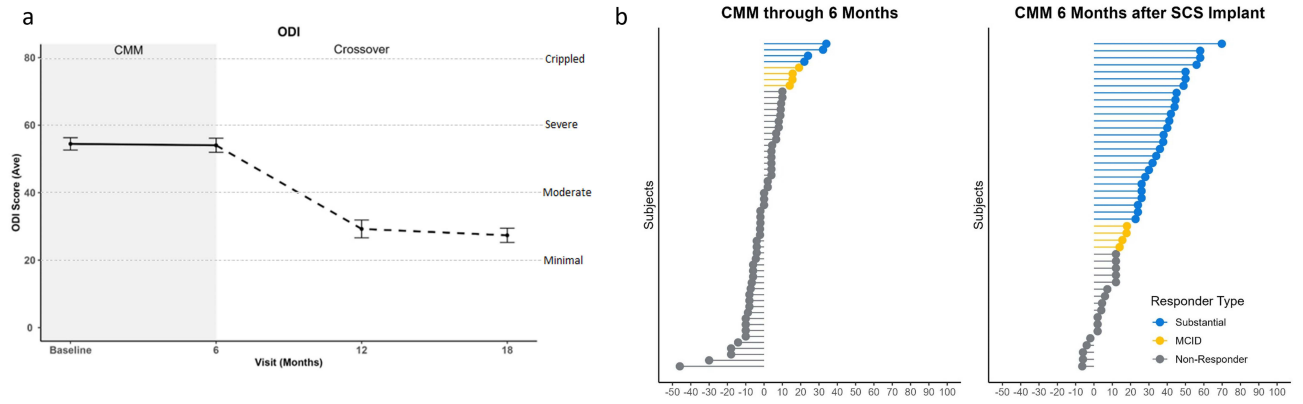

Figure 3 13.6% of CMM group reported ≥ 13pt decrease at 6M. 86% of the patients elected to cross over. (**a**) At the 12M F/U, ODI scores decreased by 25.5 ± 20.4–2x the MCID, p <0.000001. (**b**) 65% were considered responders with at least a 13-point improvement. 56% were substantial responders, defined as an ODI change of at least 20 points. All scores were sustained through 18 months ODI scores continued improving through 18 months, with 80% reporting ≥ 13pt decrease and 63% improving by at least 20 points.

Quality of Life

Most symptom domains (anxiety, depression, fatigue and sleep disturbance) on the PROMIS 29 questionnaire reported at least one category change from baseline mild-moderate to normal to mild symptoms reporting while pain interference improved from moderate-severe range to mild-moderate range after receiving SCS therapy. Patients previously reported mild-moderate symptoms for the physical (34.0 ± 4.5) and social functions (39.5 ± 6.2) with no change after 6M of CMM. These symptoms improved to mild (physical function- 41.1 ± 6.3) and normal (social function – 47.9 ± 9.1) after SCS therapy – Figure 5. All PROMIS-29 changes were statistically significant ($p < 0.05$, see Table S2).

Medication Usage

At baseline, 22 patients reported opioid usage. At the 6M follow-up, 20% (4/20) reported decreasing/discontinuing the use of opioids (3 reductions and 1 discontinuation). During the 12M and 18M follow-up, after 6 and 12 months of SCS implant, the Opioid Morphine Milligram Equivalent (MME) change mean ± SD from baseline (26.7 ± 18.4) was 8.6 ± 18.2 (12M average: 18.2 ± 19.4;18M average; 15.6 ± 20.5). Three (17%) patients reported opioid discontinuation with 5 (28%) patients reducing the opioid dosage. At the 18M visit, 6 (33%) patients had discontinued usage with 3/18 (17%) patients reporting decreased dosage. Reductions (6M of SCS vs 6M of CMM) were reported also for anti-convulsant (28.6% vs 16%), anti-depressant (7.1% vs 0%), and anti-anxiety medications (25.0% vs 0%).

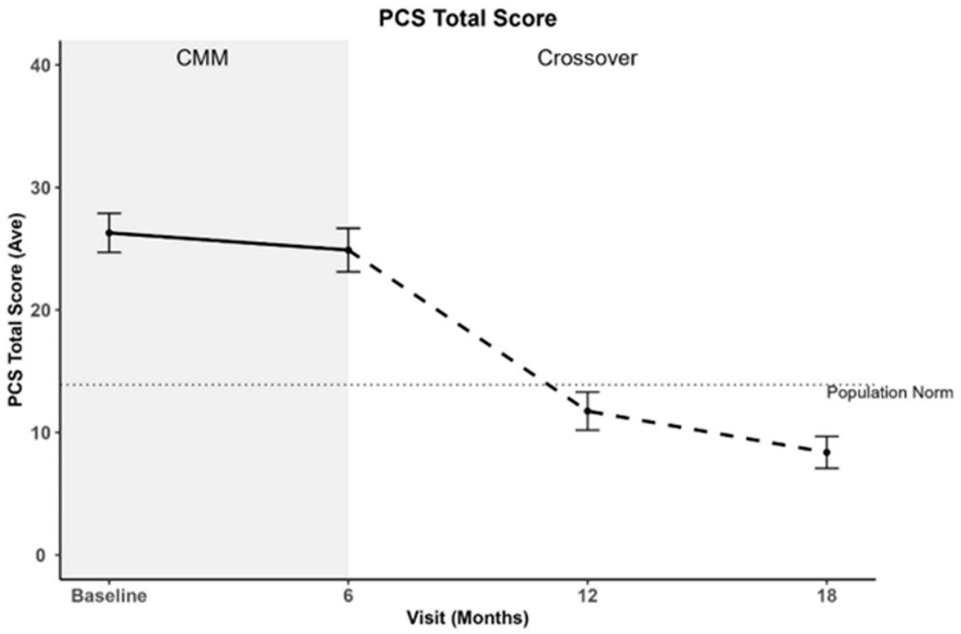

Figure 4 Patients in CMM group reported an average ± SD of 11.7 ± 11.0 at 12M, better than the population norm (13.85). Results improved before the 18M visit to an Average ± SD = 8.4 ± 9.0.

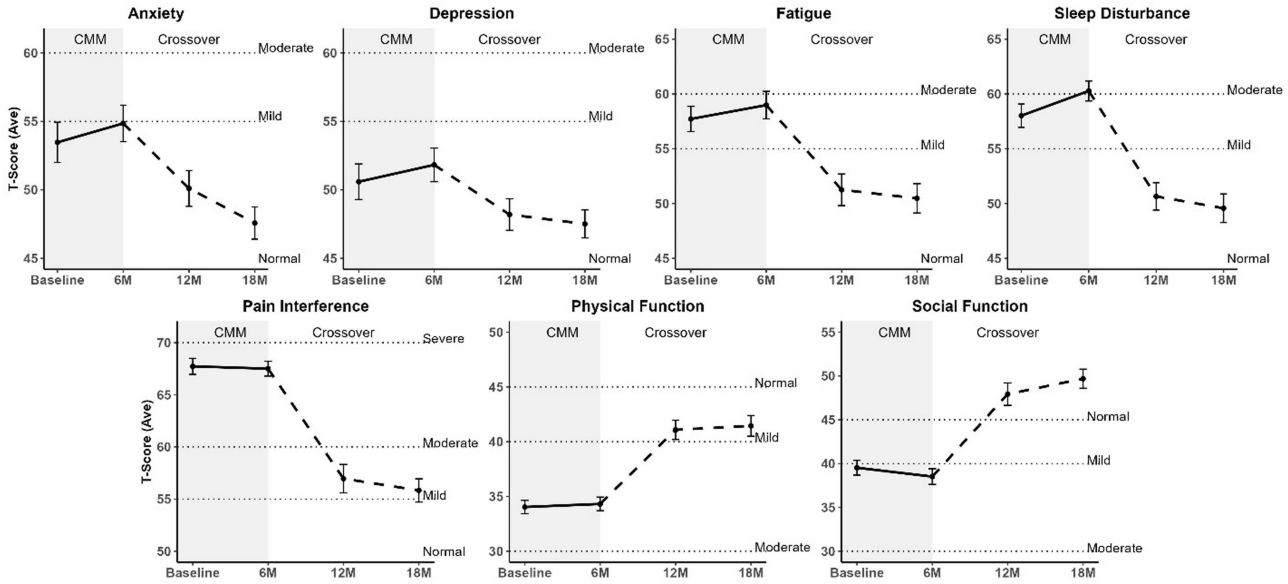

Figure 5 Patients in CMM group reported improvements in all PROMIS 29 domains when compared to their baseline and 6M scores. Patients reported normal scores for Anxiety, depression, Fatigue, Sleep disturbance and social function. Patients reported mild symptoms for pain interference and physical function.

Health Care Utilization

Patients' demand on healthcare resources related to other pain management options decreased. At baseline, patients reported using physical therapy (94.5%, 52/55), chiropractic therapy (52.7%, 29/55), massage therapy (34.5%, 19/55), acupuncture (18.2%, 10/55), injection therapy (83.6%, 46/55), and radiofrequency ablation/rhizotomy (49.1%, 27/55). In contrast, patients reported less physical therapy (6%, 3/50), chiropractic therapy (8%, 4/50), massage therapy (6%, 3/50), injection therapy (6%, 3/50), and radiofrequency ablation/rhizotomy (4%, 2/50) after SCS therapy. No patients received acupuncture in the 6 months after the SCS implant.

Table 2 Average Cost (2021 US $) per Patient During the 6-Month of CMM and 6 Months Post SCS

	During CMM (N = 50)	Post SCS Permanent Implant (N = 50)
Physical Therapy		
Mean (SD)	325 (957)	201 (723)
95% CI	[127–702]	[56–487]
Chiropractic Therapy		
Mean (SD)	50 (221)	46 (175)
95% CI	[11–144]	[11–115]
Injection Treatment		
Mean (SD)	978 (1484)	206 (986)
95% CI	[618–1442]	[26–721]
Ablation Procedure		
Mean (SD)	470 (1259)	157 (820)
95% CI	[157–836]	[0–473]
Total Cost		
Mean (SD)	1823 (1953)	609 (1957)
95% CI	[1326–2389]	[254–1566]

Using data from the Optum Market Clarity multi-payer claims database, patients spent an average of $1823 on healthcare resources under CMM therapy. After SCS implant, patients reported an average decrease of $1214 for an expenditure of $609 – Table 2. The cost of the SCS implant was not imputed for this analysis.

Safety Event Reporting

No events were reported by patients undergoing CMM therapy. Post SCS implant, 10 patients reported a device-related event. Four systems were surgically explanted (2x infection, 1x persistent pain at IPG, 1x damage to the IPG) – Table 3.

Table 3 Device Related Safety Events and Resolution Reported by the Cross Over Cohort

Event Description (Number of Patients)	AE Classification	Resolution
Infection (2)	SADE	System Explant
Seroma at the Lead Incision Site (1)	ADE	Apply pressure dressing
Infection (2)	ADE	Medication
Damage to the IPG or leads causing the system to fail deliver stimulation or causing the system to deliver overstimulation (1)	ADE	System Explant
	ADE	IPG reposition
Persistent Pain at The IPG Site (1)	ADE	System Explant
Lead Migration (2)	ADE	Lead Replacement
	ADE	Lead Replacement

Two patients had their leads surgically replaced and one patient required IPG repositioning. Two patients received medication treatments for infection and one patient had a seroma treated conventionally. No deaths were reported. All reported device related adverse events were known complications and followed expected frequencies. There were no explants for the loss of efficacy.

Discussion

Multiple studies previously indicated that SCS provided superior pain relief and improvements in quality of life when compared to CMM.[15,31–33]

Patients in the DISTINCT study reported severe pain and disability for over a decade, having failed numerous therapies. Common diagnoses included degenerative disc disease, spondylosis, spinal stenosis, lumbar radiculopathy and scoliosis that were not amenable to surgery. Upon enrollment, this group of patients were randomized to receive CMM therapy for an additional 6M under expert guidance. With very nominal changes in baseline pain score, disability, and quality of life (Table S1, 86% (70/81) of patients crossed over to the SCS arm after the 6M follow-up. None of the patients initially assigned to the SCS group chose to cross over to the CMM arm. After 6 months of passive recharge burst therapy, pain was reduced by an average of 60% with 71.4% of patients reporting at least a 50% reduction. Within 6 months of implant, patients reported a 25.5 pt decrease in ODI disability score, 2x the MCID score. The ODI responder rates were 65% for a 13-point improvement, and 56% for a substantial responder's rate with a ≥20 points improvement. Patients also reported decreased catastrophizing, opioid usage and improved quality of life (QoL) assessed with the PROMIS-29 questionnaire.

Participants in this crossover cohort experienced both treatments under similar conditions, which helps to control for confounding variables and reduces bias. Additionally, the results of economic models assessing the cost-effectiveness of spinal cord stimulation (SCS) are dependent on input parameters. By comparing each participant to themselves, crossover studies can help reduce variability due to individual differences, making it easier to detect treatment effect. These patients were randomized to CMM despite having received CMM in the past, as it has been previously reported that therapies such as physical therapy, medication, and injections work better in "expert centers, under expert guidance" than in the general primary care world.[34] Despite expert care, none of these patients reported improvements under CMM, and in some patients worsened on measured outcomes. Approximately 36% and 40% of the patients reported worsening pain and disability within 6 months of CMM, while 42% and 15% reported no change (Table S1). This highlights out an important detail about overusing CMM in chronic spine pain patients; at best it is ineffective, at worst it is costly, and the patient's underlying condition may continue to worsen. All 23 patients experiencing worsening conditions under CMM observed improvements after 6 months of SCS, with 9/14 patients reporting some improvement and 5 returning to baseline values.

This is particularly interesting because not only did patients in the CMM arm have worsening condition but CMM over multiple years accounts for increased expenditure without improved outcomes. DISTINCT crossover patients reported using less conventional therapy post implant resulting in an average cost savings of $1214. The cost of the SCS implant was not imputed for analysis.

Two patients reported serious adverse events (infections) requiring system explant, while eight others reported adverse events resolved with two explants, revisions, or more conservative measures. All infections occurred within 3 weeks and other adverse events requiring revisions occurred within 4 months of the implant.

This unique patient group received both CMM and SCS therapy. Our analysis provides robust evidence supporting the effectiveness of SCS in managing chronic pain, particularly when compared to conventional medical management. Patients reported improvements not just for pain, but for disability, function, and overall quality of life while observing a reduction in healthcare expenditure.

Integration of SCS therapy into the continuum of care for low back pain patients should be considered earlier for most patients who have no surgical remedy for their diagnosis.

Conclusion

SCS showed superiority over CMM in patients receiving both therapies, with sustained improvements in pain, disability, function and wellbeing, accompanied by decreased healthcare usage and expenditure post-implant. This detailed analysis on the "crossover" cohort, who after failing a decade or more of CMM, randomized to six more months of CMM (in expert centers) failed to improve in pain, functionality, or psychological measures, shows robust improvements in pain, functionality, psychological measures and quality of life. Further, it shows that chronic spinal patients failing to respond to CMM decline further in terms of functionality during futile attempts at CMM. Finally, SCS decreased the need for ongoing expensive CMM modalities in this crossover cohort.

Data Sharing Statement

All relevant data are included within this article or the Supplemental Material.

Ethical Consideration

This study was registered with ClinicalTrials.gov (NCT04479787). All patients were informed about on trial purpose and consent was obtained from all patients prior to enrollment. All sites/study documents received institutional review board (IRB- IRB-Copernicus Group (WCG® IRB), Partners Human Research Committee IRB – Boston, BRANY IRB, and RIH Research Protection Office IRB) approval prior to patient enrollment. The study is conducted in accordance with the US Code of Federal Regulations and the World Medical Association Declaration of Helsinki.

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Disclosure

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