PAIN MANAGEMENT
2025, VOL. 15, NO. 1, 27–36
https://doi.org/10.1080/17581869.2025.2449810

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RAPID COMMUNICATION

Real-world healthcare utilization and costs of peripheral nerve stimulation with a micro-IPG system

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ABSTRACT

Aim: To characterize real-world healthcare resource utilization (HCRU) and costs in adults with chronic pain of peripheral nerve origin treated with peripheral nerve stimulation (PNS) using the micro-implantable pulse generator (IPG).

Materials & Methods: This retrospective observational study (9/1/19–1/31/23) linked patients from the Nalu medical database to the OM1 Real-World Data Cloud (RWDC). Eligible patients received the micro-IPG implant for PNS, were identifiable in both databases, and had ≥ 12 months of RWDC pre/post-implantation claims data. Primary outcomes were all-cause HRCU and medical costs (12 months pre- and post-implantation); secondary outcomes were all-cause pharmacy costs, including opioids, over the same time.

Results: Patients ($N = 122$) had a higher mean (standard deviation; SD) number of outpatient visits pre-implantation (5.7 [5.4]) than post-implantation (4.9 [5.7]). Mean (SD) total medical costs were 50% lower, from $27,493 ($44,756) to $13,717 ($23,278). Median (first-third quartile [Q1-Q3]) medical costs were 57% lower, from $11,809 ($4,075–$31,788) to $5,094 ($1,815-$13,820). Mean (SD) pharmacy costs ($n = 77$) were higher post-implantation ($22,470 [$77,203]) than pre-implantation ($20,092 [$64,132]), while median (Q1-Q3) costs were lower (from $2,708 [$222 -11,882] to $2,122 [$50–9,370]). Post-implantation, the proportion of patients using opioids was 31.4% lower.

Conclusion: Patients with PNS using the micro-IPG had reduced HCRU, costs, and opioid use.

PLAIN LANGUAGE SUMMARY

Title: Healthcare Use and Costs with a Peripheral Nerve Stimulation Device for Chronic Pain

Summary: This study reviewed the medical records of 122 adults who received peripheral nerve stimulation (PNS), a treatment for chronic pain, to understand how PNS affects patient healthcare use and costs. Healthcare use and costs in the year before PNS were compared with the year after. The results showed that PNS helped reduce the number of doctor's visits and medical expenses. After starting PNS therapy, the average number of outpatient doctor's visits was lowered from 5.7 to 4.9 per year, and total medical costs were cut in half, from $27,493 to $13,717. In addition, the number of patients using opioids went down by 31.4%.

ARTICLE HISTORY

Received 25 October 2024
Accepted 23 December 2024

KEYWORDS

Administrative claims; analgesics; chronic pain; economic evaluation; electric stimulation; implantable neurostimulators; opioids; real-world evidence

1. Introduction

Chronic pain is persistent or recurring pain lasting ≥3 months [1]. According to the United States Centers for Disease Control and Prevention (CDC), 52 million people (approximately 1 in 5 US adults) have chronic pain [2]. Peripheral nerve pain is a particularly severe manifestation of chronic pain resulting from disease or nerve injury [3], estimated to affect one-third of US chronic pain patients [4]. Additionally, 7% of US adults, or > 17 million people, have high-impact or intractable chronic pain (ie, pain that interferes with work or life on most days or every day) [2,5]. Research confirms that chronic pain substantially impairs quality of life (QoL) [6], is associated with lost productivity (both absenteeism and presenteeism) [6–9], and contributes to high healthcare costs and resource utilization (HCRU) [9,10]. For example, the economic burden of managing peripheral neuropathic pain alone was estimated to be $348 billion in the US in 2022 [4].

Multiple factors contribute to these healthcare costs, and chronic pain treatment is complex, multidisciplinary, and changes for individual patients over time. Despite guidelines indicating that initial therapy should prioritize nonpharmacologic care, the pharmacotherapeutic management of chronic pain, using opioid and non-opioid medications, often in combination, remains a treatment mainstay [11]. Even with pharmacologic treatment, up to 50% of patients with chronic pain become drug-refractory or unable to tolerate the adverse effects of long-term pharmacotherapy, and continue to suffer

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/17581869.2025.2449810

Article highlights

- Peripheral nerve stimulation (PNS) is indicated to treat severe, intractable chronic pain of peripheral nerve origin; however, technical limitations of older PNS devices resulted in poor outcomes which limited the use of this therapy.
- Newer technology has overcome the limitations of the older PNS devices, resulting in higher pain reductions and responder rates, which has increased the clinical use of PNS.
- Newer PNS devices include a system that uses a micro-implantable pulse generator (micro-IPG) with advanced treatment programming and lead configurations, as well as magnetic resonance imaging compatibility, never before available for PNS.
- The micro-IPG's diminutive size (volume <1.5 cm^3) and external battery allow for minimally invasive implantation, reducing the risk of postoperative complications and eliminating the need for battery replacement surgeries.
- This retrospective observational study evaluated real-world healthcare resource utilization (HCRU) and costs before and after micro-IPG implantation in patients with chronic pain of peripheral nerve origin; in the 12 months following implantation, patients with had reduced HCRU, healthcare costs, and opioid use.
- These findings, along with recent results from the COMFORT PNS randomized controlled trial showing that the use of the micro-IPG for PNS was highly effective and safe in reducing chronic pain, suggest that PNS should be considered for use in patients with chronic pain of peripheral nerve origin.

with intractable pain [12–15]. In addition, long-term opioid use is no longer recommended due to the serious risk of overdose and dependency, as well as a lack of evidence showing long-term efficacy in chronic pain [16]. Specifically, the US Department of Health and Human Services (DHHS) and CDC recommend that these drugs only be prescribed when the benefits outweigh the risk, and then used for the shortest duration possible [11,16]. This consideration has led clinicians to prioritize management strategies that target structural, inflammatory, or disease-related causes of pain, with the goal of reducing the long-term need for analgesics [17].

Several chronic pain guidelines, including from the DHHS, recommend interventional nonpharmacologic pain treatments such as peripheral nerve stimulation (PNS) [11,18–20]. PNS involves the permanent surgical placement of an implantable pulse generator (IPG) attached to electrical leads that deliver current to specific neurons that innervate the area of pain [20–22]. PNS treatment provides centrally and peripherally mediated analgesic effects, and PNS has been shown to modulate both inflammatory and pain-inhibition pathways [23]. Historically, the primary drawbacks to PNS have included device-related technical limitations and physical discomfort or pain due to the implant itself (eg, pocket pain at the implantation site), reported by up to 64% of patients [24–26]. Technological advances have led to the development of the micro-IPG (Nalu Medical, Inc; Carlsbad CA), a device with advanced treatment programming and lead configurations previously only available in traditionally sized spinal cord stimulation (SCS) devices. The micro-IPG's programming includes stimulation patterns, not available in other PNS devices, that invoke multiple mechanisms of action to block pain signals from the brain [27,28]. The diminutive size of the micro-IPG (volume <1.5 cm^3) allows for a minimally invasive surgical implantation procedure, reducing the risk of postoperative complications, including pocket pain. Additionally, because the system's battery and control system are worn outside the body, the need is eliminated for battery replacement surgeries [28]. In 2019, the micro-IPG received US Food and Drug Administration (FDA) clearance for long-term or permanent implantation in patients with PNS experiencing severe, intractable chronic pain of peripheral nerve origin, and separately for SCS in patients with chronic, intractable pain of the trunk and/or limbs, including unilateral or bilateral pain [29]. The device is also compatible with magnetic resonance imaging (MRI), eliminating the need for explant surgeries in patients requiring MRIs [30].

Recently published results from the COMFORT randomized controlled trial (RCT) of the micro-IPG in patients with chronic, intractable peripheral neuralgia showed that PNS neurostimulation with the micro-IPG was consistently highly effective and safe compared to conventional medical management (CMM) alone. COMFORT results showed that 88% of micro-IPG-treated patients met the primary endpoint (≥50% reduction in patient-reported pain scores), with an average pain reduction of 70%, compared to approximately 3% of patients treated with CMM ($p < 0.001$) [31]. The COMFORT trial also confirmed the micro-IPG's strong safety profile, with no reports of pocket pain or serious adverse device events [31,32].

Given the clinical benefits of PNS using micro-IPG, there is the potential for reduced healthcare costs with this treatment. No data exist, however, describing real-world HCRU and costs for patients with chronic pain treated with PNS therapy using the micro-IPG device. As such, this descriptive analysis characterizes HCRU and healthcare costs among patients with chronic pain who received PNS using the micro-IPG.

2. Materials & methods

2.1. Study design, objectives, and data source

This retrospective observational cohort study of patients who received the micro-IPG for PNS was conducted on patients with relevant data between 1 September 2019 and 31 January 2023 (study identification period; Figure S1). The primary outcome objectives were to describe the baseline demographic and clinical characteristics of patients who received the micro-IPG; characterize all-cause HRCU; and estimate the cost of all-cause medical care in the 12 months prior to and following micro-IPG implantation. The secondary outcome objective was to characterize all-cause pharmacy costs and opioid use in the 12 months prior to and following implantation of the micro-IPG. The index date was set as the date of implant receipt, the baseline period comprised the period leading up to the index date, and the follow-up period comprised the 12 months following the index date. Note that the estimated costs of care reported are nominal and based on the available charge amounts provided with medical and pharmacy claims.

Data were generated by linking patients from the manufacturer's patient database to the OM1 Real-World Data Cloud (OM1 RWDC; OM1 Inc., Boston MA). Permission was obtained from OM1 Inc. to use the information in the OM1 RWDC for the purposes of this study. The manufacturer's database contains limited information provided voluntarily by the patient,

including name, age, indication for implant, and date of procedure, with information collected as part of an institutional review board (IRB)-approved patient registry (WCG IRB Solutions, Princeton, NJ). The OM1 RWDC is a multi-source dataset derived from linked, de-identified, individual-level healthcare claims and electronic medical records (EMR) data. EMR data include healthcare provider diagnoses, laboratory results, and medication/prescription history linked to patients' medical and pharmacy claims records, which contain billing and coding history for inpatient and outpatient encounters from acute care facilities, ambulatory medical and surgery centers, specialty clinics, and commercial and hospital pharmacies. The OM1 RWDC dataset was determined to be exempt from IRB approval (Advarra; Columbia, MD). To link patients from the manufacturer's database to OM1 RWDC, patients were tokenized (based on name, date of birth, and sex), de-identified, and then mapped to information existing in the OM1 RWDC.

2.2. Study population

Patients had to be ≥18 years of age, identifiable in both the manufacturer's database and the OM1 RWDC, implanted for PNS during the study identification period, and have ≥12 months of medical claims data in the OM1 RWDC prior to and following the index date. Patients were excluded if they had a diagnosis of stroke, myocardial infarction, or cancer/evidence of cancer treatment during the study period, or if they had evidence of implant revision or removal during follow-up. All patients who met these selection criteria were included in the primary objective cohort. The secondary objective cohort was restricted to patients who also had ≥12 months of pharmacy claims data pre- and post-index date in the OM1 RWDC.

2.3. Clinical and demographic characteristics and outcome measures

Index demographic characteristics included age, sex, race/ethnicity, geographic location, and insurance type. Baseline clinical characteristics included Charlson Comorbidity Index (CCI), select comorbidities (including major depressive disorder, bipolar disorder, and anxiety) defined based on ≥ 2 International Classification of Diseases diagnosis codes ≥30 days apart; body mass index (BMI); smoking status; and physical therapy use. Among patients with pharmacy claims data, receipt of short- or long-acting opioids (including buprenorphine, codeine, fentanyl, hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone, tapentadol, and tramadol) were described for both the baseline and follow-up periods.

All-cause HCRU encounters, along with medical and pharmacy costs were collected for the baseline and follow-up periods. The index date was excluded from HCRU and cost analyses, with the intention of avoiding misattributing implant or other day-of-implant costs to either baseline or follow-up outcomes. All-cause HCRU and medical cost components included outpatient, emergency room (ER), inpatient, and additional services. Additional services included laboratory, diagnostic, or imaging encounters; telehealth or virtual visits; home visits; or prescription/refill encounters. Pharmacy costs comprised all-cause pharmacy charges. All costs were nominal (i.e., reflected in the available charge amounts) and are reported as such.

2.4. Statistical analysis

Because of the descriptive nature of the study, no prespecified hypotheses were formally tested. Continuous variables were summarized using descriptive statistics, including means, standard deviations (SD); medians; and interquartile ranges (presented as first and third quartiles [Q1 and Q3]). Categorical variables were summarized using counts and percentages. Because this was preliminary and descriptive research, and since healthcare costs typically do not follow a normal distribution, both mean and median summary statistics were determined to be useful for this analysis [33]. Median per-patient costs reflect the typical patient experience [34], while mean per-patient costs can be used to estimate medical costs for the full patient group, which can be of value from the payer perspective [33]. Data were reported as recorded, with no imputation of missing data. All statistical analyses were performed using SAS (Cary, North Carolina, US) version 9.4.

3. Results

3.1. Baseline characteristics

Of 828 patients identified from the manufacturer's database and linked to the OM1 RWDC (Figure 1), 122 were eligible and included in the primary objective cohort, and 77 in the secondary objective cohort. The primary reasons for attrition were not having ≥12 months of medical claims data in the OM1 RWDC, either pre- or post-index (22.5% and 45.8% of patients, respectively). Fewer than 2% of patients were excluded for evidence of implant revision or removal.

For the primary objective cohort, the mean (SD) duration of the baseline and follow-up periods was 92.7 (16.4) and 18.4 (5.6) months. On the index date, mean patient age was 67.7 years (Table 1; all patients were ≥35 years of age); over one-half were female (58.2%); and a plurality were White (28.7%) and resided in the geographic South (41.8%). Medicare coverage was the most common insurance type (52.5%). Patients' mean (SD) CCI was 2.0 (1.8). Chronic pain was the most common comorbidity (62.3%), followed by anxiety disorders (26.2%) and depression (23.8%). Nearly one-half of patients showed baseline opioid use (45.5%).

The origin of peripheral nerve pain was captured for a subset of 53% of patients (65/122). In these patients, sites of pain origin included the lower back (35%), knee (26%), shoulder (12%), lower leg (11%), head/neck (9%), arm (3%), and trunk (3%). The nerves treated included axillary, brachial plexus, cluneal, femoral, genicular, intercostal, medial branch, median, occipital, peroneal, saphenous, sciatic, suprascapular, tibial, and trigeminal.

3.2. Healthcare resource utilization

Table 2 shows HCRU during the baseline and follow-up periods. The mean (SD) number of outpatient visits was

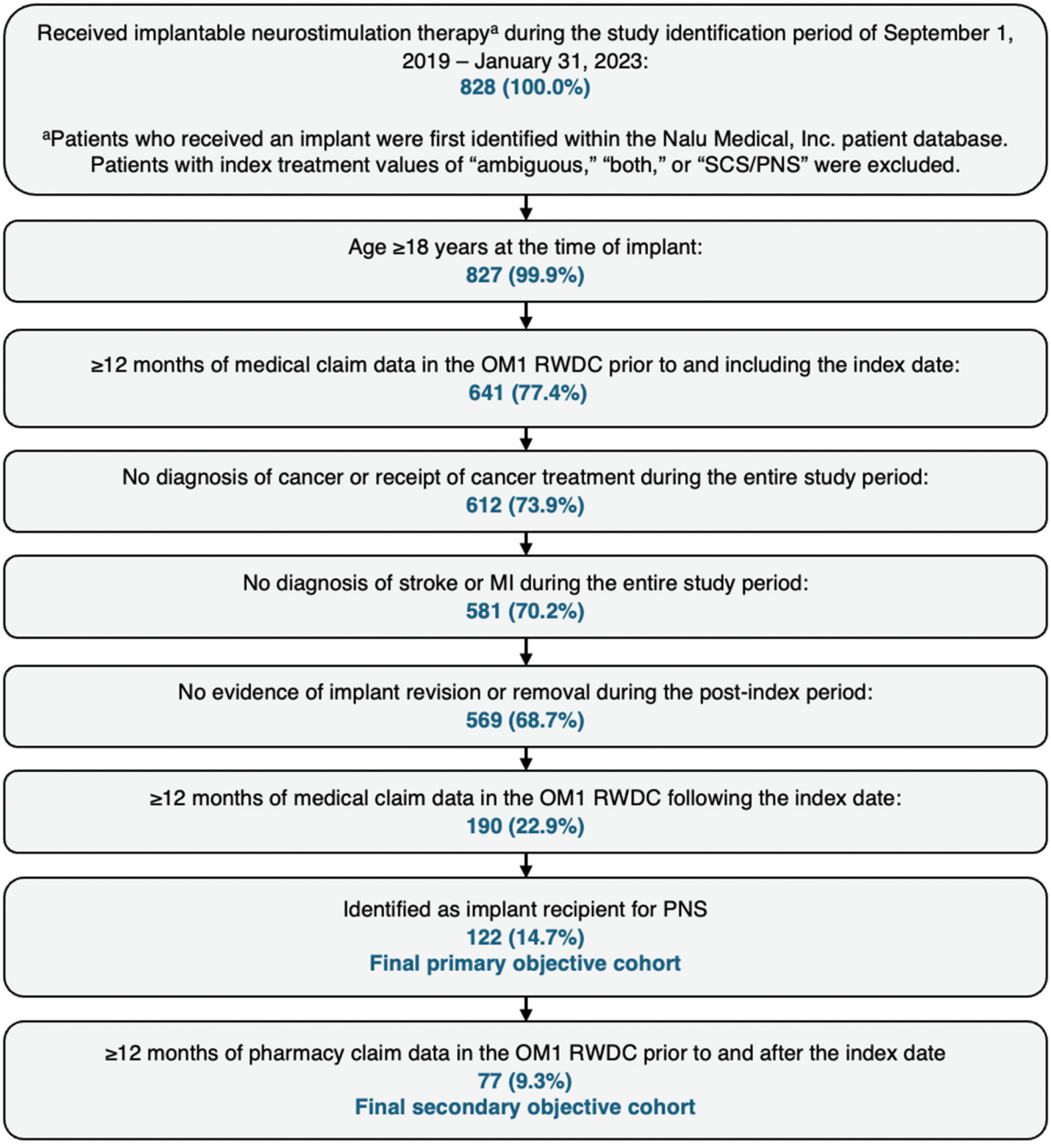

Figure 1. Patient attrition.

Abbreviations: MI = myocardial infarction; PNS = peripheral nerve stimulation; RWDC = Real-World Data Cloud; SCS = spinal cord stimulation.

numerically higher prior to implantation (5.7 [5.4]) than after (4.9 [5.7]), whereas the mean (SD) number of ER visits was unchanged (pre-implantation, 0.3 [0.8]; post-implantation, 0.3 [0.9]). The mean (SD) number of inpatient visits were also similar both before after implantation (0.1 [0.5] and 0.2 [0.6]).

3.3. Healthcare costs

Table 2 and Figure 2 show mean and median healthcare costs during the baseline and follow-up periods. Mean (SD) total medical costs lowered by 50%, from $27,493 ($44,756) prior to implantation, to $13,717 ($23,278) after implantation. The primary cost drivers, before and after implantation, were outpatient and additional services, both of which were numerically lower post-implantation. Mean (SD) outpatient service costs lowered 61% from $18,837 ($30,885) to $7,379 ($14,335) and additional services costs lowered 38% from $8,049 ($25,228) to $5,020 ($18,296).

Similarly, median (Q1-Q3) total medical costs were 57% lower, changing from $11,809 ($4,075–$31,788) prior to implantation to $5,094 ($1,815-$13,820) after implantation. With respect to component costs, median outpatient costs were 77% lower, changing from $5,841 ($1,064-$25,834) prior to implantation to $1,334 ($271-$5,737) after implantation, and additional services costs were 39% lower, changing from $1,333 ($158-$4,340) to $815 ($0-$3,492).

Table 1. Baseline demographic and clinical characteristics.

Characteristic		PNS ($n = 122$)
Age at index, years	Mean (SD)	67.7 (11.9)
	Median (Q1-Q3)	68.5 (60.0–76.0)
Age category at index, n (%)	18–34 years	0 (0.0)
	35–54 years	17 (13.9)
	55–64 years	25 (20.5)
	65–74 years	44 (36.1)
	75+ years	36 (29.5)
Sex, n (%)	Female	71 (58.2)
	Male	51 (41.8)
Race, n (%)	Asian	1 (0.8)
	Black or African American	2 (1.6)
	White	35 (28.7)
	Other	2 (1.6)
	Unknown	82 (67.2)
Ethnicity, n (%)	Hispanic or Latino	0 (0.0)
	Not Hispanic or Latino	37 (30.3)
	Unknown	85 (69.7)
Index year, n (%)	2019	1 (0.8)
	2020	10 (8.2)
	2021	72 (59.0)
	2022	39 (32.0)
Geographic region, n (%)	Northeast	12 (9.8)
	Midwest	18 (14.8)
	West	40 (32.8)
	South	51 (41.8)
	Unknown	1 (0.8)
Insurance coverage, n (%)	Commercial	27 (22.1)
	Medicare	64 (52.5)
	Medicaid	2 (1.6)
	Multiple	7 (5.7)
	Other/unknown	22 (18.0)
BMI, n (%)	Normal weight (18.5–24.9 kg/m^2)	1 (0.8)
	Overweight (25.0–29.9 kg/m^2)	3 (2.5)
	Obesity (≥30 kg/m^2)	1 (0.8)
	Unknown or not reported	117 (95.9)
Smoking status, n (%)	Current smoker	1 (0.8)
	Former smoker	2 (1.6)
	Never smoker	5 (4.1)
	Unknown or not reported	114 (93.4)
CCI	Mean (SD)	2.0 (1.8)
	Median (Q1-Q3)	2 (0–3)
	Min, max	0, 8
CCI category, n (%)	0–1	56 (45.9)
	2–3	46 (37.7)
	4–5	13 (10.7)
	6+	7 (5.7)
Comorbidities, n (%)	Chronic pain	76 (62.3)
	Anxiety disorders	32 (26.2)
	Major depressive disorder	29 (23.8)
	Fibromyalgia	11 (9.0)
	Bipolar disorder	4 (3.3)
Physical therapy, n (%)	Yes	15 (12.3)
	No	107 (87.7)
Short or long-acting opioids, n (%)[a]	N	77
	Yes	35 (45.5)
	No	42 (54.5)

[a]Assessed only among those with pharmacy claims data.
Abbreviations: CCI = Charlson Comorbidity Index; PNS = peripheral nerve stimulation; Q = quartile; SD = standard deviation.

3.4. Pharmacy costs and opioid use

Table 2 and Figure 2 show mean and median pharmacy costs during the baseline and follow-up periods for the secondary objective cohort. Mean pharmacy costs were numerically higher at follow-up than baseline, while median pharmacy costs were numerically lower at follow-up. Specifically, median (Q1-Q3) costs were 22% lower, changing from $2,708 ($222–11,882) to $2,122 ($50–9,370). As shown in Figure S2, the percentage of patients with opioid use was lower in the follow-up period, decreasing by 31.4% after implantation.

4. Discussion

This is the first descriptive analysis of real-world HCRU and costs for patients with chronic pain treated with PNS using the micro-IPG device. In the year following micro-IPG implantation, total mean and median healthcare costs decreased by more than 50% compared to the prior year (-$13,776 and -$6,715, respectively). This was driven primarily by lower outpatient and additional services costs. These reductions reflected corresponding median changes in HCRU; for example, the median number of outpatient visits decreased by 25% and the mean direction of change for total medical, outpatient, and additional services costs aligned with the corresponding medians. This suggests that healthcare costs likely decreased with micro-IPG used in patients with chronic peripheral nerve pain. Furthermore, the broad distribution of treated anatomic areas (from head to lower leg) indicates that the impact of PNS essentially applies, regardless of where in the body PNS is used. Median overall pharmacy costs (all drugs) were 22% lower from baseline to follow-up, while corresponding mean pharmacy costs rose by 12% from baseline to follow-up. Last, opioid use was 31% lower following micro-IPG implantation.

The current findings align with available prior research showing reductions in healthcare expenditures following PNS device implantation [35–37]. The one existing US economic analysis of PNS patients is a 2004 retrospective, single-center evaluation of costs and HCRU (1990–1998) in patients with a number of chronic neuropathic pain conditions who received SCS ($n = 168$), PNS ($n = 20$) or SCS-PNS ($n = 8$). Over a mean 3.1 years, neurostimulation for pain management resulted in HCRU reductions, including hospitalizations, ER and physician office visits, nerve blocks, radiologic imaging, and surgical procedures. This translated into a net annual savings of $30,221, with cost benefits accruing within 2 years of implantation [36]. International research also reports cost reductions with PNS therapies. An analysis (2013–2016) of PNS plus optimized medical management (OMM) vs OMM alone in 116 patients with back pain, conducted alongside the multicenter SubQStim RCT [38], found 9-month per-patient healthcare costs (excluding device implantation) of £1,082 for PNS-OMM and £1,238 for OMM alone. These changes were driven by fewer healthcare visits and reduced medication use [35]. A 2020 Dutch 3-month cost-utility analysis of PNS as add-on to SCS in 52 patients with chronic low back pain found a 61% cost reduction with SCS-PNS, with mean (SD) total costs of €1,813,864 (€109,782) for the SCS-PNS patient group vs €1,103,637 (€123,425) for SCS alone [37].

It is worth noting that health economics data for SCS show similar outcomes to PNS, further supporting the overall value of neuromodulation to treat chronic pain [15,39]. A 2023 US retrospective analysis of 97 patients with painful diabetic neuropathy treated with SCS found mean (SD) total healthcare cost reductions of 16% at 6 months, from $25,028 ($19,300)

Table 2. Healthcare resource utilization and costs in the 12-month baseline and 12-month follow-up periods.

		PNS ($n = 122$)	
Healthcare Resources	Statistic	Baseline	Follow-up
Outpatient visits	Mean (SD)	5.7 (5.4)	4.9 (5.7)
	Median (Q1-Q3)	4 (2–9)	3 (1–6)
Outpatient costs	Mean (SD)	$18,837 (30,885)	$7,379 (14,335)
	Median (Q1-Q3)	$5,841 (1,064–25,834)	$1,334 (271–5,737)
ER visits	Mean (SD)	0.3 (0.8)	0.3 (0.9)
	Median (Q1-Q3)	0 (0–0)	0 (0–0)
ER costs	Mean (SD)	$419 (1264)	$718 (2,172)
	Median (Q1-Q3)	$0 (0–0)	$0 (0–0)
Inpatient stays	Mean (SD)	0.1 (0.5)	0.2 (0.6)
	Median (Q1-Q3)	0 (0–0)	0 (0–0)
Inpatient costs	Mean (SD)	$188 (778)	$599 (2,612)
	Median (Q1-Q3)	$0 (0–0)	$0 (0–0)
Additional service[a] encounters	Mean (SD)	0.0 (0.0)	0.0 (0.0)
	Median (Q1-Q3)	0 (0–0)	0 (0–0)
Additional service[a] costs	Mean (SD)	$8,049 (25,228)	$5,020 (18,296)
	Median (Q1-Q3)	$1,333 (158–4,340)	$815 (0–3,492)
Total medical costs	Mean (SD)	$27,493 (44,756)	$13,717 (23,278)
	Median (Q1-Q3)	$11,809 (4,075–31,788)	$5,094 (1,815–13,820)
Pharmacy costs[b]	**N**	**n = 77**	
	Mean (SD)	$20,092 (64,132)	$22,470 (77,203)
	Median (Q1-Q3)	$2,708 (222–11,882)	$2,122 (50–9,370)

[a]Defined as services that were neither outpatient, ER, nor inpatient.
[b]Assessed only among those with pharmacy claims data.
Abbreviations: ER = emergency room; PNS = peripheral nerve stimulation; Q = quartile; SD = standard deviation.

pre-implantation to $20,970 ($21,351) ($p < 0.001$) post-implantation. This included decreased outpatient, inpatient, and medication costs. The authors projected that implant costs would be recouped approximately 3.5 years after implantation [15]. Additionally, a 2020 systematic review confirmed that SCS is economically favorable, with long-term reductions in healthcare expenditures [39].

Both the present study and prior research [40,41] show lower opioid use with PNS treatment for chronic pain. A 2014 prospective, multicenter, observational study evaluated medication usage before and for up to 6 months after PNS device implantation for chronic low back pain in 105 patients in Austria and Switzerland. At baseline, 76.2% of patients used oral or transdermal opioids; at 6 months, this decreased to 42.9% [41]. Given the ongoing, federal call for non-opioid solutions to chronic pain [11,16], as well as the high excess healthcare costs incurred by patients with chronic opioid use (estimated to range from $6,000 to $21,000 annually) [4,42–48], PNS therapies represent a clinically beneficial and financially viable option.

This real-world data analysis shows that patients with intractable, chronic peripheral nerve pain who received PNS with the micro-IPG had lower median healthcare costs and fewer outpatient visits in the year following treatment. These findings are relevant for physicians and payers, especially when considered alongside the substantial efficacy and safety benefits seen with micro-IPG used for PNS in the 2024 COMFORT RCT [31]. At 3, 6, and 12 months post-implantation, COMFORT patients who received PNS with the micro-IPG had responder rates of 83.7%, 88.1%, and 86.6%, respectively ($p < 0.001$ for all). Mean patient pain scores were reduced at the same timepoints by 67%, 70%, and 73% ($p < 0.001$ for all). At 6 months, 98% of PNS patients reported being very satisfied or satisfied with the micro-IPG, and 79% found the device very comfortable or comfortable. To date, there have been no unanticipated serious adverse device effects (ADEs), device- or procedure-related serious adverse events, or reports of pocket pain. All non-serious ADEs have resolved without sequelae. The COMFORT study is following patients for 36 months [31,32].

The COMFORT findings are consistent with prior micro-IPG research [28,49,50], including real-world data from 185 patients who received a micro-IPG SCS or PNS implant. In this 2022 analysis, 88.6% of patients achieved a ≥ 50% reduction in pain, 83.8%-88.6% showed improvement in various measures of QoL and overall function, and 80.5% showed high compliance with micro-IPG use [50]. Finally, the COMFORT-2 trial, a multicenter, prospective, open-label RCT, is currently underway to confirm the effectiveness and safety of PNS plus CMM versus CMM alone in the treatment of chronic, intractable pain [51].

5. Strengths and limitations

This study is an important addition to the limited research on HCRU and costs among patients using PNS therapies. While comparable in size to other evaluations of neurostimulation devices [15,35–37], this study had a relatively small sample size with no formal statistical testing implemented due to the relatively recent introduction of the micro-IPG to the market (2019) [29]. The small sample size was due primarily to the filtering of patients with fewer than 12 months of medical claims data following the index date. As such, outcomes are more sensitive to individual patient healthcare utilization and needs. Patient cost outliers may have affected the overall cost patterns observed, especially in cases where mean and median patterns diverged, warranting additional research. In addition, missing data made it difficult to characterize this population in reference to the general population of patients with severe intractable chronic pain of peripheral nerve origin. Despite these missing data, this study population represents a real-

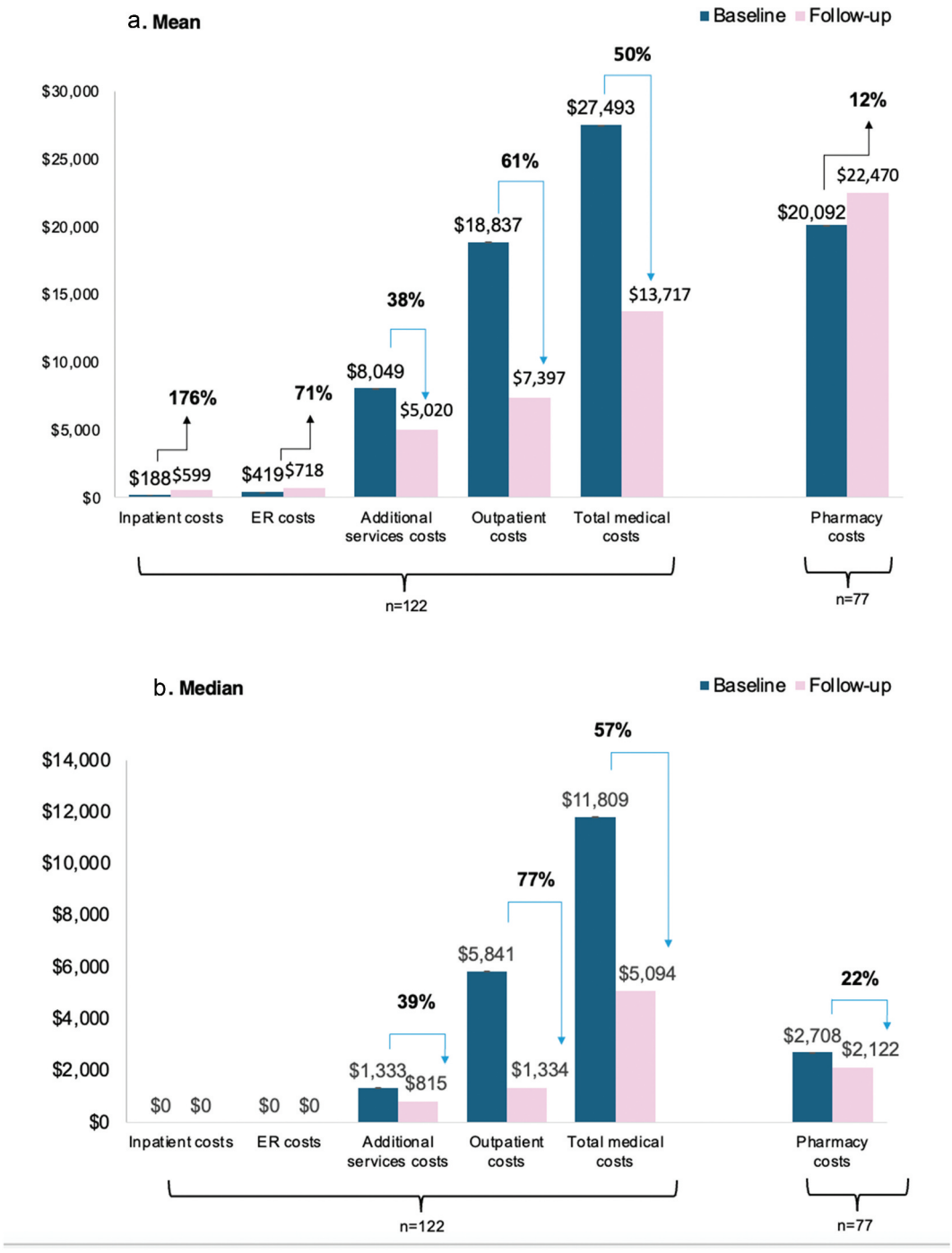

Figure 2. Mean (a) and median (b) healthcare resource costs in the 12-month baseline and 12-month follow-up periods for patients treated with micro-ipg for PNS.
Abbreviations: ER = emergency room; IPG = implantable pulse generator; PNS = peripheral nerve stimulation.

world cross-section of the US chronic pain population. Additionally, the study eligibility criteria were developed to be reflective of actual PNS patients. Patients with a cancer diagnosis were excluded, for example, because it is common for oncology patients to receive regular MRIs. Because patients with earlier PNS implants cannot receive MRIs, cancer centers do not currently treat patients with PNS. Missing data included limits on available race and ethnicity (missing for approximately two-thirds of patients) insurance type (unknown for approximately one-fifth of patients), and BMI and smoking status (unknown for ≥ 90%).

It is also not known whether or to what extent the COVID-19 pandemic influenced patient healthcare utilization and therefore the results of this study in 2020 and 2021. Finally, cost estimates were based on available nominal charge amounts from medical claims, not the actual amount paid, and the cost of implantation, day-of-implant costs, or revisions were not included in the analysis.

6. Conclusions

This study helps to address the lack of US evidence evaluating healthcare costs and resource utilization with PNS in patients with chronic pain of peripheral nerve origin. In the 12 months following PNS device implantation, patients treated with the micro-IPG had reduced HCRU, healthcare costs, and opioid use compared to conventional, baseline treatment alone. When considered alongside robust COMFORT RCT efficacy and safety data, this research shows that the use of the micro-IPG for PNS should be considered for use in patients with chronic pain of peripheral nerve origin.

Author contributions

All authors of this work affirm that they have made substantial contributions to the conception or design of the study, or to the acquisition, analysis, or interpretation of the data. Additionally, each author has actively participated in drafting the manuscript or critically reviewing it for significant intellectual content. All authors have given their final approval for the version to be published and agree to be accountable for all aspects of the work. Furthermore, they are committed to ensuring that any questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

HK was responsible for conceptualization, investigation, supervision, writing, reviewing, and editing. BT was responsible for conceptualization, data curation, formal analysis, investigation, methodology, resources, software, supervision, validation, visualization, writing, reviewing, and editing. PT was responsible for conceptualization, investigation, writing, reviewing, and editing. PM was responsible for conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing, reviewing, and editing. KS and BF were responsible for data curation, formal analysis, investigation, resources, software, validation, visualization, reviewing, and editing. CM was responsible for conceptualization, formal analysis, investigation, methodology, resources, software, validation, visualization, writing, reviewing, and editing.

Conflict of interest disclosures

HK serves as a consultant for and receives research support from Abbott, is a member of the Medical Advisory Board for Nervonik, and is a member of the Speaker Bureau for Averitas Pharma. BT has nothing to disclose. PS serves as a consultant for Medtronic, Saluda Medical, Nalu Medical, Inc., Biotronik, and AIS Healthcare; receives royalties from Averitas Pharma for the Qutenza® patch; holds stock in Nalu Medical, Inc., Saluda Medical, electroCore®, and SPR Therapeutics; and is an employee of electroCore®. PM is an employee of Nalu Medical, Inc. with stock options in the company. KS, and BF have nothing to disclose. CM is on salary and holds equity in OM1, Inc.

Funding

This study was funded by Nalu Medical, Inc. Nalu Medical funded the conduct of this study and made the decision to submit this manuscript for publication.

Ethical disclosure statement

Nalu Medical's database contains limited information provided voluntarily by the patient, including name, age, indication for implant, and date of procedure, with information collected as part of an institutional review board (IRB)-approved patient registry (WCG IRB Solutions, Princeton, NJ). The OM1 Real-World Data Cloud (OM1 RWDC; OM1 Inc., Boston MA) is a multi-source dataset derived from linked, de-identified, individual-level healthcare claims and electronic medical records data. The OM1 RWDC dataset was determined to be exempt from IRB approval (Advarra; Columbia, MD). To link patients from Nalu Medical's database to OM1 RWDC, patients were tokenized (based on name, date of birth, and sex), de-identified, and then mapped to information existing in the OM1 RWDC. Because patient data were de-identified, written informed consent was not sought.

Acknowledgments

The authors would like to thank Caitlin Rothermel, MPH of MedLitera for her writing and editorial assistance; Ms. Rothermel was compensated for her contributions to the work by Nalu Medical, Inc.

Data sharing statement

All data were de-identified. Data will not be shared, and the dataset is not publicly available.

Meeting presentation

Thapa B, Feldman B, Martin P, et al. Description of real-world healthcare resource utilization and costs among patients receiving long-term peripheral nerve stimulation therapy from a micro-IPG system. Presented at the American Society of Interventional Pain Physicians 26th Annual Meeting, April 4–6, 2024; Dallas, TX.

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