EFFECTIVENESS OF SPINAL CORD STIMULATION (SCS) IN REDUCING OPIOID CONSUMPTION IN PATIENTS WITH CHRONIC NON-CANCER PAIN

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ABSTRACT

Research Question: Do adults taking prescription opioids for chronic, non-cancer, pain have a reduction in opioid usage following spinal cord stimulator (SCS) implantation?

Background, significance, and rationale: Chronic pain is a prevalent and serious condition that impacts many. Few studies have examined how spinal cord stimulator implantation changes perceived pain and subsequent opioid consumption before and after SCS.

Materials and Methods: A retrospective study investigated the opioid consumption of 26 adults at three different times (1) Baseline (2) SCS implant date, and (3) 6 months post-SCS implant. Mean opioid consumption was calculated over the month prior and after to visit of (1), (2), and (3) to generate three separate 3-month averages. Opioid consumption was measured using Morphine Milligram Equivalents (MME). A series of paired-sample *t*-tests were conducted.

Results: Our participant population had a significant reduction of MMEs from baseline to 6-months post-SCS implantation ($p < .001$). While patients' MME decreased from SCS implant date ($M = 35.73$) to 6-months post-SCS implantation ($M = 24.64$), this difference was not significant but revealed a trend ($p = .11$).

Conclusions: In our study, patients using opioids for chronic non-cancer pain management, SCS modulated the perception of pain and noxious stimuli detections, resulting in a subsequent decrease in opioid consumption.

RESEARCH QUESTION

Do patients who have undergone permanent spinal cord stimulator implantation have a change in their daily Milligram Morphine Equivalents (MMEs) consumption? Our team predicts that following spinal cord stimulator implantation, a patients' opioid-class medication consumption will decrease. Furthermore, although quality measurements will not be assessed, we predict that the reduction of MMEs will be due to a reduction of perceived pain thus, improving the quality of life for each individual.

The following research objectives facilitate the achievement of this aim:

1) To identify patients with chronic, non-cancer, pain that are on a maintenance dose of opioid class medication and collect their demographic and dosage information.
2) To determine the timeline of each patients' chronic pain journey including their baseline MME and date of SCS implantation.
3) To assess the Texas Prescription Monitor Program (PMP) to evaluate the change in opioid class medication dosages throughout SCS implantation and 6-months post implant.
4) To calculate the change MME throughout each patients' baseline to implant date to 6 months post-implant.

CHAPTER 1

INTRODUCTION AND SIGNIFICANCE

Pain is an unpleasant but necessary communication from the body to the brain that an injury may have occurred. Although pain may be an uncomfortable experience, its role is vital in bridging the gap between the world around us to the body so one can adapt.

There are a multitude of stimuli that may activate pain receptors in the body and manifest as a painful sensation. Pain receptors, known as nociceptors, are present throughout the entire body and can respond to a plethora of external stimuli. Heat, pinch, pressure, and others all have the opportunity to trigger free nerve endings to send a nociceptive (painful) message up to the brain. Once that nociceptive receptor is triggered, a message is sent up to the brain via the major ascending pathway for pain, the spinothalamic tract.[1,2]

Acute pain and chronic pain are the two major classifications of pain. Acute pain is characterized as a brief response that serves a biological purpose to help the body. Acute pain is what is colloquially thought of as "pain" – i.e. stubbing a toe or getting a splinter. This type of pain is not only short in duration but is not accompanied by any long-term activation from the nociceptive receptor and subsequently not transmitted via the spinothalamic tract after the injury has occurred. Long-term stimulation of nociceptive stimuli can lead to a constant and unhelpful activation of the spinothalamic tract – even after that stimulus is removed. This unregulated pathway of the nociceptive receptor communicating to the spinothalamic tract, in the absence of

a stimuli, is a pathophysiological process where acute pain transitions to chronic pain.[3] Chronic pain is not helpful and is considered to be a state of disease.[4]

According to the most recent estimate from the Center for Disease Control and Prevention (CDC), an estimated 51.6 million adults in the United States alone, or 20.9% of the population, have chronic pain.[5] This estimate is even higher than the study prior in 2016 that estimated 20.4% of adults suffered from chronic pain.[5] Unsurprisingly, chronic pain has been cited not only as one of the most common reasons adults pursue medical care[6], but as a significant healthcare expense.[7] Chronic pain has also been shown to have linkage to numerous psychological conditions. Research has shown that depression and anxiety are higher in this population.[8,9] Additionally, patients with chronic pain have a reduced perceived quality of life[10] and an overall shorter life expectancy.[11]

The downstream consequences of chronic pain not only bleed over into other aspects of an individuals' health but impacts other aspects of their life as well. Patients with chronic pain on average have poorer work performance, miss more days from work, and perhaps accordingly, have increased unemployment rates compared to their coworkers.[12] The combination of increased unemployment rates and increased healthcare cost due to medical visits can lead to a more challenging financial situation and impact the financial stability and wellness of that person and their family. Patients with chronic pain have elevated rates of bankruptcy.[13]

Treating pain – weather chronic or acute – is a challenging task. Multiple studies have commented that pain is not only the number one reason a patient presents to the emergency department[14], but is one of the most challenging symptoms to assess and accurately treat.[15] Given the prevalence and importance of treating pain, it is vital that clinicians are accurately educated on the available treatment options, as well as recommend sustainable and effective ones. One important distinction to make is that treating acute and chronic pain are very different. Acute pain is short-lived, and treatment is aimed at finding the insulting injury and making sure that patient is comfortable. Opioid analgesics are a major tool at the disposal of clinicians in treating acute pain due to the accessibility and quick onset of symptomatic relief that opioid-class medications provide.[16] Despite the efficacy in the acute pain setting, opioids for chronic pain are less than ideal.

Opioid class medications are powerful analgesics that act through three receptors: mu, delta, and kappa. Opioid receptors are found systemically; however, have a high concentration throughout the brain and as such, play a key role in modulating behavior and mood.[17] Mu-opioid receptors are predominately implicated in analgesic properties.[18] Opioid receptors are unique since they are recruited and expressed in response to rewarding stimuli. Multiple studies have shown that when opioid medications are distributed to mice after a given behavior, that behavior occurs more.[19] Such behavior reinforcement occurs through the mesolimbic dopaminergic signaling system. Although the exact mechanism by which opioid-receptors "tap" into this dopamine circuity may be incompletely understood, what is known is that the two processes are undoubtably linked. This neurobiological framework is what contributes to the tolerance, reinforcement, and eventual addictive potential of opioids.

Opioid abuse and addiction can put patients at risk of overdose and subsequent death. Opioid-receptors have a high prevalence in the respiratory system. High concentrations can bind to lung parenchyma and stimulate respiratory depression and lead to apnea.[20] Although respiratory depression rates vary on the administration and type of opioid medication, the risk is always present given the location of opioid-receptors.

In 2017, two thirds of the overdose deaths that occurred in the United States were at the hands of an opioid-class medication.[21] Synthetic opioid deaths continues to rise at concerningly high rates. From 2017 to 2018, opioid deaths increased 10%.[22] Since the turn of the century, opioid overdose deaths have across the board increased 6-fold.[23] With the opioid epidemic claiming more lives each year and chronic pain becoming more common every day, the need for safe alternatives to opioid-analgesic becomes more crucial each day.

The earliest description of Spinal Cord Stimulation (SCS) was in 1967.[24] SCS is a form of long-term analgesic therapy that can and has been used as an alternative to prescription opioids for chronic pain.[25] SCS essentially is the percutaneous placement of electrodes within the epidural space of the spinal cord canal.[26] The electrodes within the canal extend superiorly and communicate with certain dorsal horns in the spinal column.

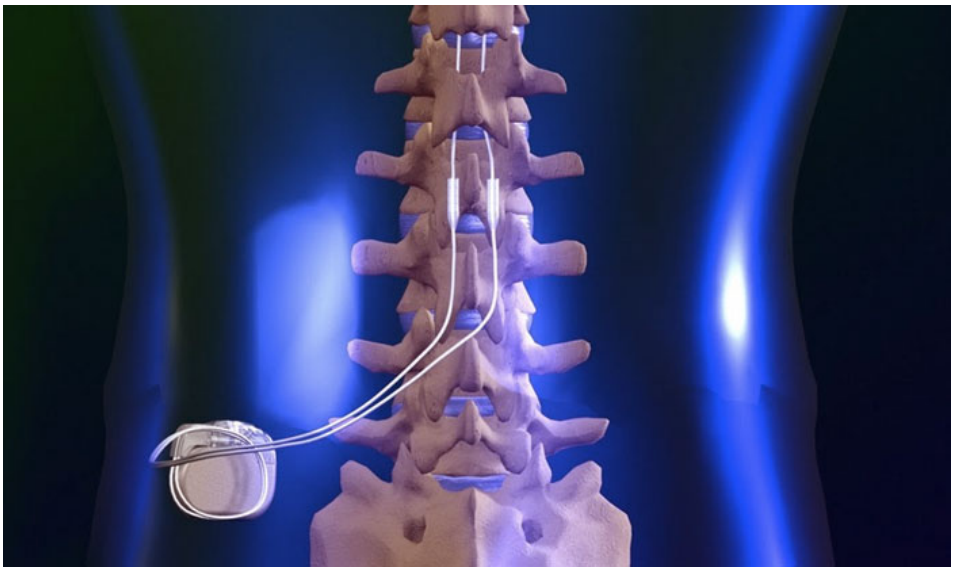

Figure 1: Artistic depiction of spinal cord stimulator electrodes extending up the dorsal column. Acquired from University Pain and Spine Center.[27] Image accessed on November 4, 2023.

Conventional SCS is theorized to modulate pain by reducing the perception of pain from the spinothalamic tract by stimulating an adjacent sensory pathway – the dorsal column. The dorsal column is the other major ascending sensory tract within the spinal cord responsible for detection of vibration and pressure.[28] Stimulation of the dorsal column fibers may alter the sensory reception of nociception and thereby, reduce overall pain in patients. This theory, the gate theory of pain, is the leading explanation by which SCS has improved patients' quality of life. The gate theory of pain suggests that the more non-painful (pressure or vibration) sensory information one detects, the more that nociceptive (painful) signal may be "drowned out".[29]

SCS utilizes the gate theory of pain to send constant non-painful, high-frequency waveforms via the dorsal column. This constant stimulation serves to minimize the perception of chronic pain via continuous stimulation of the spinothalamic tract – thus reducing pain.[30] Electrodes of the

SCS implants require virtually no daily care and permanent implants have shown to be effective for multiple years after implantation.[31]

Although SCS has strong efficacy and a clinical following within the pain medicine specialty for chronic pain management, research on whether patients' prescriptions change following the implantation of SCS is limited. After all, the goal of SCS as a therapy is to not only provide long-term relief for patients with chronic pain, but to reduce the number and dosage of opioid-class medications one takes each day. Opioid consumption is most commonly quantified into Morphine Milligram Equivalents (MME). MMEs convert opioid medications and their associated dosages into a standard unit – the milligram amount of morphine required to achieve the same therapeutic affect as the opioid of consumption.

The goal of this project is to expand upon the limited literature describing the change in opioid prescription consumption after spinal cord stimulator implantation. Our hypothesis is that SCS provides a meaningful analgesic effect to facilitate the reduction of MMEs over time in our participant population.

The significance of this project cannot be overstated as millions of people suffer from chronic pain every day. Currently, chronic pain is primarily treating with long-term opioid-class medications. Prescription opioids have shown to be effective; however, have a myriad of consequences. The risk for abuse and addiction are high and have contributed to the thousands of deaths by overdose each year. With rising rates of overdose deaths and increasing prevalence of chronic pain, new and effective chronic pain treatments need to be explored.

The introduction and significance chapter presents the background and context for this research project. The history, physical basis, and current adopted theory have been presented. The research aims and objective are defined, and the significance of the project has been addressed. The materials and methods will outline the research philosophy, design, and methodology. The results chapter will present the date in a clear and concise format. Finally, the discussion, future directions, and conclusion chapters will provide a framework for what impact the study has on the field and how to move forward.

CHAPTER 2

MATERIALS AND METHODS

This study aims and rationale are two-fold. 1) To provide data into how prescription opioid usage changes throughout a patient's SCS journey. 2) To expand our limited understanding in literature as to how SCS therapy can positively impact a patient and be an effective long-term therapy.

2.1. Subject Identification and Study Population

Our study population is from a private practice called the Advanced Pain Institute of Texas in Lewisville, Texas. Medical information from our participants were obtained through the medical charts of this private practice from October 2017 to March 2022. Every participant underwent an SCS implantation and were followed by the private pain practice throughout their implant and postoperative periods. Our inclusion criterion for this study included (1) Age above 18 years; (2) Not pregnant; (3) Having been on long-term opioid-class medication for maintenance of their chronic pain prior to spinal cord stimulator implant; (4) Underwent spinal cord stimulator implantation within the study periods; and (5) Must have failed other non-invasive treatment modalities for management of their chronic pain, and who are currently not candidates for spinal surgery.

A review of all patients at the Advanced Pain Institute of Texas who underwent spinal cord stimulator implantation between October 2017 and March 2022 were collected. Patients were included if they met all criteria for our study and those that did not, were excluded. The medical

records were accessed using password protected desktop and laptops. The subject population were stratified by age, gender, and degree of opioid use [i.e. high or low].

2.2. Study Design

Our study has a retrospective cohort study design. This study is chart-review in nature and as such was considered exempt from further reviewing by the institutional review board (IRB) at Texas Christian University. This study was approved by the office of research compliance at the university.

This chart review was conducted between the dates of June 2022 and October 2022 and was completed in three stages: subject identification, chart review, and statistical analysis. Participants were enrolled in the study if they were prescribed and currently taking opioid-class medication for chronic pain, underwent SCS within the study period, and met the remaining inclusion criteria for the study.

The gold standard for determining daily opioid consumption was utilized for this study – morphine milligram equivalents (MME).[32] MME were calculated at three points in time for each participant in the study:(1) Initial date of service [Baseline]; (2) Date of permanent SCS implantation; and (3) 6 months post permanent SCS implant. Each of these three points in time were determined using the preceding and flanking months – a 3 month-average of MME was calculated. 3-Month averages were used for each of the three periods in time to increase the data points and as a result, improve the accuracy of what each participants true MME was for that period of time.

For example, a participant in the study who first came to the Advanced Pain Institute of Texas in February 2019 would have their 3-month baseline that determine their MME for that period of time as an average from the months January 2019, February 2019, and March 2019. Consequently, if this same patient underwent spinal cord stimulator implantation during the month of July 2019, the months of June, July, and August of 2019 would be averaged to generate a three-month average for MME at date of SCS. Finally, this patient's final MME would be estimated six months after implant (January 2020) and as such December 2019, January 2020, and February 2020 would be averaged together for the MME value at time of 6-months postoperative.

An important note is that the interval between each participant's initial date of service to the pain practice [Baseline] and the actual date they underwent their SCS procedure was variable. Understandably, this range occurred due to participant's each unique scenario and the varying amount of time each decided that proceeding with SCS was the right decision for them and their chronic pain. Despite the variability between times (1) and (2), the interval between points (2) and (3) obviously were the same as they were all 6-months in length from implant date to postoperative.

The electronic medical record (EMR) was accessed to record and identify when each patient presented to the pain practice, underwent SCS, and 6-months postoperatively. To calculate the MME for each participant, our team accessed the Texas prescription monitoring program (PMP) – a state-mandated mechanism for evaluating how much and where each patient is getting their opioid-class medication from. The PMP is a program that collects and tracks prescription data on

all controlled substances (Schedule II, III, IV, and V). Not only are all opioids considered controlled substances, therefore all are regulated, but given their abusive nature, a majority of opioid are Schedule II or Schedule III (high schedule). The PMP has shown to be an effective program for clinicians to determine the number of scheduled medications their patients are on, in addition to tracking the trend in dosages. Furthermore, the PMP is monitored from the programs' perspective to identify both patients who have multiple prescribers and clinicians who prescribe the most.

2.3. Statistical Analysis

The approach to descriptive statistics in this study was the evaluate the change between our stated 3 points of time that were of interest to us for each participant: (1) Presentation to the Pain Practice; (2) SCS implant date; and (3) 6-months post permanent implant. A series of paired *t*-tests were performed for the analysis. A *t*-test from point (1) and point (3) as well as between points (2) and (3) were done. SPSS was the utilized statistical software for running such analyses.

CHAPTER 3

RESULTS

This chapter provides the results from the study discussed in the prior chapter. All statistical analyses were conducted by statistician Dr. Marcel Kerr in the SPSS statistical analysis software. The variables of interest for such analyses were daily morphine equivalents at two separate points in time.

3.1. Participant Characteristics and Selection

29 participants met the inclusion criteria and had zero exclusion criterion from the initial chart review. After further review, three participants underwent SCS implantation; however, never followed-up in clinic at the pain practice postoperatively after implant. Given the loss of follow-up for these three participants, the Texas PMP was not accessed and consequently a morphine milligram equivalent value for 6-months post SCS implant could not be identified and as a result these participants were intentionally left out of the analysis. 26 participants were included in the final analysis.

The 26 participants with chronic, non-cancer, pain has a mean age of 62.5 years with a standard deviation (SD) of 10.33 years at the time of SCS implantation. Participant ages ranged from 42 years of age to 80 years of age. Fifteen patients (58%) identified as female and eleven (42%) identified as male. Fourteen (54%) of participants did not have an ethnicity / race documented on

their medical record, ten (38%) of the participants had “Caucasian / white” designated on their medical records and two participants (8%) has “mixed race” designated.

3.2. Statistical Analysis Results

Paired *t*-tests were conducted for our study.

1) From initial date of presentation to the pain practice and 6-months postoperatively from SCS permeant implant
2) At date of SCS and 6-months postoperatively from SCS permanent implant

The first *t*-test from initial date of presentation to the pain practice and 6-months postoperatively from SCS permeant implant had a significant result with a ($p < .001$). The average baseline MME for our study population was 52.63 with a standard deviation of 45.08 MME. Standard error mean for this analysis was a moderate 8.84. The MME at 6-months postoperative was a much lower 24.64 MME with a standard deviation of 31.97 MME. Standard error mean for this analysis was 6.27. The effect difference was large with a value of ($d = 0.84$).

The second *t*-test from date of SCS and 6-months postoperatively from SCS permanent implant was not significantly difference; however, did result in a trend with a p value of ($p = 0.109$). The mean MME value at time of SCS implant date was 35.73 with a standard deviation of 52.78. Standard error mean for this analysis was 10.35. The effect difference was small with a value of ($d = 0.34$).

Our participants were stratified into several groups with subsequent analyses conducted to investigate the changes in MME. Participants were stratified on the basis of age, sex, and

baseline MME consumptions (high/low). Gender was stratified into male and female identifying. Age was stratified into above age 60 years and below 60 years of age. MME consumption of high and low were stratified on above 50 MME and below 50 MME. Due to the absence of direction on MME classification for high and low usage, industry standards were challenging to assess. We used the median age and median MME of our sample to split our participants for the remaining *t*-test analyses. Statistical significance was not yielded for the remaining analyses.

CHAPTER 4

DISCUSSION AND INNOVATION

This chapter will identify and interpret the results from chapter 3. Such interpretation will be followed with a discussion of how the results may impact the literature and what limitations our study has. Thereafter, recommendations for future research will be discussed and conclusions will be drawn.

4.1. Investigation and Key Findings

1) Patients had a significant reduction in MME from presentation to the pain practice compared to 6-months post spinal cord stimulator implant ($p < .001$).

2) Although there was not a statistically significant change in MME from SCS implant date to 6-months postoperatively, there was a trend ($p = .11$).

3) The results suggest that spinal cord stimulation meaningfully reduces a patients' pain and therefore, may require less daily opioid-class medication to stabilize their pain.

4.2. Interpretation of Results

Our study analyzed how a patient's MMEs (opioid consumption) changed throughout the time from when the patient presented to the pain practice to their implant date and through postoperatively (6-months after SCS). Our hypothesis was correct, and the results support this, that opioid consumption would reduce following spinal cord stimulator implantation.

The average morphine equivalents for our participants group (26 individuals) went down from their baseline compared to their SCS implant date to their 6-month post implant date (52.63 to 35.73 to 24.64, respectively). The subsequent reduction from baseline to 6-months post-op was a significant finding ($p < .001$). Conversely, from SCS implant date to 6-months after implant, the results were not significant ($p = .11$). A 50% overall reduction in MME was seen in our participant pool from baseline to 6-months post.

Amongst the 26 participants in our study, over three-quarters (77%) experienced an overall decrease in their opioid consumption from baseline to 6-months post implantation (n = 20). Of this group, half (n=10), completely eliminated the amount of opioid-class medication they took on a daily basis. The remaining 6 participants had differing results. Half, (n=3), had no change at all in their MME throughout the study period. The other half, (n=3), experienced an interesting increase in their morphine equivalents.

The interval between implant date to 6-months post-op, did not change – that is to say that every patient had an interval of exactly 6 months. Conversely, the interval was not this way for the baseline (initial presentation to pain practice) to SCS implant date. Each participant had a unique conversation with their physician to decide if the treatment was right for them and if so, what timeline made sense given their story. 556.7 days was the mean for the amount of time it took a participant from presentation to the pain practice to undergo SCS. The standard deviation for this was 313.73 days with a range of 4 days to 1093 days. Each individual gets to drive their own

care. That is to say that some patients decided that SCS was the intervention they wanted to go to immediately, and others may have failed other less invasive treatment options before attempting SCS.

Our findings are similar to prior literature that found a trend[33] or a significant change in opioid consumption after SCS implant.[34–36] Our study did not continue past 6-months after implant and as such, it is reasonable to say that this reduction may or may not persist for the years to come.. Some studies have shown SCS reducing MME both at the 6-month and 2-year follow-up periods[37,38] while others founds different results. Kumar et. al. revealed a decrease of morphine equivalents at the 6-month follow up for the SCS group, compared to the conservative medical management group, but no difference in the 2 year follow-up area.[39]

SCS can be delivered at differing volume and frequencies which is important to mention. As such, this may influence the degree by which MME may be reduced. Kapural and colleagues described that HF10 therapy (SCS at 10kHz) as an approach to SCS reduced morphine equivalents more than the traditional model of SCS.[40] Our results contribute to the ever-growing body of literature that describes evidence-based medical approachs for dealing with chronic pain. Furthermore, this adds to the literature supporting spinal cord stimulation as a safe and effective invasive option for patients who choose to pursue this option. To our team's knowledge, this novel study is the first to measure and track a patient's MME through their chronic pain journey – through presentation to clinic then through SCS date and finally through the postoperative period. Additionally, the 3-month average approach was unique and unlike anything described in the literature.

While the majority (77%) of participants observed a decline in MME following the implantation of a spinal cord stimulator, a myriad of factors unrelated to the SCS implant itself could account for this reduction. One potential explanation is that participants engaged in discussions with their physicians about tapering off their opioid prescriptions. Considering the adverse effects associated with prolonged opioid use, it is plausible that physicians advised a reduction in morphine equivalents, leading to fewer opioid-class medications being prescribed or lower dosages, resulting in a gradual decrease in morphine equivalents over time. Another plausible explanation is that participants received fewer prescriptions for opioid-class medications both around the time of the implant and during the postoperative period. This approach may have been adopted to evaluate their subjective pain experience without the modifying effects of opioids.

4.3. Limitations

Due to our study's design and structure, there are several limitations we faced. First, a sample size of 26 participants is quite small. Given the limited population during the study dates, the power of the study as a result is quite low. Secondly, the population of our participants was homogenous. Many of the participants did not designate an ethnicity on their medical record and as a result, the ethnicity diversity of our study is limited. Of the participants that did select an ethnicity, almost all identified as white. Third, our study measured the amount of prescribed opioid-class medication, not the amount taken – the Texas PMP that was used to access this information only provides this.

Despite our study findings that a change in MME was found after SCS, what remains unknown is if our participant received opioid-class medications from other avenue (i.e. street drugs, old medications, etc.). Fourth, there was an inherent variability between initial presentation to the pain practice and their SCS date – as each participants decided at differing times that SCS was the correct treatment decision for them and their chronic pain journey. Fifth, the unique 3-month average of MMEs that our study used for descriptive statistics may overestimate or underestimate MMEs for that period of time if one of the months within each period was particularly higher or lower than the other two.

CHAPTER 5

FINAL ANALYSIS

This chapter features the key findings of this project as well as the research aims and questions that have been asked. The impact and lasting impression from this study will also be discussed. Finally, we will discuss future directions and conclude.

5.1. Conclusions

Opioid consumption following spinal cord stimulator implantation remains incompletely understood. The association by which these factors influence each other need to be studied for future guidance. Our results build to the limited literature on how SCS not only may be a safe and effective long-term therapy but may suggest MME can decrease following such a procedure. The opioid epidemic in the United States and the world is not going away and as such, more research needed to be done to improve the quality of life for our patients who are suffering from opioid-related consequences and deaths.

5.2. Future Directions

Given the retrospective study design and small sample size (n = 26) of our project, more research should be conducted on this topic. Future studies should replicate this study using larger sample sizes and incorporate pain scales (1-10) throughout their SCS recovery period to quantify the perception of pain in addition to the reduction of MME. Additionally, more research into the long-term efficacy of SCS should be explored. While SCS remains a solid option for chronic

pain, studies describing their long-term efficacy have yet to be explored given the modernity of the technology.

COMPLIANCE

This study has IRB approval through Texas Christian University. The chart review nature of our study rendered our study exempt from IACUC and all required CITI trainings were completed prior the beginning of the study.

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VITA

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