Observational Study

Cost-Utility and Cost-Effectiveness Analysis of Spinal Cord Stimulation for Chronic Refractory Pain in the Context of Developing Country

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Background: Spinal cord stimulation (SCS) is an effective treatment for chronic refractory pain. The evidence of pain reduction, improvement of function, quality of life, and cost-effectiveness are strong in developed countries. Nevertheless, there is still a lack of economic studies of SCS in the context of low- and middle-income countries.

Objectives: To evaluate the cost-effectiveness and cost-utility of additional SCS to conventional management (CMM) in patients with chronic refractory pain in Thailand.

Study Design: Prospective observational study.

Setting: The pain clinic at Siriraj Hospital, a tertiary care center in Thailand.

Methods: This study recruited patients undergoing SCS implants due to refractory pain to CMM from varieties of conditions and followed up to 36 months. The clinical outcomes, quality of life, and costs of treatment were collected before and after SCS implantation. A decision tree and Markov model were developed to estimate the total lifetime costs and health benefits of SCS using a societal perspective. The results were presented as an incremental cost-utility ratio (ICUR) in 2021 Thai Baht (THB) per quality-adjusted life year (QALY) gained and an incremental cost-effective ratio (ICER) in 2021 THB per numeric rating pain score (NRS) reduction.

Results: Twenty-nine patients who underwent SCS implantation reported pain intensity and increased utility at every point in time. Compared to pre-implantation, the QALY gained in both rechargeable and non-rechargeable SCS was 2.13 QALYs. The economic analysis showed the ICUR in the rechargeable and non-rechargeable SCS + CMM group was 660,106.96, and 620,120.59 THB/QALY gained, respectively, which was higher than Thais' willingness-to-pay (WTP) threshold at 160,000 THB/QALY gained. Pain score reduction was 2.49/10 at the 3-year point, and the ICER was 496,932.08 and 337,341.77 THB/NRS reduction for rechargeable and non-rechargeable SCS, respectively.

Limitations: As this is a single-center prospective cohort study, the results might be subject to selection bias and may not truly represent all patients from a developing country. The cost-effectiveness results should also be carefully interpreted for generalizability.

Conclusion: Spinal cord stimulation is effective in pain control and improves the quality of life for patients with chronic refractory pain. However, the ICUR of SCS is above the WTP, leading to the interpretation that SCS is still not a cost-effective treatment in the current context in Thailand.

Key words: Spinal cord stimulation, effectiveness, quality-adjusted life year, incremental cost-utility ratios, cost-utility analysis, cost-effectiveness analysis, willingness to pay, developing country

Registration: This study was registered at thaiclinicaltrials.gov (Identifier number: TCTR20210923001).

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Chronic pain affects one fifth of the adult population globally and impacts quality of life, productivity (1-3), and economy (4-5). Moreover, a portion of these patients suffers from chronic refractory pain, a condition that is recalcitrant to conventional treatments or even surgery, from a variety of conditions such as failed back surgery syndrome or complex regional pain syndrome. Chronic refractory pain from these conditions not only brings suffering to millions of people but also leads to a detrimental quality of life. For example, it is estimated that failed back surgery syndrome affects 30% of patients undergoing lumbar spinal surgery, with an annual incidence of 33 per 100,000 per year and an overall prevalence of 610 per 100,000 of the general population (5-6). The overall prevalence of complex regional pain syndrome is 20-90 per 100,000, with an annual incidence of 5-45 per 100,000 per year (7). More importantly, the quality of life, measured by EQ-5D-5L (range: 0-1), is as low as 0.15 (8) in patients with failed back surgery syndrome and 0.2-0.3 (9) in complex regional pain syndrome, whereas the utility level is at 0.87 (10) in average Americans and 0.83 in Thais (11).

Spinal cord stimulation (SCS) is a neuromodulative treatment that is indicated for chronic neuropathic or ischemic pain in patients who had attended fully conventional treatment with limited success (12-13). The evidence of the effectiveness of SCS is strong not only for pain reduction but also for improving function and quality of life in chronic refractory pain from failed back surgery syndrome, complex regional pain syndrome, peripheral vascular diseases, and refractory angina (12-13). Moreover, even if the cost of the treatment is initially high, long-term economic studies in North America and Europe (14-17) show the treatment is cost-effective in the long term when compared to conventional treatment (15-16) or surgery (17).

Even if the evidence of the effectiveness (5,17) and cost-utility (15-17) of SCS for refractory pain from aforementioned conditions are clear in developed countries (5,14-17), a systematic study in the context of low- and middle-income countries including Thailand has not been elucidated. The lack of data and research from these parts of the world poses an important barrier to improving pain management (18). In Thailand, where the cost of labor, Gross National Income, and willingness-to-pay (WTP) are lower (19), the results of the cost-utility study are still unknown but must be different.

We hypothesized that SCS is still cost-effective in Thailand. The primary goal of this study is to evaluate the cost-utility of additional SCS to conventional medical management (SCS + CMM) compared with conventional medical management alone before the SCS implantation (CMM) in chronic refractory pain patients in Thailand by comparing the incremental cost-utility ratio (ICUR) with Thai's WTP. The secondary goal of this study is to evaluate the effectiveness of SCS for patients suffering from refractory pain by pain intensity and health-related quality of life. Lastly, the cost-effectiveness ratio (ICER) of additional SCS to conventional medical management is calculated by additional cost per numeric rating pain score (NRS) reduction.

Methods

Study Population

This prospective observational study recruited patients undergoing SCS implants due to refractory pain at Siriraj Hospital between April 2015 and March 2021, then followed up to December 2021. All patients suffered from refractory pain, despite appropriate conventional treatment, including pain medication, physical therapy, other pain interventions, or surgery. The causes of pain were from a variety of conditions, including failed back surgery syndrome, inoperable peripheral vascular diseases, complex regional pain syndrome, and neuropathic pain (Table 1). The baseline cost, clinical data, and utility before SCS implantation were collected. Subsequently, the patients who underwent a successful SCS trial and subsequent implantation were followed up for at least 3 years to collect the aforementioned data after the implantation.

Sample Size Calculation and Ethics Approval

Based on the utility from the study by Kumar et al (16), the average utility for adding SCS to CMM was 0.391 (SD 0.070), and the average utility in CMM alone was 0.480 (SD 0.080). Two independent means were compared with the ratio of 1:1, a significance level of 0.01, and a power of 90%; the sample size was 22 patients per group. Sample size and power calculation by nQuery Advisor version 5.0 (Statistical Solutions Ltd. Cork, Ireland). The study was approved by the Institutional Review Board of Siriraj Hospital (certificate of approval: Si 441/2019).

Procedure

Patients were recruited and screened for the SCS trial by the consensus of pain physicians. They were followed up 3-10 days after the trial to determine the results of the trials. SCS implantation was considered if they reported at least a 50% reduction in pain intensity from baseline during the trial period. If the SCS implantation was not offered, the treatment continued with conventional treatments.

Data Collection

We collected patients' demographic and initial clinical data during the outpatient visit at the enrollment. All patients were asked to answer the questionnaires before SCS implantation and after at the 1st, 3rd, 6th, and 12th month and every year during follow-up visits.

The demographic data consists of age, gender, work status, education, and salary. Clinical data consists of diagnosis, pain locations, comorbidities, duration, current medication, previous treatment, and pain intensity. The comparison of categorical data was done by chi-square and normal-distributed continuous data by t-test.

Health Related Quality of Life (HRQoL) Data

Patients' quality of life worldwide was evaluated by EQ-5D-5L health questionnaires (20) (Thai version) (11). The data obtained from the questionnaire was applied to the calculation of the utility score by using a program, which was developed by the Health Intervention and Technology Assessment Program (HITAP) that has been validated specifically for Thai people. The utility score ranges from 0 to 1, with 0 meaning death and 1 meaning complete health.

Resources Consumption and Costs

The resource consumption was collected using a societal perspective. The costs were collected from 1 year before the implantation as the cost for CMM only and at an approximately 3-year period after SCS implantation. Data retrieved included direct medical resource consumption and costs such as standard care, complication care, medication, laboratory analyses, trial and implantation of SCS, and inpatient and outpatient services.

Currently, only the Medtronic Company Inc USA provides SCS services in Thailand. Information about the cost of spinal cord stimulation hardware was gained from the company. The non-rechargeable implantable pulse generator (IPG) (PrimeAdvance SureScan, Medtronic, MN, USA) typically lasts 4 years and costs 667,400 Thai Baht (THB). The rechargeable IPG (Intellis ResoreSensor, Medtronic, MN, USA) typically lasts 9 years and costs 1,065,000 THB (data as of April 2020).

Direct nonmedical costs, including food and transportation were retrieved from the HITAP; the standard cost list was last updated in 2009 from published literature in Thailand (21). The costs were adjusted to 2021 THB using the Thai consumer price index (CPI) (22). They were distributed into the pre- and post-SCS implantation periods. According to the societal perspective and the recommendations of Thai health technology assessment guidelines (23), indirect costs were not included because we assumed that lost or impaired ability to work or engage in leisure activities due to morbidity would be captured in the disutility of quality-adjusted life year (QALY).

Data Analyses

The baseline patient characteristics and diagnoses are shown in Table 1. A decision tree was used to explore the clinical pathway at 3 years, then extended to a 3-month cycle length Markov model to determine costs and outcomes over the lifetime (Fig. 1). This decision tree (Supplemental Fig. 1) and the Markov model were adapted from the study by Kemler et al (15). Input parameters, including transitional probabilities, both direct medical and nonmedical costs, and utilities, were applied to the economic model.

In a decision tree, the period before SCS implantation was classified into the CMM only and was considered suboptimal or no pain relief. The periods after SCS implantation, after the decision point at 3 years, every 3 months, were classified into 4 health states, including optimal pain relief with or without complications (at least 50% pain reduction from baseline), sub-optimal pain relief with or without complications, and no pain relief (0% pain relief or increased pain intensity more than 50% of visit at 3 years) and death (supplemental Fig. 1).

Table 1. *Patients' characteristics at study enrollment time.*

Characteristics	n = 29
Age: average (range)	47.4 (15-79) years
Gender (Male: female)	16:13 patients
Diagnosis (n, %)	
Failed back surgery syndrome	16 (55.17%)
Neuropathic pain	6 (20.69%)
Peripheral vascular disease	4 (13.79%)
Complex regional pain syndrome	3 (10.34%)
Baseline average pain intensity, NRS (mean ± SD, 0-10)	6.24 ± 1.83
Baseline utility (mean ± SD, 0-1)	0.46 ± 0.18

In our Markov model (Fig. 1), all patients were rotated every 3 months throughout the patient's lifespan (19) to each 4 health states according to transitional probability (Tp), which is modified from Taylor et al's Markov model (24) (Table 2). The battery replacement was calculated at every 4 years for non-rechargeable and at 9 years for rechargeable IPG until the age of 65-year-old. Nevertheless, the effect of SCS was assumed to last throughout the patient's lifespan. The complication rates referred to Taylor et al's study (24) due to larger sample size and longer follow-up.

The results were presented as ICUR in THB/QALY gained. The WTP threshold of 160,000 THB/QALY gained was the ceiling threshold in Thailand (19) and was used to determine if the interventions were cost-effective in terms of ICUR (25). The discount rate of 3% was applied to all future costs and outcomes in the model.

A one-way sensitivity analysis was conducted and presented in a tornado diagram. Multivariate probabilistic sensitivity analyses (PSA) were used to explore the uncertainties of parameters in the decision analysis using 1,000 Monte Carlo simulations on Microsoft Excel 2019 (Microsoft Corp., Redmond, WA) (26), and the results were presented as a cost-effectiveness plane and cost-effectiveness acceptability curves (CEAC) to show the probability of rechargeable and nonrechargeable IPG being cost-effective within the range of WTP threshold.

Results

Initially, 46 patients underwent the SCS trial. Only 30 patients reported significant pain relief (more than 50% pain reduction) and subsequently underwent SCS implantation and were recruited into this study. However, one patient was excluded due to missing data and the inability to interpret the result. The data before SCS implantation were considered CMM only, and data up to 3 years after the implantation was considered SCS + CMM. The demographic data of 29 patients in this study are shown in Table 1. The number of participants during each follow-up time point is shown in Fig. 2.

The Effectiveness and Cost-Effectiveness of SCS Treatment

The results showed the patients who underwent

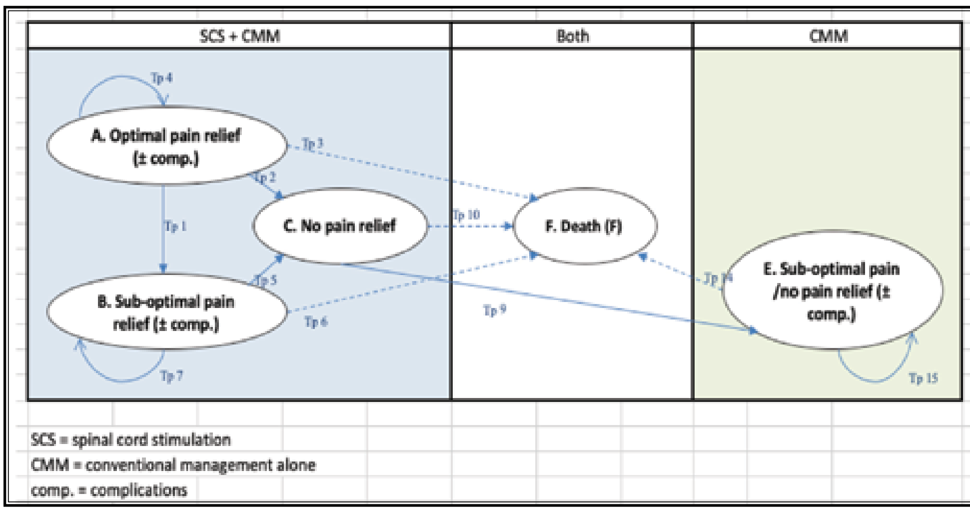

Fig. 1. *Markov model. Time horizon = lifetime. Transition probability = arrows. Cycle length = 3 months. CMM, conventional medical management; SCS, spinal cord stimulation.*

Table 2. *Model input – Transitional probability.*

Model input parameters		Value per 3 months	References
Transitional probability of decrement in achieving satisfactory pain with SCS [optimal pain relief to sub-optimal pain relief]		0.015	Taylor et al (24)
Transitional probability of failing SCS from year 3 onward [any pain relief to no pain relief]		0.005	Taylor et al (24)
Mortality rate		ASMR	WHO lifetable (27)
Complication probability	SCS + CMM group CMM group	0.18 0	Taylor et al (24)

SCS, spinal cord stimulation; CMM, conventional management; ASMR, age-specific mortality rate; WHO, World Health Organization.

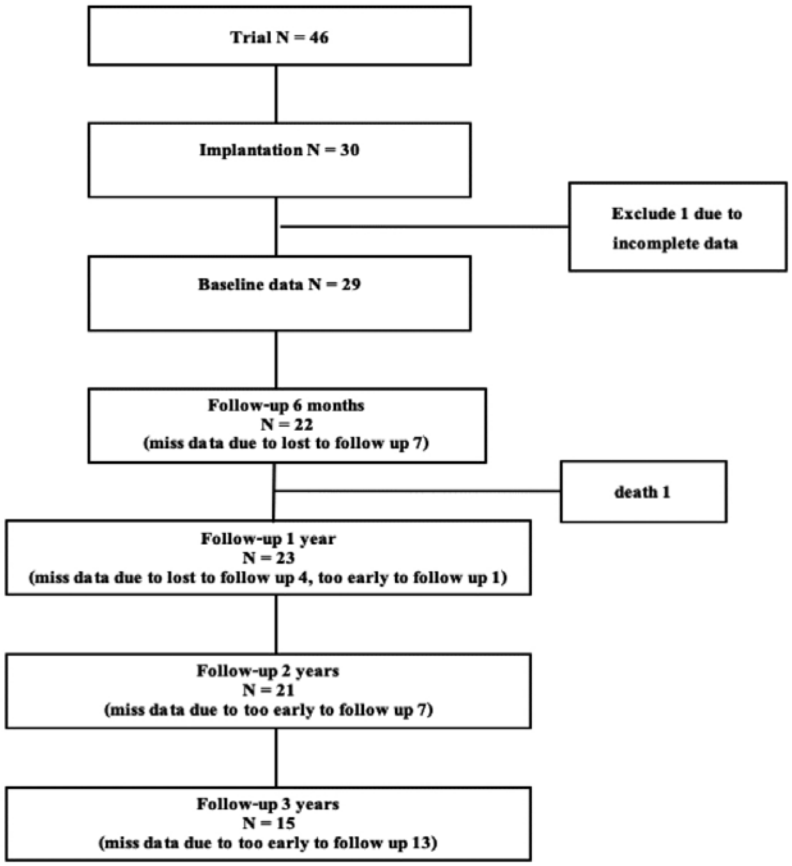

Fig. 2. *Number of participants during follow-up.*

SCS implantation reported a significant reduction in pain intensity. The NRS (0-10) was reduced from baseline at 6.24 ± 1.83 to 3.46 ± 2.15, 3.72 ± 2.35, 4.05 ± 2.66, and 3.75 ± 2.67 at 6 months, 1, 2, and 3 years, respectively. The incremental cost of adding SCS to CMM over 3 years was 1,238,046.29 THB for rechargeable SCS and 840,446.29 THB for nonrechargeable SCS. The ICERs at 3 years were 496,932.08 and 337,341.77 THB/NRS reduction (2.49/10) for rechargeable and nonrechargeable SCS, respectively.

The clinical utility (range: 0-1) increased from 0.46 ± 0.18 to 0.68 ± 0.19, 0.66 ± 0.23, 0.64 ± 0.28, and 0.74 ± 0.23 at 6 months, 1, 2, and 3 years respectively. The mean and standard deviation of pain scores and utility at each time point are shown in Fig. 3.

There were 4 incident reports of complications after SCS implantation. Two patients reported premature battery depletion within one year after the implantation and needed battery replacement. Additionally, 2 patients reported pocket site infection, which needed surgical debridement and courses of systemic antibiotics, and one patient needed IPG replacement. There is no report of neurological complication or lead migration which needed revision.

Cost-Utility, Lifetime Horizon Analysis

The cost-utility compared incremental costs of the SCS + CMM period and the CMM-only period (THB) per QALYs gained over the lifetime horizon. Lifespan and mortality rates of the patients were calculated from the age-specific mortality rate (ASMR) of the Thai population (average life span of 79 years old) (28). The total lifetime QALYs in the SCS + CMM was 10.34 QALYs higher compared with the CMM period of 8.22 QALYs. The utility in each health state is shown in Supplemental Table 1. Additionally, the linear prediction of pain intensity and utilities showed a coefficient of determination range (R2) of 0.65 (0-1), which demonstrated a strong inverse correlation between pain intensity and utilities.

Base-Case Analysis

The incremental costs of rechargeable SCS + CMM

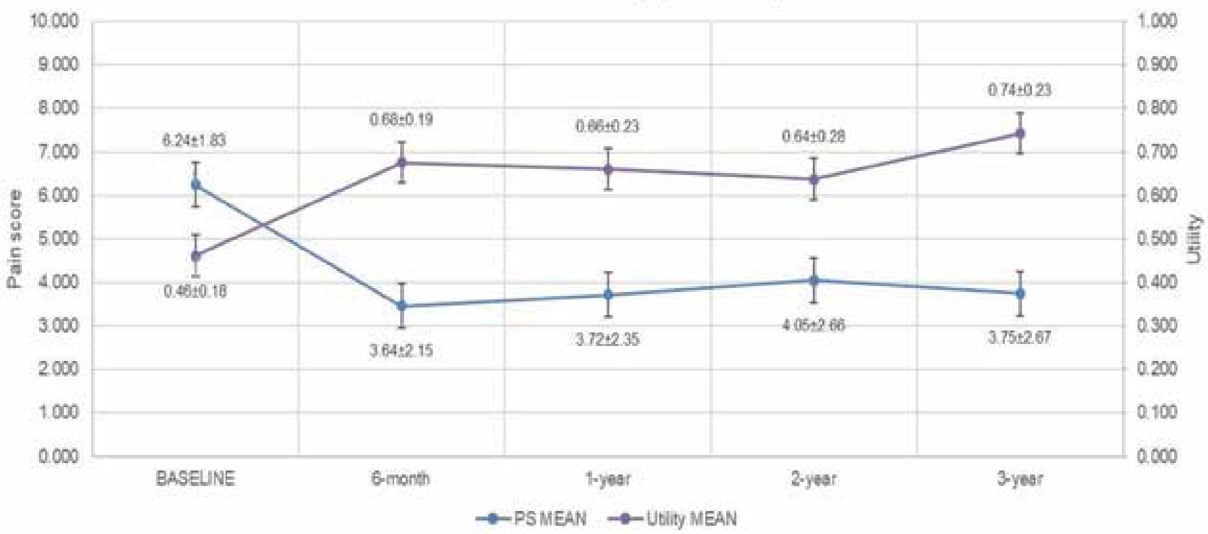

Fig. 3. *Mean and standard deviation of pain score and utility at each time point.*

and nonrechargeable SCS + CMM compared with CMM were 1,403,045.22 and 1,318,054.91 THB, respectively. The group of SCS + CMM gained 2.13 QALYs over the lifetime in both rechargeable and nonrechargeable IPG. The rechargeable IPG provided the ICUR of 660,106.96 THB/QALY gained, whereas the ICUR of the nonrechargeable IPG was 620,120.59 THB/QALY gained. Due to the Thai WTP threshold of 160,000 THB/QALY gained, none of the scenario options were cost-effective compared to CMM alone. The results of the base-case analysis are shown in Table 3.

Sensitivity Analyses

The results of one-way sensitivity analyses of the non-rechargeable SCS + CMM group compared with the CMM group were plotted in tornado diagrams (variation in cost, utility, and transitional probability of 20%, longevity of 3-5 years) (Fig. 4). The one-way sensitivity analyses of rechargeable SCS can be found in Supplemental Fig. 2 (longevity of 9 years).

The highest impacted variables on the higher ICURs for both types of SCS were 1) the utility value of the CMM group for sub-optimal pain relief (E); 2) the utility value of the SCS+CMM group for optimal pain relief (A); 3) utility value of the SCS + CMM group for sub-optimal pain relief (B); and 4) probability of complication in CMM.

In the case that the longevity of rechargeable SCS (Intellis) can be varied, the longevity will be the 5th rank in both models, followed by the cost of SCS, and the cost of IPG as the 6th and 7th rank. Nevertheless, in any circumstance, the sensitivity analysis showed that within the ranges of any variables, the results still remained higher than the Thai WTP threshold.

Threshold Analyses

Threshold analysis showed there were at least 6 discount scenarios per group in order to overcome the current ICUR, as shown in supplemental Tables 2 and 3. For an example of scenario number 2 in Supplemental Table 2 and number 1 in Supplemental Table 3, the costs of rechargeable or non-rechargeable SCS and IPG needed to be reduced by approximately 70% and 80% to be considered cost-effective, compared with CMM.

Probabilistic Sensitivity Analyses (PSA)

In the base-case analysis, the probability of either rechargeable or nonrechargeable SCS + CMM being cost-effective was impossible at the Thai WTP threshold when compared to CMM alone (Fig. 5). However, the cost-effectiveness acceptability curve showed that when the WTP threshold was increased, the probability of SCS + CMM being cost-effective was gained (Fig. 6). When considered at the WTP threshold of 1,600,000 THB/QALY gained (the WTP threshold in North America) (16), there are 98.9% and 99.7% probability of being cost-effective of rechargeable and nonrechargeable SCS (Fig. 6).

Discussion

The study demonstrated that spinal cord stimulation is effective for pain reduction and improved the quality of life of patients suffering from chronic refractory pain in Thailand. However, the hypothesis that SCS is still cost-effective in the current context of Thailand is rejected; the incremental cost-utility ratio is still above the Thai WTP threshold.

Our study showed the SCS treatment reduced pain and improved utility for a variety of chronic pain conditions, including failed back surgery syndrome, complex regional pain syndrome, peripheral vascular diseases, and neuropathic pain in patients who had moderate-to-high pain intensity (average pain score of 6.24 ± 1.83 of 10) and low quality of life (average utility of 0.46 ± 0.18) despite appropriate conventional treatment. Our outcome regarding the clinical benefits of SCS is consistent with previous clinical studies in developed countries (12-16). Moreover, the study also showed the negative impact of pain and quality of life, as the higher pain intensity is strongly correlated with lower utility ($R^2 = 0.65$).

There only are 2 types of SCS available in Thailand: rechargeable and nonrechargeable IPG. Nevertheless, our economic model analysis showed the ICURs of both SCS models in Thailand ranges around 20,000 USD/QALY gained (19,379-20,628 for rechargeable IPG respectively), which exceeds the current WTP threshold of Thailand of 5,000 USD/QALY gained. These results from base-case analysis make SCS not likely to be cost-effective in the current situation (cost of treatment and WTP) for a chronic refractory pain patient in Thailand. In comparative studies from developed countries, Kumar et al (16)

Table 3. *Incremental costs, QALYs gain, and ICUR from the base-case analysis.*

Outcomes	CMM only	SCS + CMM	
		Rechargeable	Nonrechargeable
Total cost/ patient (THB)	833,451.09	2,236,496.31	2,151,506.01
QALYs/patient	8.22	10.34	10.34
Incremental cost (THB)		1,403,045.22	1,318,054.91
QALY gained		2.13	2.13
ICURs (THB/ QALY gained)		660,106.96	620,120.59

SCS, spinal cord stimulation; CMM, conventional medical management; QALYs, quality-adjusted life years; ICURs, incremental cost-utility ratios.

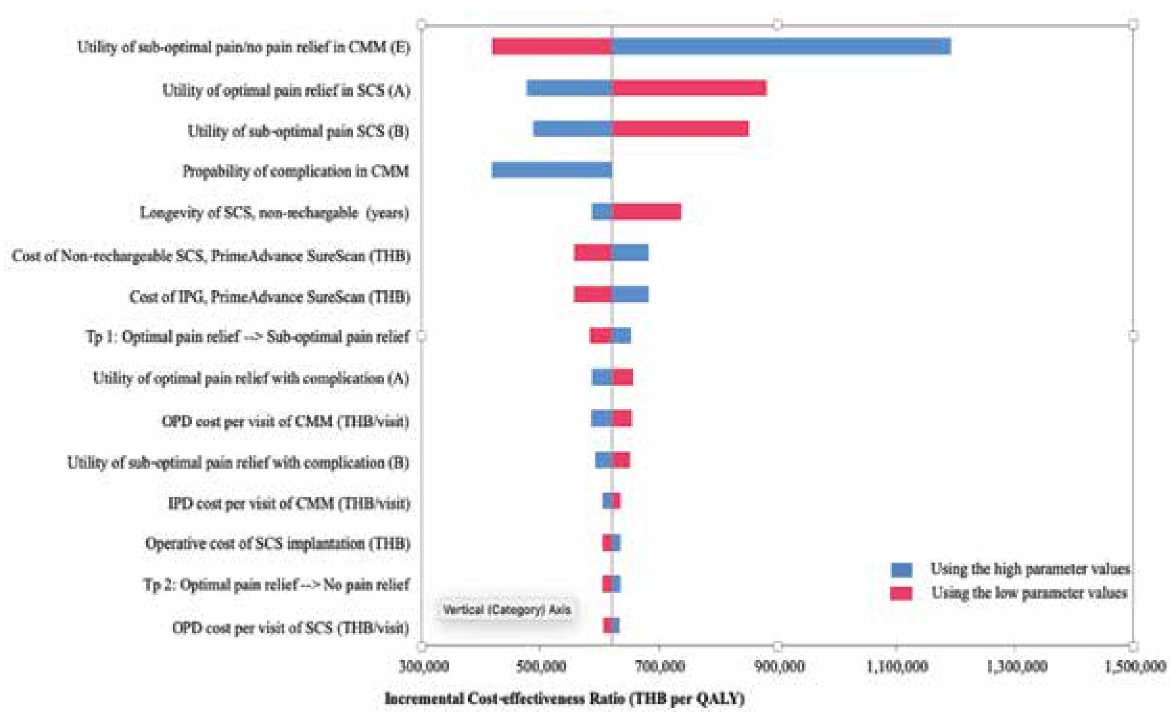

Fig. 4. *Tornado diagram of nonrechargeable SCS + CMM group versus CMM group.*
SCS = spinal cord stimulation. CMM = conventional medical management. Tp = transitional probability

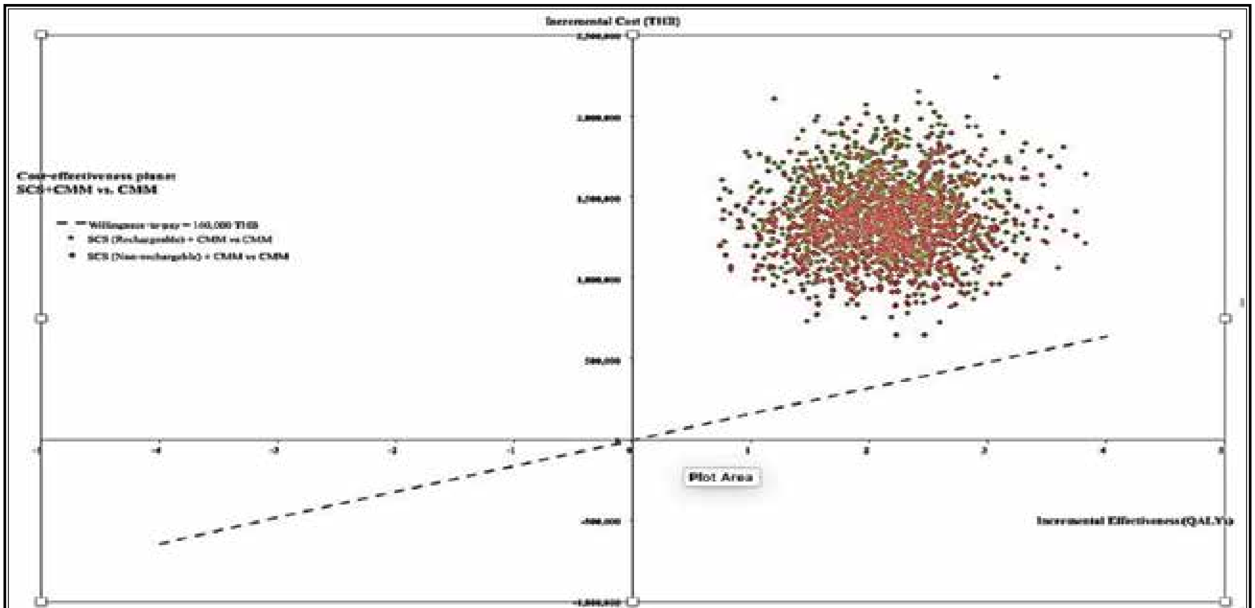

Fig. 5. ***Cost-effectiveness plane of SCS (rechargeable and nonrechargeable) + CMM compared with CMM group. X-axis represents incremental QALY.***
Y-axis represents incremental cost (THB). The majority of simulations are clustered and stay above the willingness to pay of 160,000 THB. Time horizon = lifetime.
SCS, spinal cord stimulation; CMM, conventional medical management; QALYs, quality-adjusted life years; THB, Thai Baht.

Fig. 6. ***Cost-effectiveness acceptability curves (CEAC).***
Y-axis represents the probability of spinal cord stimulation (SCS) providing a cost-effective outcome alternative to conventional medical management (CMM). X-axis represents different willingness-to-pay thresholds.

reported that SCS was cost-effective in Canada due to the ICUR of SCS from the study of 7,317-8,831 USD/QALY gained being below the Canadian WTP threshold (39,370 USD/ QALY gained). Kemler et al (15) also demonstrated the cost-utility of SCS in the UK by showing the ICUR of SCS from the study of 4,879 USD/QALY gained, below the UK's WTP threshold (27,397 USD/QALY gained) (Table 4: In order to compare, we converted to all currencies to USD by the following ratio: 1 USD = 32 THB, 1.27 CAD, or 0.73 Pound). The main reasons why SCS is not cost-effective in

Table 4. *Comparison of the results from economic analysis among studies in different countries.*

Studies	Conditions	Cost of SCS – Cost of CMM = incremental cost (USD)	QALY gained	ICUR (USD/ QALY gained)	WTP (USD/QALY gained)
Kumar et al (16) (Canada)	Chronic pain, including FBSS, CRPS, PAD, and RAP	131,054 to 143,595 – 117,164 to 128,130 = 10,171 to 18,723 (1)	1.39 to 2.21	7,317 to 8,831	39,370
Kemler et al (15) (UK)	CRPS	118,863 – 109,280 = 9,583	1.96	4,879	27,397
Our study (Thailand)	Chronic refractory pain, including FBSS and CRPS	67,235 to 69,891 - 26,045 = 41,190 to 43,846 (2)	2.13	19,379-20,628	5,000

FBSS, failed back surgery syndrome; PVD, peripheral vascular diseases; CRPS, complex regional pain syndrome; RAP, refractory angina pectoris; SCS, spinal cord stimulation; CMM, conventional medical management; QALYs, quality-adjusted life years; ICURs, incremental cost-utility ratios. Note: (1)(2) The table represents ranges of cost and QALY in Kumar et al (16) based on different diagnoses, whereas the range in our study is based on different types of IPG.

this context are due to the higher ICUR in this study and the lower WTP in Thailand.

ICUR is calculated by the difference of cost ([cost in SCS + CMM group] - [cost in CMM group]), divided by the QALY gained ([QALY in SCS + CMM group] - [QALY in CMM group]). Compared to the study by Kumar (16) et al and Kemler (15) et al, the QALY gained in our study is in the comparable range (within the range of 96% to 153%), whereas the difference of the cost of SCS + CMM and CMM is 2-4 times higher (220% to 458%). The higher difference between the cost is plausibly the main reason of the higher ICUR in Thailand.

The higher ICUR in Thailand can be explained by the larger gap between the cost of CMM and SCS + CMM compared to the context of developed countries. Our study showed the cost in the SCS + CMM group is about half (50% to 58%), compared to Kumar (16) and Kemler studies (15). Nevertheless, the cost in the CMM group in Thailand is only about one fifth (20% to 24%), even much lower, resulting in the disproportional lower cost of CMM and wider incremental cost.

The same explanation can apply to the higher ICER in this study as well. The ICER study by Zucco (5) was about 2,990 USD/NRS reduction (societal perspective, 1 USD = 0.88 Euro), whereas our data showed ICER of 10,219-15,054 USD/NRS reduction (non-rechargeable and rechargeable SCS respectively). The pain reduction is comparable in both studies (2.57 in Zucco's study vs 2.57 in our study); however, the incremental cost after the treatment resulted in a different ICER (7,556 USD in Zucco's study vs 26,264-38,689 USD in our study). The difference between the cost of CMM and SCS, not the effectiveness or utility gain, is the main reason of higher ICUR and ICER in our context.

There are several possibilities to match the ICUR with WTP in Thailand. The first possibility is to adjust the WTP: according to the PSA, the probability of being effective is zero at current WTP threshold. However, if the WTP threshold increases to 1,600,000 THB/QALY gained, the similar threshold in North America, the probability of SCS being cost-effective is almost 100%. Nevertheless, the decision on the WTP threshold and price policy are beyond the scope and authority of this study. The second possibility is to reduce the cost of equipment: the threshold analyses showed many discount scenarios in order to reduce the current ICUR, including a 70% to 80% cost reduction of the SCS. As the longevity of the IPG is one of the factors in deterministic sensitivity analysis for ICUR of rechargeable SCS, the third possibility of having a newer model of SCS that can make the IPG last longer may reduce the ICUR. Finally, regarding health policy, the policymakers generally consider various aspects other than the cost-effectiveness outcome alone, including prevalence and severity of disease, the effectiveness of an intervention, applicability to a local context, economic impact, ethical issues, and budget (28).

This study used local data as much as available and, to the best of our knowledge, is the first study on the cost-utility of spinal cord stimulation in the context of low- and middle-income countries. However, there are several limitations in this study as well. Firstly, the data was derived from a single-center prospective cohort study. The clinical results might be subject to selection bias as there was no randomization. Secondly, the data from the CMM group were retrieved retrospectively from the period before the SCS implantation and assumes that there is no change in utility and pain intensity over time. Thirdly, the analysis was based on a symptom (refractory pain) of heterogeneous, conditions (failed back surgery syndrome, complex regional pain syndrome, peripheral vascular diseases), which might not represent the exact cost and QALY gained in individual conditions. However, due to the small sample size, the subgroup analysis of each diagnosis will not be reliable. Lastly, due to the limited number of patients who can afford spinal cord stimulation in Thailand, the study was able to collect only a small sample size of patients, which may not represent the chronic refractory pain patients from the whole country or other low- and middle-income countries. A larger multi-center study is needed in the future to address these limitations.

There are many countries that have economies and reimbursement systems comparable to Thailand (29). Nevertheless, the deterministic factors for the outcome of economic analysis, including the level of universal health coverage, cost of health care, cost of living, and willingness to pay, are highly variable in each country (29). Our cost-effectiveness results should also be interpreted with caution in terms of generalizability, even for low- and middle-income countries. Nevertheless, we believe that the information from this study can guide economic studies for the individual country and setting for the decision on payment and reimbursement to the related parties in the future.

Conclusion

The study demonstrated spinal cord stimulation as an effective treatment for chronic refractory pain and could improve the patients' quality of life. However, the economic evaluation showed SCS is not cost-effective in the current context of Thailand, due to a higher incremental cost-utility ratio and a lower willingness-to-pay threshold, compared to developed countries. Adjustments to the cost of equipment, an increase of the willingness-to-pay threshold, the use of a model with longer longevity, or a combination of these strategies can be plausible solutions for the application of this high cost and high technology in the context of Thailand.

Authors Contributions

NZ: design, recruitment, analysis, MS preparation; NS: data collection, analysis; NC: data collection, analysis, MS preparation; SW: design; CK: analysis, MS preparation; PP: analysis, MS preparation

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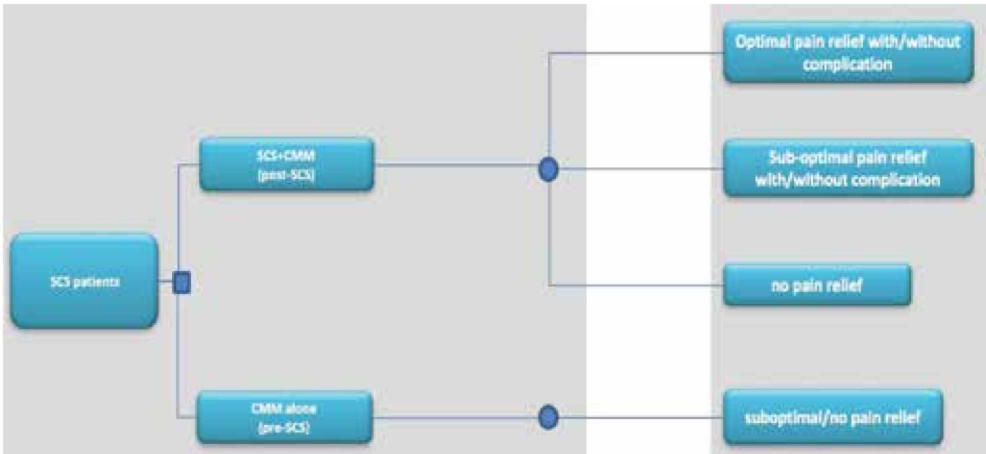
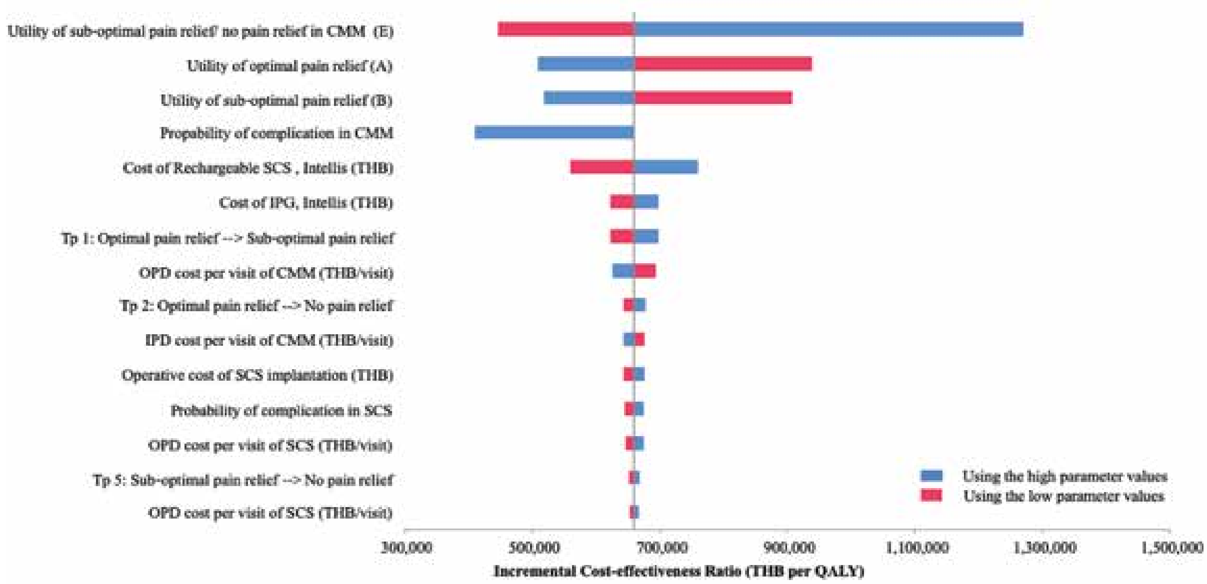


Supplemental Fig. 1. *Decision tree.*



Supplemental Fig. 2. *Tornado diagram of rechargeable SCS + CMM group versus CMM group. (Note, as the Intellis model has a fixed longevity of 9 years, the longevity is not ranked in sensitivity analysis. However, if the longevity can be variable from 9-18 years, this factor will be in the 5th rank). SCS = spinal cord stimulation, CMM= conventional medical management, TP = transitional probability.*

Supplemental Table 1. *Utility in each health states. (average utility in each stage, n = frequency of chance of staying in each stage) Optimum pain relief = pain score reduction of at least 50%; sub-optimum pain relief = pain reduction of less than 50%; no pain relief = 0% pain relief or more pain, more than 50% of visit at 3 years. SCS, spinal cord stimulation; CMM, conventional medical management.*

Group	Health state	utility	Reference
SCS+CMM	Optimal pain relief (n =43)	0.824 ± 0.13	Data from present cohort
	Sub-optimal pain relief (n =39)	0.560 ± 0.22	Data from present cohort
	No pain relief (n=4)	0.370 ± 0.30	Data from present cohort
CMM	Sub-optimal pain relief (n = 18)	0.461 ± 0.18	Data from present cohort
Complication	Utility decrement	-0.121*	Taylor et al24, 2002

Supplemental Table 2. *Threshold analysis of 6 discount scenarios for rechargeable SCS. Spinal cord stimulation set (SCS) and only internal pulse generator (IPG).*

Scenario	%Reduction to meet ICUR (SCS)	Final price of rechargeable SCS	%Reduction to meet ICUR (IPG)	Final price of rechargeable IPG
	0%	1,065,000.00	0%	770,000.00
1	65%	372,750.00	93%	54,179.22
2	70%	319,500.00	80%	156,999.80
3	80%	213,000.00	53%	362,640.97
4	85%	159,750.00	40%	465,461.55
5	90%	106,500.00	26%	568,282.13
6	95%	53,250.00	13%	671,102.71

Supplemental Table 3. *Threshold analysis of 6 discount scenarios for non-rechargeable SCS. Spinal cord stimulation set (SCS) and only internal pulse generator (IPG).*

Scenario	%Reduction to meet ICUR (SCS)	Final price of non-rechargeable SCS	%Reduction to meet ICUR (IPG)	Final price of non-rechargeable IPG
	0%	667,400.00		418,900.00
1	70%	200,220.00	77%	97,453.30
2	80%	133,480.00	67%	139,452.99
3	85%	100,110.00	62%	160,452.84
4	90%	66,740.00	57%	181,452.68
5	95%	33,370.00	52%	202,452.53
6	100%	0	47%	223,452.38