Observational Study

Cost-effectiveness of Radiofrequency Denervation for Zygapophyseal Joint Pain

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Background: Chronic pain is a leading cause of disability. Radiofrequency denervation (RFD) is effective when performed according to guidelines for patients with correctly diagnosed zygapophyseal joint pain (ZJP). However, the cost-effectiveness of this method has not been fully explored.

Objective: The aim of this study was to analyze whether RFD is cost-effective for ZJP from a societal perspective.

Study Design: Cost effectiveness study based on an observational study.

Setting: An interventional pain management clinic in central Sweden.

Methods: Patients - This cost-effectiveness study was performed for all patients (n = 873) assessed between 2010 and 2016 at a specialized interventional pain clinic in Sweden. Those diagnosed with ZJP (n = 331, 37.9%) were treated with RFD and followed up for 1 year after the RFD. Using data collected from national registers, we determined the health care costs, medication costs, the patients' time and travel costs, and the patients' ability to work. The effects of RFD on quality-adjusted life years (QALY) and cost/QALY gained were calculated.

Results: On average, patients reported very low health-related quality of life (HRQoL; EQ-5D index: 0.212). After RFD, HRQoL increased significantly to 0.530 ($P < 0.0001$). Drug consumption and specialized health care consumption were reduced by 54% and 81%, respectively, and the cost/QALY gained from a societal perspective was 221,324 Swedish krona (USD ~26,008). The sensitivity analysis showed that the treatment was cost-effective in all scenarios evaluated, using the patients as their own controls. The cost/QALY gained from a health care perspective was 72,749 Swedish krona (USD ~8,548).

Limitations: The results are based on data collected at one center. The results need to be compared with those from pain rehabilitation programs and should be confirmed using data from other centers.

Conclusions: Patients referred for RFD in Sweden report extremely low HRQoL. HRQoL significantly increased following RFD in patients with ZJP. Medications and health care consumption decreased after RFD. RFD was cost-effective, and the sensitivity analysis yielded stable results in different scenarios. Therefore, RFD is a cost-effective treatment that meets the Swedish National Board of Health and Welfare criteria for a high priority treatment.

Trial Registration: The study was registered at ClinicalTrials.gov (NCT01835704) with Protocol ID SE-Dnr-2012-446-31M-1. https://clinicaltrials.gov/ct2/show/NCT01835704

Key words: Chronic pain, interventional pain management, zygapophyseal joint pain, radiofrequency denervation, cost-effectiveness, QALY gained

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Chronic pain is a widespread condition (1-3) that causes much suffering to affected individuals with a significant cost to society (4,5). In the World Health Organization Global Burden of Disease studies, lower-back pain has remained the leading cause of disability since 1990 (6).

Interventional pain management (IPM) strategies, including radiofrequency denervation (RFD) to treat zygapophyseal joint pain (ZJP), have shown promising effects in patients with chronic spinal pain (7-13). A diagnosis of ZJP is established if nerve blocks performed on 2 occasions both relieve ≥ 80% of the pain during the period of local anesthesia (7,14,15). To date, however, the long-term health and economic effects of RFD have not been comprehensively evaluated, despite the importance of such evaluations for decision makers (16). The National Institute for Health and Care Excellence (NICE) evaluated RFD for lumbar zygapophyseal joints in patients diagnosed and treated according to international clinical guidelines (7,14,15), and concluded that this method could be cost-effective for treating lumbar pain in adequately diagnosed patients (17).

In designing the present study, we aimed to investigate the effects of RFD on health-related quality of life (HRQoL) and determine the costs from a societal perspective. We used the cost per quality adjusted life years (cost/QALY) as the study main outcome, using the patients as their own controls.

Methods

Aim and Design

The aims of this study were to (i) describe the characteristics of patients referred to a specialist clinic and treated with RFD, (ii) compare the patients' HRQoL at the first visit and when they were diagnosed with zygapophyseal joint pain (ZJP) and ready for treatment, (iii) calculate the QALYs gained by treating those diagnosed with ZJP with RFD, and (iv) investigate whether interventional methods to identify ZJP and subsequently treat with RFD is cost-effective in terms of cost/QALY gained.

Study Setting and Population

The setting was a specialist IPM clinic in central Sweden (Stockholm County). Patients assessed between 2010 and 2016 were included in the study. Of the 873 patients assessed, 331 (37.9%) were diagnosed with ZJP in either the lumbar (200), thoracic (76) or cervical (55) region and underwent RFD of the tested joints. Sociodemographic and clinical variables were collected for all assessed patients, and the outcomes were analyzed for patients who underwent RFD (Table 1).

Description of the Intervention

First, a physician performed a pain analysis using a semi-structured interview (Supplement 1). Then, a diagnostic medial branch block (MBB) was performed at the suspected location (Fig. 1). The patients completed a form hourly for 7 hours to report any reductions in pain from before the block. The results were confirmed during the following encounter(s). Two MBBs performed at the same level on two different occasions, and if both instances reduced the pain by ≥ 80%, the patient was diagnosed with ZJP (7,14,15). Patients with ZJP were offered RFD at the tested levels. The MBBs and RFD were performed according to the Spine Intervention Society guidelines (14). Patients not diagnosed with ZJP after a series of negative tests were referred back to their source with recommendations for further treatment.

'No Treatment' Comparison

A "no treatment" comparison was constructed by analyzing changes in HRQoL before treatment. Baseline data were collected at the first visit. During the following encounters, diagnostic nerve blocks were performed to determine the location of the pain focus (Figs. 1 and 2). The number of tests needed and the time they took varied considerably among the patients. The patients' HRQoL was assessed before the RFD, which yielded a second measurement for untreated patients. The change in HRQoL between these 2 measurements was calculated and the correlation with the timespan between the assessments was calculated.

Data Collection

Data were prospectively collected and entered into the databases. Demographic data were collected by the physician during the first assessment. Linked data on medication and health care consumption were obtained from national registers (Swedish National Board of Health and Welfare, NBHW).

The patients completed questionnaires covering sick leave, psychological distress, and HRQoL at the time of the assessment, at the time of RFD, and at 3, 6, and 12 months after RFD. A short telephone interview was performed 1 month after RFD to ask how long the patients experienced pain after treatment (Fig. 2).

Table 1. *Description of the patients at first assessment.*

	Interventional Pain Management	
	All patients assessed n = 873	**Patients diagnosed with zygapophyseal joint pain n = 331 (37.7%)**
Age, year mean (SD) range	52 (15.7) 16-94	51 (15.6) 17-89
Age > 66, n	n = 176	n = 60
Women n (%)	n = 550 (63%)	n = 218 (66%)
Men n (%)	n = 323 (37%)	n = 113 (34%)
Pain duration, months mean (SD) range	110 (113.4) 0.1-768	122 (124.3) 2-744
Sick-leave n (%)	Missing data 3 (0.3%)	Missing data 1 (0.3%)
0%	226 (33%)	77 (29%)
25%	46 (7%)	21 (8%)
50%	76 (11%)	34 (12%)
75%	38 (5%)	18 (7%)
100%	308 (44%)	120 (44%)
Pain onset cause		
Unknown	40 (5%)	4 (1%)
Transport/traffic	104 (11.9%)	45 (13.6%)
Surgery	61 (7.0%)	24 (7.3%)
Other trauma	182 (20.8%)	75 (22.7%)
No trauma	486 (55.7%)	183 (55.3%)
Pain localization	Missing data 40 (5%)	Missing data 4 (1%)
Head	23%	23%
Neck	38%	43%
Upper extremity	23%	25%
Chest/thoracic	30%	38%
Lumbar	64%	74%
Abdomen/perineal	24%	28%
Lower extremity	18%	21%
ZJP diagnosed in region:		
Cervical Thoracic Lumbar		55 (16.6%) 76 (23.0%) 200 (60.4%)
HAD-anxiety HAD-depression mean(SD)	7.2 (4.5) 7.7 (4.4)	6.9 (4.3) 7.9 (4.5)
EQ-5D index mean(SD)	0.252 (0.313)	0.212 (0.279)
EQ-VAS mean(SD)	43 (19.4)	42 (18.2)

SD, standard deviation; HAD, Hospital Anxiety and Depression scale; EQ-5D, EuroQol five-dimensional questionnaire; EQ-VAS.

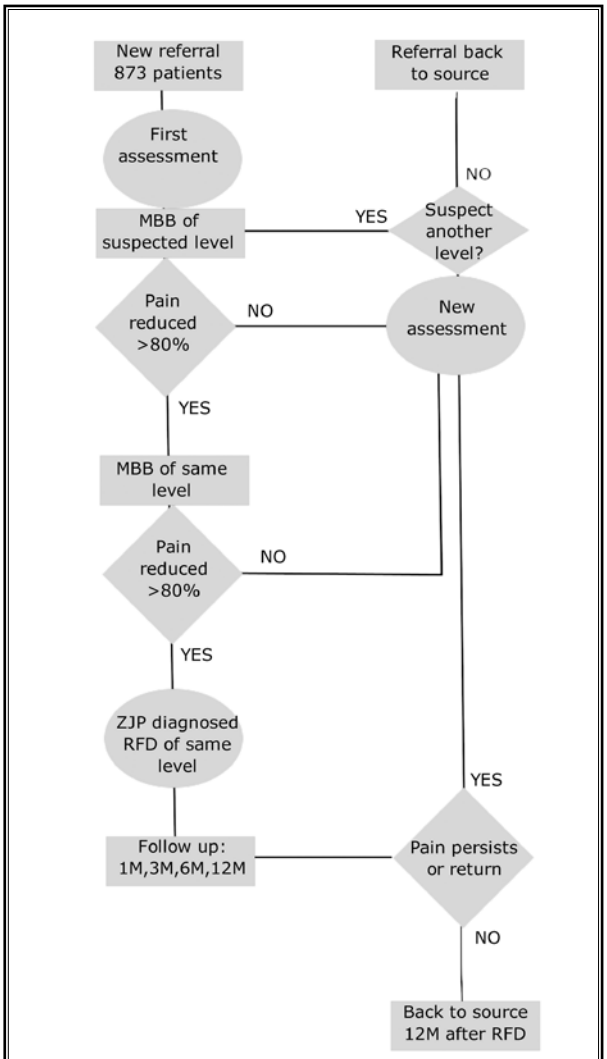

Fig 1. *Flowchart of tests, treatments and follow-up.*

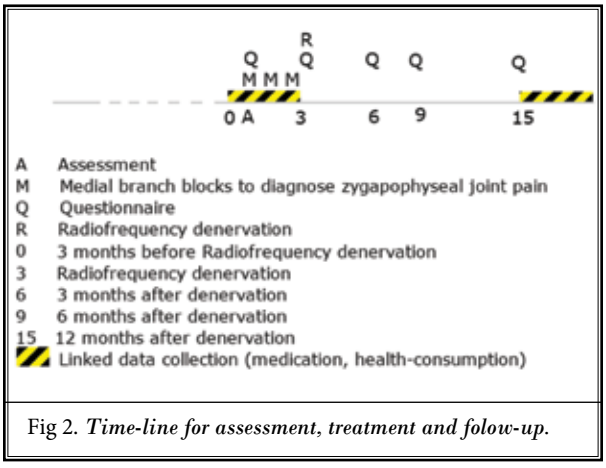

Fig 2. *Time-line for assessment, treatment and folow-up.*

Health Outcomes

HRQoL was measured using the EQ-5D index and the EuroQol visual analog scale (EQ-VAS (18) under license from EuroQol). We used the time-trade-off-derived UK value set to calculate the EQ-5D index (18-20). Psychological distress was measured using the Hospital Anxiety and Depression Scale (HAD) (21-26).

Intervention Costs

The number of visits to the clinic and the number of procedures performed were measured for all patients (n = 873). The unit costs (per visit and procedure) were obtained from the reimbursement price list for Swedish public procurement 2010 to 2016 (Supplement 2).

Medications

Data on prescribed and dispensed drugs were collected for all treated patients (n = 331). In Sweden, people can purchase prescribed drugs for a 3-month consumption period at any time. Data were obtained for 3 months before and 15 months after RFD. Drugs associated with the treatment of chronic pain were identified using the Anatomic Therapeutic Chemical Classification codes (Supplement 3) (27).

Health Care Consumption

The patients' use of all types of specialized health care was obtained from the Swedish NBHW registers for the same period as for drugs and analyzed similarly (Fig. 2). Only health care associated with chronic pain (i.e., with relevant diagnoses according to the International Classification of Diseases 10th revision codes) were included (Supplement 4).

To calculate the unit cost per visit, we used data from the Swedish Association of Local Authorities and Regions (28). For specialist outpatient visits, the average cost was calculated as Swedish krona (SEK) 3,792 per outpatient visit and SEK 11,423 per day for inpatient care (Table 2). Daycare visits, defined as inpatient care < 24 h, were handled similarly to the outpatient visits, with an estimated average cost of SEK 3,792.

Patient Costs

The patients' time spent at the IPM clinic and the travel costs were estimated for all visits. The time and travel costs associated with attending the clinic for diagnostic procedures were classified as diagnostic costs, whereas the time and travel costs associated with RFD were classified as treatment costs (Table 3). We used the Swedish average wage in 2016 as the unit cost for time (SEK 217 per hour including 32.46% payroll tax) (29). We included 4 hours and SEK 540 in travel cost (300 km/186 miles, SEK 1.8 per km) per visit (30).

Ability to Work and Sick Leave

The self-reported ability to work was recorded at the time of assessment and at each follow-up visit as 0%, 25%, 50%, 75%, and 100%, of their capacity (31). To place a monetary value on these changes, we used the average hourly wage of SEK 217 (29). Full-time work was estimated as 1880 h per year or 40 h per week. After RFD, many patients are temporarily unable to work for a few weeks. Therefore, we included a sick-leave period of 4 weeks after RFD as a treatment cost for all patients aged < 67 years whose prior ability to work was ≥ 25% of their capacity (Table 1).

Statistical Methods

Descriptive statistical methods were used. The Tukey Kramer test was used for parametric variables and Wilcoxon test was used for pairwise comparisons. A P value of < 0.05 was considered to indicate statistical significance. For medications and health care use, the baseline cost was calculated for the 3 months preceding RFD, while the 3 months from 1 year after RFD was regarded as the outcome period. If the baseline costs were higher than the outcome period costs, the reduction was considered a consequence of the treatment. Productivity gains were calculated for the individual patients and were summed to determine the total productivity gain for all patients combined. Changes in the EQ-5D index were transferred into QALYs by calculating the area under curve for the mean EQ-5D index versus time (Figs. 2 and 3). We assumed that the EQ-5D index changed evenly between measurements. All calculations were made in Swedish krona (SEK) in 2016 values. The US-dollar (USD):SEK exchange rate was 1:8.51 in 2016. All analyses were conducted using JMP 14.0.0 (SAS Inc., Cary, NC).

Sensitivity Analysis

Sensitivity analyses were performed for all variables that could affect the outcome. We diagnosed ZJP among 37.9% of the patients assessed, but according to prior studies, the prevalence of ZJP may vary between ~30% (lumbar region) to ~50% (cervical region) (32-34). Therefore, sensitivity analyses were performed assuming that 30% and 50% of the patients received RFD. We also examined the effect of a 10% increase/decrease in treatment costs and health care use. A

sensitivity analysis of the time and travel costs first considered the recruitment of local patients (2 h per visit and 50 km /31 miles travel), and second considered an accompanying person and a full day's visit (16 h per visit and 300 km/186 miles travel). Because the mean duration of pain after RFD was 2 weeks in these patients, we considered different durations of sick leave (2 or 4 weeks) to determine its effect on costs. In addition, because the improvement in pain after RFD often lasts for > 1 year (9,10,36,37), we determined the costs under the assumption that the effect on HRQoL would last for 2 or 4 years. Finally, we calculated the cost utility from a health care perspective to yield values that can be compared with previously published cost utility studies.

Ethics

All patients provided informed consent for inclusion in the study, for the use of their medical records, and for data collection and analysis. The regional ethics board in Umeå, Sweden approved the study (Dnr 2012-446-31M, Dnr 2017-542-32M). The study was registered at ClinicalTrials.gov (NCT01836666) with Protocol ID SE-Dnr-2012-446-31M-2.

Results

Characteristics of the Assessed Patients

During the study period (2010-2016), 873 patients were assessed at the clinic. After a total of 2,759 visits and 3,788 procedures, 331 patients (37.9%) were diagnosed with ZJP and underwent RFD (Table 1). Fifty-five patients diagnosed with cervical, 76 with thoracic, and 200 with lumbar ZJP. There were slightly more women (63% assessed, 66% treated. $P = 0.279$) than men. The mean duration of pain before assessment was 110 months. Most of the patients were working (67% of assessed and 71% of treated patients) (Table 1).

HRQoL and Psychological Distress at the Initial Assessment

The mean EQ-5D index score at the initial assessment was 0.252 among assessed and 0.212 among diagnosed patients (Table 1). In patients diagnosed with ZJP, there were no significant differences in the EQ-5D index, EQ-VAS, HADS-anxiety, or HADS-depression scores among various age groups or which level the

Table 2. *Cost per outpatient visits in specialized care and inpatient care-days 2016 according to the Swedish Association of Local Authorities and Regions.*

	Outpatients		Inpatients	
	Specialized care		Specialized care	
	Cost per visit (SEK)	Visits (n)	Cost per day (SEK)	Care days (n)
Physician, somatic care	3428	8 333 000	13 113	5 924 147
Advanced day-care	5866	1 079 000	-	-
Physician, psychiatric care	4750	831 000	5 126	1 590 007
Average cost	3 792 SEK/visit		11 423 SEK/care day	

Average cost for outpatient visits was calculated depending on how many visits of each kind there were during 2016. For inpatient care an average was calculated between somatic care and psychiatric care.

Table 3. *Cost calculations in the analysis.*

	Costs	Reduced costs
Assessment	Health care costs for assessment (pain analysis) and diagnostic procedures performed on all patients assessed, until a zygapophyseal joint pain has been diagnosed. Time to attend during assessment and visits when diagnostic procedures were performed Time and travel expenses to reach the unit for all visits	
Treatment	Health care costs for radiofrequency denervation Time to attend Time and travel expenses to reach unit	
Medication	Medication after treatment	Medication before treatment
Health service consumption	Outpatient visits after treatment Inpatient ward-days after treatment Inpatient day-care days after treatment	Outpatient visits before treatment Inpatient ward-days before treatment Inpatient day-care days before treatment
Sick-leave	Cost for sick-leave during 1 month after radiofrequency denervation Patients on sick-leave after treatment	Patients on sick-leave before treatment

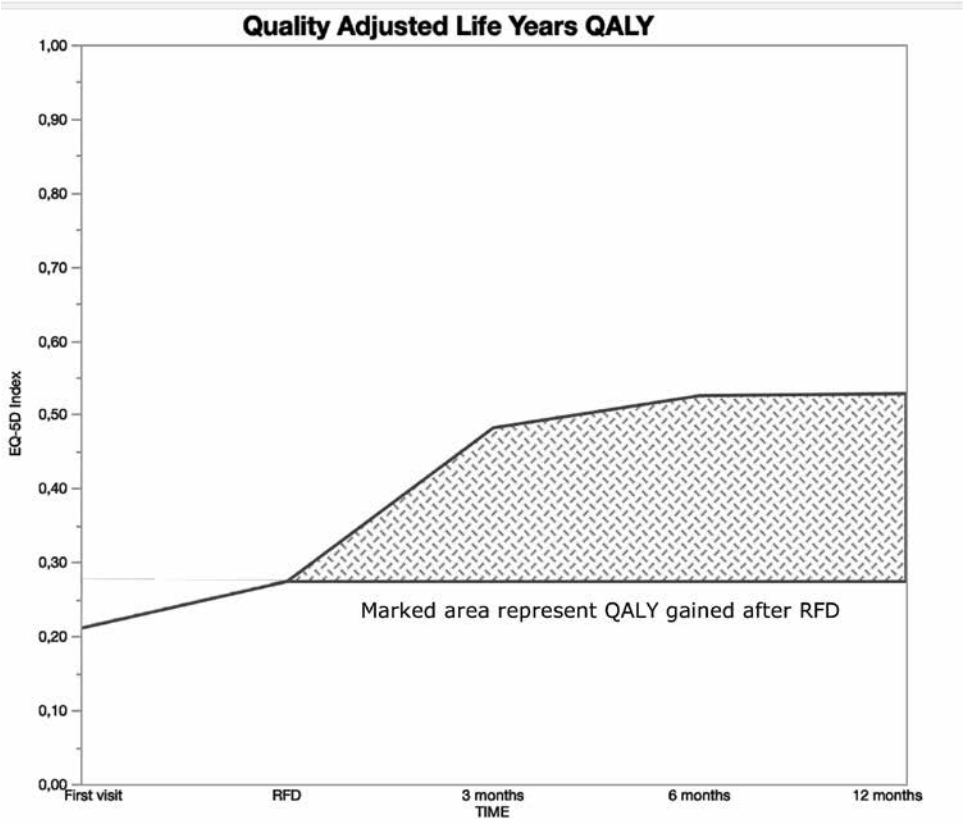

Fig 3. *Changes in health-related quality of life after treatment.*

pain was localized to (Table 4). The EQ-5D index was significantly lower among patients who were unable to work but there were no significant differences in EQ-VAS, HADS-anxiety, or HADS-depression scores according to the patient's ability to work.

Changes in HRQoL Between Initial Assessment and RFD

In patients diagnosed with ZJP, the mean EQ-5D index was not significantly different between the first visit and the time of RFD (0.212 vs 0.274, $P = 0.092$). The mean to diagnose ZJP was 86 days, with a range of 2 days to 2.5 years. There was no time-dependent improvement in HRQoL before RFD. There was a weak correlation between the change in HRQoL and the time between the measurements (r = -0.12, $P = 0.036$). Patients were therefore used as their own controls in subsequent analyses.

Changes in HRQoL at 12 Months After RFD

The mean duration of pain after RFD was 13.1 days, and it did not differ significantly according to gender or ability to work (Table 5). The mean EQ-5D index increased significantly (from 0.212 to 0.530, $P < 0.0001$) between the initial assessment and 12 months after RFD. This increase was consistent in all age-groups, in both genders, and in all pain regions.

Health Care Costs

The total costs associated with assessing and diagnosing ZJP was SEK 14.9 million, or SEK 45,060 per patient, based on 3,788 procedures and 2,759 visits (Table 6).

The total treatment cost was calculated as SEK 2.3 million, or SEK 6,908 per patient.

The annual pain-related medication cost at 1 year after treatment had decreased by SEK 1.1 million in patients treated with RFD based on an annual reduction of 68,628 defined daily doses. The cost of pain-related health care use decreased by SEK 8.2 million for outpatient care and by SEK 0.08 million for inpatient care.

Table 4. *Health-related quality of life and psychological distress at the time of assessment in patients divided by age or sick-leave.*

	Patients diagnosed with zygapophyseal joint pain			
Age group	**EQ-5D Index mean (SD)**	**EQ-VAS mean (SD)**	**HAD-anxiety mean (SD)**	**HAD-depression mean (SD)**
≤ 17 n = 1	0.088 n = 1	30 n = 1	14 n = 1	12 n = 1
18-29 n = 28	0.239 (0.290) n = 28	41 (15.4) n = 27	8.2 (5.5) n = 20	8.0 (4.7) n = 20
30-44 n = 88	0.209 (0.303) n = 88	44 (20.5) n = 81	7.3 (4.4) n = 73	7.8 (5.0) n = 73
45-66 n = 154	0.222 (0.283) n = 154	42 (17.9) n = 143	6.5 (4.1) n = 131	8.1 (4.4) n = 131
≥ 67- n = 60	0.179 (0.233) n = 60	38 (16.3) n = 47	7 (4.3) n = 51	7.6 (3.8) n = 51
All n = 331	0.211 (0.280) n = 331	42 (18.2) n = 299	6.9 (4.3) n = 276	7.9 (4.5) n = 276
Work ability %	EQ-5D index mean (SD)	EQ-VAS mean (SD)	HAD anxiety mean (SD)	HAD depression mean (SD)
0	0.137 (0.238)#*	39 (17.8)	7.3 (4.6)	8.5 (4.4)
25	0.267 (0.293)	39 (17.8)	7.1 (3.9)	7.4 (4.2)
50	0.187 (0.252)	39 (19.8)	6.1 (4.1)	7.6 (5.1)
75	0.373 (0.294)#	50 (14.8)	4.4 (3.2)	6.1 (3.7)
100	0.340 (0.314)*	48 (18.3)	6.9 (3.9)	7.3 (4.4)
Region with ZJP	EQ-5D index mean (SD)	EQ-VAS mean (SD)	HAD anxiety mean (SD)	HAD depression mean (SD)
Cervical	0.256 (0.285)	48 (19.6)	6.6 (4.0)	7.2 (4.6)
Thoracic	0.218 (0.290)	42 (19.1)	7.8 (4.4)	7.9 (4.4
Lumbar	0.205 (0.276)	40 (16.6)	6.6 (4.3)	8.0 (4.5)

* $P < 0.0001$, # $P = 0.0010$

SD, standard deviation; EQ-5D, EuroQol five-dimensional questionnaire; EQ-VAS, EuroQol visual analog scale; HAD, Hospital Anxiety and Depression scale; ZJP Zygapophyseal Joint Pain.

Ability to Work

The total cost of 4 weeks' sick leave after RFD was estimated to SEK 3.9 million. The self-reported ability to work increased after RFD, and the increase was valued at SEK 1.1 million (Table 1). Among the 271 patients of working age (< 67 years old), there were 5 fewer who were unable to work and 3 more who reported a capacity of 100%. Overall, 31 patients reported an increase in their ability to work and 19 who reported a reduction in their ability to work, resulting in an average of 2.75 patients with an increased full-time ability to work.

QALY and Cost Per QALY Gained

At one year after treatment, the total QALY gained was 48.08, or 0.145 QALYs per patient. The total cost was SEK 10.6 million, or SEK 32,149 per patient. Thus, the cost/QALY gained was SEK 221,324 (Table 1), which is below the threshold value for acceptable cost-effectiveness in Sweden (SEK 500,000/QALY gained) (37,38).

Sensitivity Analysis

In all sensitivity analysis scenarios, the cost-effectiveness ratio remained within the moderate range for cost-effectiveness according to the Swedish NBHW (SEK 100,000–500,000) (37,38).

The factors that had the greatest effect on the cost/QALY gained were how many of the assessed patients were diagnosed with ZJP and treated; the duration of the increase in HRQoL; the number of patients that required sick leave after treatment; and how long sick leave lasted. In this study, we did not consider sick leave for the 18% of the patients who were aged > 66 years. Table 7 shows the results of the sensitivity analyses with different values for the number of diagnosed patients,

Table 5. *Effects of treatment on health-related quality of life (EQ-5D and EQ-VAS) and psychological distress (HAD) according to sick-leave.*

	Before				Duration of pain after treatment	12 months			
Work ability	**EQ-5D Index mean (SD) n**	**EQ-VAS mean (SD) n**	**HAD-A mean (SD) n**	**HAD-D mean (SD) n**	**Days mean (SD) n**	**EQ-5D Index mean (SD) n**	**EQ-VAS mean (SD) n**	**HAD-A mean (SD) n**	**HAD-D mean (SD) n**
0%	0.137 (0.238) n = 179	39 (18) n = 156	7.3 (4.6) n = 154	8.5 (4.4) n = 154	11.9 (11.9) n = 179	0.407 (0.377) * n = 77	51 (24) # n = 77	7.2 (6.0) n.s. n = 22	7.3 (5.1) n.s. n = 22
25 %	0.268 (0.293) n = 18	39 (15) n = 18	7.1 (3.9) n = 13	7.4 (4.2) n = 13	12.8 (11.5) n = 18	0.654 (0.219) ʀ n = 6	60 (13) ʊ n = 6	-	-
50 %	0.187 (0.252) n = 34	39 (20) n = 30	6.1 (4.1) n = 28	7.6 (5.1) n = 28	15.2 (9.1) n = 34	0.627 (0.234) * n = 16	60 (20) € n = 16	4.8 (3.3) n.s. n = 5	2.8 (2.0) ¥ n = 5
75 %	0.373 (0.294) n = 22	50 (15) n = 21	4.4 (3.2) n = 16	6.1 (3.7) n = 16	15.9 (14.4) n = 22	0.666 (0.310) þ n = 12	75 (14) * n = 12	5 (4.2) n.s. n = 2	5 (5.7) n.s. n = 2
100 %	0.340 (0.314) n = 77	48 (18) n = 73	6.9 (3.9) n = 64	7.3 (4.4) n = 64	14.3 (11.2) n = 77	0.683 (0.240) * n = 35	68 (20) * n = 34	6.6 (4.9) n.s. n = 14	6.1 (5.0) n.s. n = 14
Region	EQ-5D index	EQ-VAS	HAD-A	HAD-D	Days	EQ-5D index	EQ-VAS	HAD-A	HAD-D
Cervical	0.256 (0.285) n = 54	48 (20) n = 50	6.6 (4.0) n = 43	7.2 (4.6) n = 43	14.0 (11.4) n = 34	0.545 (0.303) * n = 24	63 (19) * n = 24	8.2 (5.2) n.s. n = 6	7.2 (4.2) n.s. n = 6
Thoracic	0.218 (0.290) n = 70	42 (19) n = 68	7.8 (4.4) n = 60	7.9 (4.4) n = 60	13.4 (12.4) n = 50	0.503 (0.346) * n = 36	57 (24) * n = 36	5.9 (5.2) n.s. n = 14	4.6 (4.9) n.s. n = 14
Lumbar	0.205 (0.276) n = 184	41 (17) n = 162	6.6 (4.3) n = 160	8.0 (4.5) n = 160	11.7 (11.1) n = 125	0.530 (0.364) * n = 83	58 (24) * n = 83	7.0 (5.5)n.s. n = 21	7.1 (5.2) n.s. n = 21
Gender	EQ-5D index	EQ-VAS	HAD-A	HAD-D	Days	EQ-5D index	EQ-VAS	HAD-A	HAD-D
Men	0.218 (0.302) n = 114	44 (19.0) n = 103	6.9 (4.5) n = 97	8.7 (4.6) n = 97	11.2 (12.0) n = 114	0.524 (0.324) * n = 51	62 (22.1) * n = 50	5.8 (6.1) n.s. n = 12	6.9 (4.8) n.s. n = 12
Women	0.209 (0.268) n = 217	41 (17.7) n = 196	7.0 (4.3) n = 179	7.5 (4.4) n = 179	14.2 (11.4) n = 217	0.533 (0.356) * n = 96	57 (23.5) * n = 96	6.9 (4.9) n.s. n = 31	6.0 (5.0) n.s. n = 31
All	0.212 (0.280) n = 331	42 (18.2) n = 299	6.9 (4.3) n = 276	7.9 (4.5) n = 276	13.1 (11.7) n = 331	0.530 (0.344) * n = 147	59 (23.1) * n = 146	6.6 (5.2) n.s. n = 43	6.3 (4.9) n.s. n = 43

* $P < 0.0001$, # $P = 0.0001$, € $P = 0.0015$, ¥ $P = 0.0024$, ʀ $P = 0.0053$, ʊ $P = 0.0081$, þ $P = 0.0137$, n.s. $P > 0.05$
EQ-5D, EuroQol five-dimensional questionnaire; EQ-VAS, EuroQol visual analog scale; HAD, Hospital Anxiety and Depression scale.

Table 6. *Calculation of costs.*

		IPM	
		Costs	**Reduced costs**
Costs for assessment and diagnostic procedures n = 873 patients Health care costs Time Travel costs Total costs:	 3,788 procedures (eTable 1 for cost/procedure) 2,759 visits * 4 h/visit 2,759 visits * 300 km/visit 	 11,030,100 2,394,812 1,489,860 14,914,772	
Treatment costs n = 331 patients Health care costs Time Travel costs Total treatment cost:	 SEK 5,500/patient 4 h/patient 300 km/patient 	 1,820,500 287,308 178,740 2,286,548	
Cost of pain-related medication	Reduction of 68628 defined daily doses (DDD) per annum (128,276 to 59,648) Antiemetics/constipation drugs -34% NSAID -70% Muscle relaxants -71% Opioids -53% Antiepileptics -66% Hypnotics/sedatives -48% Antidepressants -55%		-1,101,072
Health consumption Outpatient care Inpatient care	Reduction of 2,156 visits (2,660 to 504) Reduction of 8 care-days (72 to 64) Increase of 4 daycare days (0 to 4)		-8,175,552 -91,384 +15,168
Sick leave n = 151 patients After RF denervation Changed ability to work after 12 months	 4 weeks at SEK 34400/patient Increase of 2.75 full time work, SEK 407,906/year	 3,914,680 	 -1,121,890
Subtotal		21,091,160	-10,474 730
Total costs costs/pt		10,641,270 32,149	
Total QALY-gained after 12 months	331 pt		48.08
Cost/QALY-gained		221,324	

the number of patients > 66 years, and the duration of sick leave after RFD. All scenarios yielded a cost/QALY gained below SEK 500,000.

An increase/decrease of 10% in the treatment costs yielded a cost/QALY gained of SEK 248,052 and 194,597, respectively. A similar increase/decrease of health care consumption yielded cost/QALY gained of SEK 238,487 and 204,162, respectively. Increasing the time per visit and travel costs to 16 h and 300 km increased the cost/QALY gained to SEK 388,678, whereas reducing the time and travel costs to 4 h and 50 km changed the cost/QALY gained to SEK 169,366.

When taking a health care perspective and calculating the cost-utility using health care costs, medication costs and health care consumption, the cost/QALY gained was SEK 72,749 (~$8,548).

Discussion

Main Findings

The aims were to (i) describe the characteristics of the patients, (ii) compare the patients' HRQoL at the first visit to when they were ready for treatment with RFD, (iii) calculate the gain in QALY, and (iv) investigate

Table 7. *Sensitivity analysis. Cost/QALY gained (SEK).*

Cost/QALY gained (SEK)		Amount of patients diagnosed with ZJP			Amount of patients diagnosed with ZJP			Amount of patients diagnosed with ZJP		
		30,00%	37.9%	50,00%	30,00%	37.9%	50,00%	30,00%	37.9%	50,00%
Age of Patients	Sick-leave after RFD	Duration of effect 1 year			Duration of effect 2 years			Duration of effect 4 years		
All patients under 67 years old	No sick-leave	216434	134738	60032	101326	63079	28105	49099	30566	13619
	2 weeks	228845	147150	72444	107136	68889	33915	51915	33382	16434
	4 weeks	24157	159561	84855	112947	74700	39726	54731	36198	19250
18% retired patients	No sick-leave	221600	139904	65198	103744	65497	30523	50271	31738	14791
	2 weeks	262310	180614	105908	122803	84556	49582	59507	40974	24026
	4 weeks	303020	221324	146618	141862	103615	68641	68742	50209	33261

RFD, radiofrequency denervation; ZJP, zygapophyseal joint pain; QALY, Quality Adjusted Life Years.

whether IPM with RFD was cost-effective in terms of the cost/QALY gained.

The extremely low HRQoL reported before treatment is similar to that reported in other Swedish studies of patients with chronic pain (21,39,40). There were no significant differences in the characteristics or HRQoL between the patients diagnosed with ZJP and all patients assessed at the clinic. The most striking finding is the significant increase in HRQoL following RFD (0.212 to 0.530).

RFD for ZJP was cost-effective, with a cost/QALY gain of SEK 221,324 (USD ~26,008), which is within the range of "moderate" according to the Swedish NBHW (37,38).

The Swedish NBHW applies 4 criteria when setting priorities for health care: the severity of the condition, the effectiveness of the treatment, the cost-effectiveness of the treatment, and the evidence base. The overall judgement is based on a combination of these criteria. The severity of the condition is clearly demonstrated in this and other studies (13,21,39-41). Although few studies have examined the effectiveness of RFD for ZJP, the present study suggests that this treatment modality shows great potential in terms of improving HRQoL. If the diagnostic criteria for selecting candidates for RFD and the RFD procedure are set according to established guidelines (7,9,14,15,42,43), there is a strong evidence supporting this treatment. Although the present observational study is not perfect, it adds to the overall evidence base, and the marked improvement in HRQoL cannot be reasonably explained by a placebo effect. Based on this rationale, IPM focusing on the treatment of ZJP should be given a high rank when setting priorities in health care.

Strengths and Weaknesses of the Present Study

The strength of this study is that we took a societal perspective and did not focus solely on health care costs. Another strength is that we placed a monetary value on the patients' time, regardless of whether the patient was retired or on permanent sick leave, which means that the costs can be extrapolated to other settings with younger patients or if fewer patients are on permanent sick leave. Furthermore, the study included the procedures and costs incurred during the diagnostic process, even for patients not diagnosed and therefore not treated. A total of 3,788 diagnostic procedures were performed on 873 patients to determine the source of pain, of which 331 patients were diagnosed with ZJP (Tables 1 and 6). Therefore, the study reflects the results that can be achieved in real life when following strict guidelines for the diagnosis and treatment of ZJP. Another strength is that data on health care and medication use were obtained from Swedish national registers, thus reducing the effects of recall bias. Furthermore, we estimated the productivity loss based on the patients' self-reported ability to work, and not sickness benefits from social insurance (44), a parameter that is sensitive to changes in eligibility criteria over time (45,46).

A weakness of the study is that we only had data from a single clinic. However, with only 3 physicians, it was easier to adhere to the study protocol. Other

weaknesses of this study are its observational design and the lack of randomization and a control group. However, the duration of pain before the first assessment was very long (122 months, Table 1), and the interval between the first visit and RFD ranged from 2 days to 2.8 years, without a significant difference in the mean EQ-5D index between these time-points and no correlation between the time and the change in HRQoL. Because we found no significant improvement in HRQoL between the first visit and the time of RFD, the patients could serve as their own controls.

Comparison with Other Studies

To the best of our knowledge, the present study is one of the first cost-effectiveness studies of IPM (in this case RFD) for the treatment of ZJP. Until recently, economic evaluations of IPM have used a health care perspective and focused on therapeutic blocks as a treatment (47,48) or cost-utility was based on reimbursement costs (15,49,50). The selection process in our clinic strictly complied with international guidelines, ensuring our results are applicable in an international context. In contrast to prior cost-utility studies of different interventional techniques (47-49,51), we took a societal perspective that included not only health care costs but also the costs associated with the patients' time and the diagnostic costs incurred in patients who did not have ZJP. When calculating the cost/QALY gained from a health-care perspective, we achieved comparable results (SEK 72,749, ~$8,548) to those prior studies ($2,200 - $4,261) (47-53), although those studies were calculated using reimbursement costs and an estimation of overall costs.

The increase in HRQoL was accompanied by a reduction in pain-related medications and health care use. A reduction in pain-related medications was reported by Cunningham et al. after a pain rehabilitation program (57), and by McCormick et al. and Burnham et al. after RFD (10,58). Although Turk hypothesized that pain rehabilitation programs should be able to reduce medication costs (59), this possibility was not confirmed in published studies. In contrast, Gauthier et al (60) provided an updated review of the clinical effectiveness, cost-effectiveness, and guidelines for multidisciplinary treatment programs for patients with chronic pain and concluded that "no relevant cost-effectiveness studies were identified."

Other studies have examined the cost-effectiveness of rehabilitation programs, using reduction in sick-leave benefits as outcome (60-64). The use of HRQoL measures such as QALY for evaluating pain management has been discussed in the pain rehabilitation scientific community (57,65,66), because no latent construct has been found in QALY. However, EQ-5D and QALYs are formative measures without a latent construct, which is apparent from the absence of internal correlation (67). The present study shows that it is possible to use general measures, such as HRQoL and QALY, to evaluate treatments for chronic pain and to perform cost-effectiveness studies in this setting, as is widely done in other clinical settings. Recently, a cost-utility analysis of pain rehabilitation in primary care setting in Sweden gave comparable results as we had, although it only used a partial societal perspective (41).

Pain rehabilitation programs in specialized care are currently the gold standard for treating chronic pain in Sweden (68). The next step should be to perform a similar cost-effectiveness analysis of patients who undergo pain rehabilitation programs according to Swedish guidelines.

Conclusions

Patients referred for IPM in Sweden report extremely low HRQoL. Treatment of ZJP with RFD resulted in a significant increase in HRQoL (from 0.212 to 0.530). RFD was cost-effective, with a cost/QALY gained of SEK 221,324 (USD ~26,008). Furthermore, the sensitivity analysis demonstrated the stability of the cost-effectiveness values in different scenarios. Therefore, RFD is a cost-effective treatment that meets the Swedish NBHW criteria as a high priority treatment.

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Supplement 1. *Template for semistructured interview*

Topic	Description
Problem	What are the main pain problems? Where is it located? Radiation?
Sympathetic	Subjective autonomic nervous system problems:
	Sensory: hyperesthesia and/or allodynia
	Vasomotor: temperature asymmetry, skin color changes, color asymmetry
	Sudomotor/edema: edema, sweating, sweating asymetry
	Motor/trophic: Decreased range of motion, weakness, tremor, dystonia, trophic changes (hair, skin, nail)
	Problems to pass urine, incontinence, obstipation
	Eye-problems (focusing, pupillary adjustments)
Start	How did the pain start? Trauma? What trauma and how? How was it transferred into chronic pain?
Other problems	Other diseases? Previous problems before the chronic pain?
Previous treatments	Pain rehabilitation programs? Surgery? Interventional pain managements? Dorsal column stimulation?
Painlevel	Visual analogue scale (When the least pain, when worst pain and in average last week)
Pain description	How does it feel? Itching? Pricking? Burning? Ask the patient to describe with own words.
Worsening	What activities makes the pain worse? Getting cold? Changes during the day?
Better	Are there activities that can make the pain better?
Sleep	How long time before falling asleep?
	How many times do you wake up during the night?
	Overall perception of sleep. Do you still feel tired when waking up or are you relieved?
Medication	What medications do you take. Doses.
Work	What are you working as? On sick-leave? What percent are you working if any?
Social	Family description (children, living alone or with a partner)
	Psychological distress. Anxiety? Depression? Suicide?
Goal	Why are you here? What do you hope to achieve by attending? What do you hope we can help you with?

The interview is performed with minimal feed back, in order to receive information as free as possible from the influence of the interviewer. The aim is to collect information about feelings and believes that the patient has, regardless whether the interviewer understands it or see it as relevant. The consideration and evaluation of the information is postponed until after the physical examination.

Supplement 2. *Procured reimbursements for diagnostic and therapeutic procedures (SEK).*

Procedure	**Reimbursement**
Pain analysis assessment at first visit	3100
Assessment without other procedures	900
Interlaminar root-blocks	2400
Transforaminal root-blocks	3100
Medial branch blocks	3100
Intraarticular joint injections	1800
SI-joint injections	3400
Lateral branch blocks	3900
Radiofrequency denervation of medial branch	5500
Radiofrequency denervation of lateral branch (SI-joint)	6000
Sympathetic nervous system blockade	3100
Other nerve blocks	1800

Supplement 3. *Selected ATC-codes defining medication associated to chronic pain.*

ATC-codes (part of)	**Description**
A04A	Antiemetics and antinauseants
A06A	Drugs for constipation
M01A	Antiinflammatory and antirheumatic products, non-steroids
M02AA	Antiinflammatory preparations, non-steroids for topical use
M02AB	Capsaicin and similar agents
M03A	Muscle relaxants, peripherally acting agents
M03B	Muscle relaxants, centrally acting agents
N02A	Opioids
N02B	Other analgesics and antipyretics
N02C	Antimigraine preparations
N03A	Antiepileptics
N05A	Antipsychotics
N05B	Anxiolytics
N05C	Hypnotics and sedatives
N06A	Antidepressants
N07BC	Drugs used in opioid dependence

Supplement 4. ICD-10 codes associated to chronic pain.

ICD-Code chapter	Description	Relevance for chronic pain
A00 – B99	Infections	No
C00 – D48	Malignancies	No
D50 – D89	Diseases in blood and immunological system	No
E00 – E90	Endocrine diseases	No
F00 – F03	Dementia	No
F04 – F09	Organic psychosis	No
F10 – F19	Psychological symptoms from drugs	Yes
F20 – F21	Schizophrenic	No
F22 – F29	Psychotic symptoms	Yes
F30 – F39	Depressive and maniac problems	Yes
F40 – F48	Neurotic and stress-related syndromes	Yes
F50 – F59	Behavioral problems and insomnia	Yes
F60 – F69	Personality disorders	No
F70 – F79	Mental retardations	No
F80 – F89	Psychological retardations	No
F90 – F98	Behavioral and emotional problems	No
F99	Unspecific psychological problem	Yes
G00 – G09	Inflammatory diseases in CNS	No
G10 – G14	Atrophic diseases	No
G20 – G26	Diseases in basal gangliae	No
G30 – G32	Degenerative diseases	No
G35 – G37	Demyelinated diseases	No
G40 – G41	Epileptic diseases	No
G43 – G44	Migraine and headache	Yes
G45 – G46	Vascular diseases in the CNS-reactions	No
G47 – G47	Insomnia	Yes
G50 – G59	Mononeuropaties	Yes
G60 – G64	Polyneuropaties	Yes
G70 – G73	neuromuscular transmission diseases	Yes
G80 – G83	Cerebral paresis and hemiparesis	Yes
G90 – G99	Other neurological diseases	Yes
H00 – H59	Eye diseases	No
H60 – H95	Ear diseases	No
I00 – I99	Vascular diseases	No
J00 – J99	Respiratory diseases	No
K00 – K93	Gastrointestinal diseases	No
L00 – L99	Dermatological diseases	No
M00 – M99	Musculoskeletal diseases	Yes
N00 – N99	Urinary tract diseases	No
O00 – O99	Obstetric diseases	No
P00 – P96	Neonatal diseases	No
Q00 - Q99	Congenital problems	No
R00 – R09	Symptoms from vascular & respiratorysystem	No
R10 – R19	Symptoms from gastrointestinal system	No
R20 – R23	Symptoms from skin	No
R25 – R29	Symptoms from nerve- and musculoskeletal system	Yes
R30 – R39	Symptoms from urinary tract	No
R40 – R46	Psychological & behavioral symptoms	Yes
R47 – R49	Symptoms from speech	No
R50 – R69	General symptoms	Yes
R70 – R89	Aberrant findings in blood, urine and other bodyfluids	No
R90 – R94	Aberrant radiological findings	Yes
R95 – R99	Unknown or not defined causes of death	Yes
S00 – T98	Injuries and intoxications	No
V01 – Y98	External causes of injury and disease	No
Z00 – Z99	Other causes for health-care contact	No