Cost Utility Analysis

Cervical Interlaminar Epidural Injections In The Treatment Of Cervical Disc Herniation, Post Surgery Syndrome, Or Discogenic Pain: Cost Utility Analysis From Randomized Trials

Laxmaiah Manchikanti, MD[1,2], Vidyasagar Pampati, MSc[1], Allan Parr, III, MS4[2], Maanasa V. Manchikanti[3], Mahendra R. Sanapati, MD[4], Alan D. Kaye, MD, PhD[5], and Joshua A. Hirsch, MD[6]

From: [1]Pain Management Centers of America, Paducah, KY; [2]Louisiana State University School of Medicine, Shreveport, LA; [3]University of Kentucky, Lexington KY; [4]Pain Management Centers of America, Evansville, IN [5]Louisiana State University Health Science Center, New Orleans, LA; and [6]Massachusetts General Hospital and Harvard Medical School, Boston, MA.

Additional Author Affiliation Information on P. 428.

Address Correspondence: Laxmaiah Manchikanti, MD 2831 Lone Oak Road Paducah, Kentucky 42003 E-mail: drlm@thepainmd.com

Disclaimer: There was no external funding in the preparation of this manuscript. Conflict of interest: Dr. Kaye is a speaker for Merck. Dr. Hirsch is a consultant for Medtronic.

Manuscript received: 07-10-2019 Revised manuscript received: 07-28-2019 Accepted for publication: 08-22-2019

Free full manuscript: www.painphysicianjournal.com

Background: Neck pain is one of the major conditions attributing to overall disability in the United States. There have been multiple publications assessing clinical and cost effectiveness of multiple modalities of interventions in managing chronic neck pain. Even then, the literature has been considered sparse in relation to cervical interlaminar epidural injections in managing chronic neck pain.

In contrast, cost utility studies of lumbar interlaminar injections, caudal epidural injections, cervical and lumbar facet joint nerve blocks, percutaneous adhesiolysis demonstrated costs of less than $3,500 for quality-adjusted life year (QALY).

Objectives: To assess the cost utility of cervical interlaminar epidural injections in managing chronic neck and/or upper extremity pain secondary to cervical disc herniation, post-surgery syndrome in neck, and axial or discogenic neck pain.

Study Design: Analysis based on 3 previously published randomized trials of the effectiveness of cervical interlaminar epidural injections assessing their role in disc herniation, cervical post-surgery syndrome, and axial or discogenic pain.

Setting: A contemporary, private, specialty referral interventional pain management center in the United States.

Methods: Cost utility of cervical interlaminar epidural injections with or without steroids in managing cervical disc herniation, cervical post-surgery syndrome, and cervical discogenic or axial neck back pain was conducted with data derived from 3 randomized controlled trials (RCTs) that included a 2-year follow-up, with inclusion of 356 patients. The primary outcome was significant improvement defined as at least 50% in pain reduction and disability status. Direct payment data from all carriers from 2018 was utilized for the assessment of procedural costs. Overall costs, including drug costs, were determined by multiplication of direct procedural payment data by a factor of 1.67 to accommodate for indirect payments respectively for disc herniation, discogenic pain, and cervical post-surgery syndrome.

Results: The results of the 3 RCTs showed direct cost utility for one year of QALY of $2,412.31 for axial or discogenic pain without disc herniation, $2,081.07 for disc herniation, and $2,309.20 for post surgery syndrome, with an average cost per one year QALY of $2,267.57, with total estimated overall costs with addition of indirect costs of $3,475.38, $4,028.55, $3,856.36, and $3,785.89 respectively.

Limitations: The limitation of this cost utility analysis includes that it is a single center evaluation. Indirect costs were extrapolated.

Conclusion: This cost utility analysis of cervical interlaminar epidural injections in patients nonresponsive to conservative management in the treatment of disc herniation, post surgery syndrome and axial or discogenic neck pain shows $2,267.57 for direct costs with a total cost of $3,785.89 per QALY.

Key words: Cervical interlaminar epidural injections, chronic neck pain, cervical disc herniation, cervical discogenic pain, post surgery syndrome, cost utility analysis, cost effectiveness analysis, quality-adjusted life years

Pain Physician 2019: 22:421-431

Chronic neck pain is one of the leading sources of global disability with a substantial burden on the health care system and society, with loss of productivity and consumption of a large proportion of health care resources (1). In assessing U.S. spending on personal health care and public health and factors associated with the increase in U.S. health care spending from 1996 to 2003, Dielman et al (2,3) reported yearly spending of $87.6 billion for low back and neck pain. In this regard, expenses for low back and neck pain accounted for the third highest amount. Other studies from 1990 to 2016 have demonstrated that morbidity and chronic disability now account for nearly half of the United States health burden, despite substantial progress and improvements in health (4,5). Further, it also has been shown that neck pain ranked number 3 in the United States among the 30 leading diseases and injuries contributing to years lived with disability in 2010, whereas low back pain ranked number one (4). Even though neck pain has been estimated to be low in prevalence, the estimates of regional pain have shown neck pain as number 2 in its ranking with 32% prevalence (6). Global burden of the neck pain and disability also have shown a point prevalence of neck pain of 4.9%, with a significant proportion of patients suffering from chronic neck and arm pain with a high disability index (7).

Among the multiple causes of chronic neck and upper extremity pain, cervical disc herniation, axial or cervical discogenic pain without disc herniation, central spinal stenosis, and finally cervical post surgery syndrome have been described as common conditions leading to multiple modalities of treatments (8-31). Multiple modalities including surgical interventions have been increasing rapidly (18-22), non-steroidal anti-inflammatory agents (8,24), antiepileptic drugs (23), opioids (24-29,31), and finally interventional techniques including epidural injections and facet joint interventions (10,11). The most expensive categories are the surgical interventions with a certain rate of failure and also with the need for treatments following surgery including repeat surgery, epidural injections, physical therapy, and drug therapy (21,32). In fact, failure rates have been shown to range from 13.4% to 32% resulting in cervical post surgery syndrome (21,32). However, Rihn et al (33) in an analysis of economic outcomes of recalcitrant cervical radiculopathy concluded that anterior cervical fusion remained the dominant strategy compared with cervical epidural injections if the surgical avoidance rate of such injections was less than 50% in cervical radiculopathy. Further, they commented that if there is a greater than 50% surgery avoidance rate with injections, the cervical epidural injections would be considered a cost-effective strategy with a role in the management of cervical radiculopathy before surgery. This assessment was not based on randomized controlled trials (RCTs), it was limited to an economic analysis based on surgical practices. In fact, a systematic review and meta-analysis of the role of epidural injections to prevent surgical intervention in patients with chronic sciatica (34) showed a significant improvement with avoidance of surgery in 80% of the patients. In addition, epidural injections are also a treatment in post surgery syndrome with clinical effectiveness and cost utility (8,9,35-37). Overall, interventional techniques have been shown to be clinically effective, with appropriate cost utility with multiple interventions (8,9,33-53). Challenges with evidence assessment for cost utility analysis are that they have been reported to be redundant, inappropriate, and biased (34,54-67).

Cervical interlaminar epidural injections are the preferred methodology for cost utility analysis due to complications related to cervical transforaminal epidural injections (68,69). Thus, the use of cervical interlaminar epidural injections has been increasing steadily (10,11), despite the decline in the utilization of other interventions including lumbar interlaminar epidural injections, but less than a multitude of other interventions including facet joint interventions and sacroiliac joint interventions (36,70). The use of cervical/thoracic interlaminar epidural injections have increased 108% per 100,000 Medicare beneficiaries from 2000 to 2016, with a smaller increase of 4% noted from 2009 to 2016 compared to 101% from 2000 to 2009.

Escalating health care costs and continuous debates on the effectiveness of multiple interventions, cost effectiveness or cost utility analysis has become a cornerstone in health policy including for epidural injections (35,36,51-53,71-77). Further, multiple assessments have shown significant improvements with non-operative treatment including epidural injections with avoidance of surgery in at least 50% of the patients in cervical radiculopathy and 80% in sciatica (31,32). Despite these encouraging results, inappropriately performed cost utility analyses (78,79) have yielded either poor (78) or mixed results (79).

Based on the Spine Patient Outcomes Research Trial (SPORT) literature with 2 well publicized cost effectiveness studies of surgical versus non-operative treatment for lumbar disc herniation (75) and spinal stenosis

with and without degenerative spondylolisthesis (76), gold standards of cost utility analysis were published. These studies showed cost per quality-adjusted life year (QALY) in managing lumbar disc herniation of $69,403 and $77,600 in managing spinal stenosis without degenerative spondylolisthesis and $115,600 in managing spinal stenosis with degenerative spondylolisthesis. Based on these landmark studies by Tosteson et al (75,76), direct costs were attributed to 60% of the total in spinal stenosis and 68% in disc herniation, and 71% in spinal stenosis with degenerative spondylolisthesis, with highest indirect costs for spinal stenosis of 40%, Manchikanti et al (51-53) utilized direct medical costs at 60% and multiplied the direct cost data by 1.67%, deriving overall cost utility.

In this assessment, therefore, the present investigation sought to derive a reliable and valid overall assessment of cost utility data with assessment of direct costs and addition of indirect costs utilizing 3 cervical interlaminar epidural injection RCTs in disc herniation, discogenic pain without disc herniation or facet joint pain, and post cervical surgery syndrome with chronic neck pain and upper extremity pain with a 2-year-follow-up (80-82).

Methods

Study Design

The cost utility analysis for this assessment was performed based on 3 double-blind RCTs, which assessed effectiveness of cervical interlaminar epidural injections in managing chronic neck pain secondary to disc herniation (80), discogenic or axial pain without disc herniation or facet joint pain (81), and cervical post surgery syndrome (82). The methodology utilized in performing these studies has been described in their respective manuscripts (80-82). Appropriate diagnosis was established in all patients with disc herniation, axial or discogenic pain, and cervical post surgery syndrome based on a multitude of investigations including diagnostic facet joint nerve blocks in patients with discogenic pain. Further, all the patients had failed conservative management with a structured exercise program, physical or occupational therapy, and drug therapy.

Outcome Measures

Outcome measures included pain rating and disability status. Pain rating was determined on an 11-point Numeric Rating Scale (NRS) and disability and functional status was assessed based on a 50-point Neck Disability Index (NDI). Intermittent post treatment outcomes were assessed for 2 years. Primary outcome was determined as significant improvement of 50% reduction in pain and increase in function.

Analysis

A total of 356 patients were studied among the 3 studies. Two of the studies with disc herniation (80) and discogenic pain (81), utilized 120 patients total in each study, whereas in post surgery syndrome (82) there were 116 patients. In each trial these patients were assigned to either a control group receiving 5 mL of 0.5% local anesthetic only or an intervention group receiving 4 mL of 0.5% local anesthetic mixed with 6 mg of 1 mL of Celestone.

For analysis of the direct procedural cost utility, actual reimbursement rates by various carriers (not Medicare allowed rates) were utilized from 2018 for calculating costs for physician services and the facility costs based on each patient's payer status. Overall costs were estimated by multiplying direct procedural costs by a factor of 1.67 based on previous studies (75,76).

Results

Patient Flow

Figure 1 shows the patient flow diagram for all 3 RCTs (80-82).

Outcomes

Table 1 shows characteristics of pain relief and functional status improvement as evaluated by Numeric Rating Scale (NRS) and Neck Disability Index (NDI). There was no significant difference between patients undergoing cervical interlaminar epidural injections for either discogenic pain, disc herniation, or pain of post surgery syndrome. Figure 2 shows the proportion of patients with significant reduction in pain scores and improvement in NDI scores.

Adverse Events

No additional costs were incurred due to adverse events occurring in any of the 356 patients during the study period.

Cost Utility Analysis

Cost utility analysis was based on the quality of life improvement and cost for procedure per QALY based on the primary outcomes of pain relief and improvement in functional status. As shown in Table 2, direct

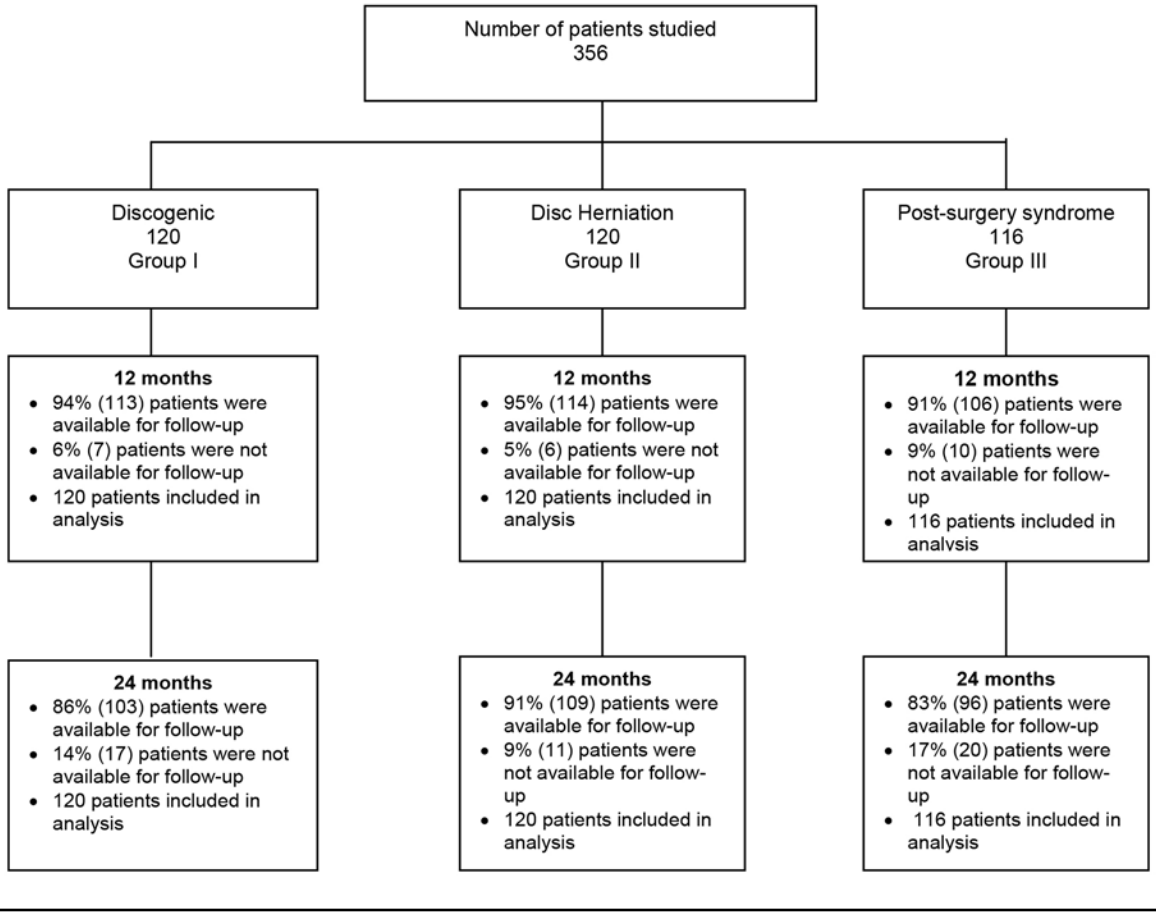

Fig. 1. *Patient flow diagram of randomized controlled trials of cervical interlaminar epidural injections.*

cost utility for one-year improvement in QALY was $2,412.31 for axial or discogenic pain without disc herniation, $2,081.07 for disc herniation, and $2,309.20 for post surgery syndrome. Overall direct procedural cost utility for one year of improvement in quality of life was $2,847.57. Average total direct cost per patient in 2 years was $22,847.57. Total costs for one-year improvement of quality of life with multiplication of direct cost by a factor of 1.67 showed cost utility of $4,028.55 for discogenic pain per QALY, $3,475.38 for disc herniation per QALY, $3,856.36 for post surgery syndrome per QALY, and $3,785.89 on average for all cervical epidural injections per QALY.

Discussion

The cost utility analysis was derived from 3 RCTs with a 2-year follow-up with data from 356 patients, nonresponsive to conservative management, undergoing cervical interlaminar epidural injections with appropriate outcomes data utilizing significant improvements defined as 50% improvement in pain and functional scores. The outcomes results showed significant improvement in 71% of the patients at the end of 2 years. The overall costs with direct costs added to extrapolated indirect costs resulting in overall cost of $4,028.55 for one year of quality of life improvement for discogenic pain. In patients with discogenic pain without disc herniation or facet joint pain, $3,475.38 for patients with disc herniation and $3,856.36 for post surgery syndrome with an overall cost utility rate of $3,785.89 for cervical interlaminar epidural injections in 356 patients. Further, there was no significant difference in patients either receiving local anesthetic alone or local anesthetic with steroids. The costs were higher,

Table 1. *Pain relief and functional status improvement evaluated by and Neck Disability Index (NDI).*

	Group I Discogenic Pain	Group II Disc Herniation	Group III Post surgery Syndrome	Pooled
Numeric Rating Score				
Baseline	7.7 ± 0.9	7.9 ± 0.9	8.0 ± 0.9	7.9 ± 0.9
6 months	3.6* ± 1.3 (78%)	3.7* ± 1.4 (78%)	3.7 ± 1.4 (76%)	3.7 ± 1.4 (77%)
12 months	3.6* ± 1.3 (78%)	3.8* ± 1.5 (72%)	3.8 ± 1.4 (74%)	3.7 ± 1.4 (74%)
24 months	3.6* ± 1.5 (75%)	3.7* ± 1.6 (70%)	3.7 ± 1.6 (71%)	3.7 ± 1.5 (72%)
Oswestry Disability Index				
Baseline	29.1 ± 5.6	29.4 ± 5.7	30.2 ± 4.9	29.6 ± 5.4
6 months	14.5* ± 5.8 (71%)	14.5* ± 6.2 (78%)	15.5* ± 6.4 (73%)	14.8* ± 6.1 (74%)
12 months	14.3* ± 5.9 (72%)	14.5* ± 6.4 (72%)	15.1* ± 6.3 (73%)	14.6* ± 6.2 (72%)
24 months	14.0* ± 6.1 (73%)	14.0* ± 6.3 (72%)	14.8* ± 6.4 (71%)	14.2* ± 6.3 (72%)

(_____) illustrates proportion with significant pain relief (≥ 50%) from baseline
* significant difference with baseline values (P < 0.001

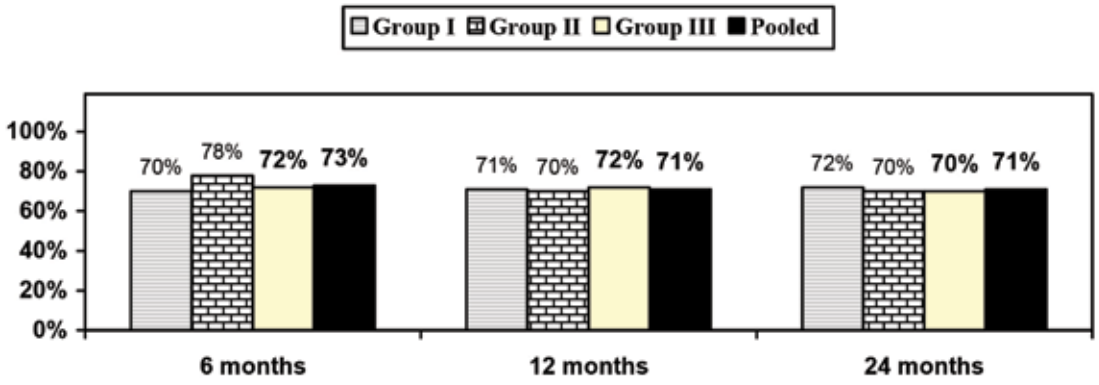

Fig. 2. *Proportion of patients with significant reduction in numeric rating score and neck disability index (>= 50% reduction from baseline).*

though statistically insignificant, in patients with axial or discogenic pain due to larger than average treatments compared to disc herniation and postsurgery syndrome [5.7 ± 2.4 versus 5.4 ± 2.6 or 2.7] with slightly lesser significant improvement per procedure compared to disc herniation, but similar to post surgery syndrome. In contrast, a lumbar discogenic pain with lumbar interlaminar epidural injections, costs were lower. The significant improvement was higher in discogenic pain group compared to central spinal stenosis.

The results of the present assessment reflect similar cost utility analysis rates with caudal epidural injections and lumbar epidural injections with or without steroids (35,51-53). For lumbar interlaminar epidural injections (51), overall cost was shown to be $3,301 and for caudal epidural injections (35) it was $3,628. These total costs were also similar to therapeutic lumbar facet joint nerve blocks with a cost of $4,432 for QALY (52), and also cervical facet joint nerve blocks with a cost of $4,261, and percutaneous adhesiolysis with a cost of

Table 2. *Analysis of cost effectiveness of cervical epidural injections in managing pain and disability of disc herniation, discogenic pain, and post surgery syndrome.*

	Group I Discogenic Pain	Group II Disc Herniation	Group III Post surgery Syndrome	Pooled
Number of patients	120	120	116	356
Total number of procedures for 2 years	689	654	627	1971
Number of treatments for 2 years per patient (mean) ± SD	5.7 + 2.4	5.4 + 2.7	5.4 + 2.6	5.5 + 2.5
Number of weeks with significant improvement for all patients in the study in weeks	8,093	7,900	7,254	23,247
Average total relief in two year per patient				
Significant improvement in weeks per procedure (mean) ± SD	11.6 + 7.7	12.6 + 12.0	11.4 + 8.6	11.9 + 9.6
Total Cost ($)				
Physician	$89,321	$95,130	$82,162	$266,614
Facility	$286,117	$221,033	$239,971	$747,121
Total	$375,439	$316,163	$322,133	$1,013,735
Cost per procedure ($)				
Physician	$129.64	$145.46	$131.04	$135.27
Facility	$415.26	$337.97	$382.73	$379.06
Total	$544.90	$483.43	$513.77	$514.33
Average total direct costs per patient in 2 years	$3,128.66	$2,634.69	$2,777.01	$2,847.57
Direct procedural improvement in quality of life ($) per one year	$2,412.31	$2,081.07	$2,309.20	$2,267.57
Indirect costs including drug costs for 1-year improvement in quality of life ($)	$1,616.25	$1,394.32	$1,547.16	$1,519.27
Total estimated costs including procedural costs, costs of medicine and other indirect costs for 1-year improvement in quality of life ($)	$4,028.55	$3,475.38	$3,856.36	$3,785.89

All the payments based 2018 allowed rates
SD = standard deviation

$4,426 (53). However, these costs are lesser than spinal cord stimulation of £5,624 (about $8,400 in 2010) for QALY (77). The costs are very similar as all other studies performed by Manchikanti et al (35,51-53) provided similar methodology and were performed in the same clinical setting with a pragmatic approach in an ambulatory surgery setting. However, these results were superior to other lumbar epidural injection studies. Whynes et al (83) with lumbar interlaminar epidural injections with £8,975 (about $13,500 in 2012) per QALY, which was more expensive than spinal cord stimulation, and short-term evaluation of cost utility by appropriate analysis by Carreon et al (78) only in failed patients with $62,175 per QALY and short-term assessment of cervical epidural injections in a 3 month pilot study in a small number of patients by Alvin et al (79) with a cost utility of $21,884 per QALY gained.

Looking at a global picture analysis of various modalities of interventions utilized in spine treatment, only 45% of the cost utility studies showed costs less than $100,000 per QALY, compared to 23% of the costs showing greater than $100,000 per QALY (72). Similar results were also reported by others even though the majority of the reviews showed greater value with non-operative treatments (73). With specific analysis in cost utility analysis in the neck pain, Furlan et al (74) showed that alternative medicine treatments such as acupuncture for neck pain was associated with significantly higher total cost compared to usual care (£1,565 versus £1,496) with $12,469 per QALY gained in patients with chronic neck pain in a systematic review and meta-analysis of efficacy, cost effectiveness, and safety. Additionally, in another systematic review of conservative treatments for neck pain and cost-effectiveness by Driessen et al (84) manual therapy plus advice and exercise compared to advice and exercise (85), showed $34,000 per QALY threshold. Further, in another study looking at evaluating cost-effectiveness of spinal manipulative therapy,

supervised exercise, and home exercises for old adults with chronic neck pain (86), inflation-adjusted cost in 2004 was $65,731 per QALY.

For obvious reasons, cost of surgical interventions is the highest in managing spinal pain (87-89). However, cost-effectiveness of surgical interventions was shown to be comparable with other modalities of treatments even though much higher than cervical interlaminar injections or cervical facet joint nerve blocks at $3,785.89 and $4,261 per QALY. Cost utility analysis showed a rate of $20,547 per QALY for posterior cervical fusion (89), whereas it was shown to be $52,816 for QALY for anterior cervical discectomy and fusion (88), with wide variation.

In modern medicine, looking at reducing the cost, improving the quality and access, as envisioned by Obamacare (90-94) there have been challenges achieving these goals. Cost utility analysis is an important aspect even though it is not part of the Affordable Care Act (ACA) or Medicare coverage policies. Thus, cervical interlaminar epidural injections are superior to other modalities of treatments, but similar to cervical facet joint nerve blocks of a different etiology with chronic neck pain. In addition, the cost utility analysis was also less if only the patients who responded to initial 2 treatments considered as responsive group compared to overall population with overall cost of $3,680.21.

Even though cost utility analysis is not utilized in making coverage determinations based on the ACA (90), in other countries, including the United Kingdom, cost-effectiveness of potential expenditures is crucial. In fact, the National Institute for Heath and Clinical Excellence (NICE) (95) in the United Kingdom is well known for assessment of cost-effectiveness and their utility in making coverage decisions. NICE accepts as cost-effective of those interventions with an incremental cost-effectiveness ratio of less than £20,000 (about $40,000 in 2008) per QALY and an incremental cost effectiveness ratio or threshold of £30,000 (about $60,000 in 2008) per QALY in extenuating circumstances.

As with many other studies, this cost utility analysis also suffers from limitations. These include extrapolation of indirect costs at 40% or multiplied by a factor of 1.67 of direct procedural costs, however this is appropriate based on highly regarded SPORT studies (24,75,76) that are used as a gold standard in spine literature in the United States and abroad. However, in this analysis we have not included extensive benefits derived by returning to work. The second disadvantage is related to a single center assessment of 356 patients recalcitrant to conservative management incorporating 3 RCTs and assessing long-term improvement, with an active control design with local anesthetic with or without steroids. The second limitation also is considered as an advantage because of pragmatic nature of the assessment with utilization of real-world evidence as promoted in recent years (96-99). The third limitation is that the present investigation used direct costs instead of Medicare allowable, which in essence uses a picture at the current time, but may be subject to variations in reimbursement rates.

The estimated costs are only applicable in a pragmatic setting such as described here. The procedures were performed in an ambulatory surgery setting with reasonable charges, and also following the appropriate guidance by not exceeding 2 procedures in the diagnostic phase, and not exceeding 4 procedures in the therapeutic phase per year. It is also estimated that the costs may be higher in a hospital outpatient setting ranging from 30% to 70% and 20% to 30% lower in an office setting (100).

Multiple limitations of this analysis include consideration of current procedural costs and extrapolation of indirect costs at 40% or multiplication by a factor of 1.67 of direct procedural costs. However, there was no benefit analyzed for return to work even though there was a significant proportion of patients returning to work. Further, the study is derived from a single center assessment of 360 patients, even though this included a large population of chronic pain patients recalcitrant to conservative management incorporating 3 RCTs and assessing long-term improvement. However, these limitations may be considered as advantages. In addition, the cost of provision of epidural injections have decreased in 2017 compared to 2016, which in fact may lower the cost utility with use of 2017 data (100).

The costs estimated here are only applicable in a practical pragmatic setting such as described here in private practice with performance of these procedures in an ambulatory surgery setting with reasonable charges (100). Consequently, the results of this analysis may not be generalizable to all settings and all populations. Further, it is estimated that cost utility may be 30% to 70% higher in a hospital setting and approximately 20% to 30% lower in an office setting (100).

Conclusion

The present analysis of 3 RCTs of cervical interlaminar epidural injections in a private practice setting in patients after failure of conservative management

shows cost utility of epidural injections at $3,785.89 per QALY. The results also showed cost effectiveness at $3,475.38 for managing disc herniation, $4,028.55 for managing discogenic pain, and $3,856.36 for managing central spinal stenosis with or without steroids with no significant differences observed among the groups for those receiving steroids or those receiving local anesthetic only.

Acknowledgments

The authors wish to thank Bert Fellows, MA, Director Emeritus of Psychological Services, for manuscript review, and transcriptionists Tonie M. Hatton and Diane E. Neihoff, for their assistance with the preparation of this manuscript. We would also like to thank the editorial board of Pain Physician for their suggestions to improve this manuscript.

Author Affiliations

Dr. Manchikanti is Co-Director, Pain Management Centers of America, Clinical Professor, Anesthesiology and Perioperative Medicine, University of Louisville, Louisville, KY, and Professor of Anesthesiology-Research, Department of Anesthesiology, School of Medicine, LSU Health Sciences Center, New Orleans, LA. drlm@thepainmd.com

Vidyasagar Pampati is a Statistician at the Pain Management Centers of America, Paducah, KY. sagar@thepainmd.com

Allan Parr, III, is a medical student at Louisiana State University School of Medicine, Shreveport, LA. aparr1@lsuhsc.edu

Maanasa Manchikanti is a student at the University of Kentucky, Lexington KY. maanasa.manchikanti@uky.edu

Dr. Sanapati is Co-Director, Pain Management Centers of America, Evansville, IN msanapati@gmail.com

Dr. Kaye is Professor, Program Director, and Chairman, Department of Anesthesiology, Louisiana State University Health Science Center, New Orleans, LA. akaye@lsuhsc.edu; alankaye44@hotmail.com

Dr. Hirsch is Vice Chair and Service Line Chief of Neurointerventional Radiology, Chief of Neurointerventional Spine, Massachusetts General Hospital and Harvard Medical School, Boston, MA. jahirsch@mgh.harvard.edu

References

1. Nordin M, Randhawa K, Torres P, et al. The Global Spine Care Initiative: A systematic review for the assessment of spine-related complaints in populations with limited resources and in low- and middle-income communities. *Eur Spine J* 2018; 27:851-860.
2. Dieleman JL, Baral R, Birger M, et al. US spending on personal health care and public health, 1996–2013. *JAMA* 2016; 316:2627-2646.
3. Dieleman JL, Squires E, Bui AL, et al. Factors associated with increase in US health care spending, 1996–2013. *JAMA* 2017; 318:1668-1678.
4. Murray CJ, Atkinson C, Bhalla K, et al; U.S. Burden of Disease Collaborators. The state of US health, 1990–2010: burden of diseases, injuries, and risk factors. *JAMA* 2013; 310:591-608.
5. US Burden of Disease Collaborators, Mokdad AH, Ballestros K, et al. The state of US health, 1990–2016: Burden of diseases, injuries, and risk factors among US states. *JAMA* 2018; 319:1444-1472.
6. Leboeuf-Yde C, Nielsen J, Kyvik KO, Fejer R, Hartvigsen J. Pain in the lumbar, thoracic or cervical regions: do age and gender matter? A population-based study of 34,902 Danish twins 20–71 years of age. *BMC Musculoskelet Disord* 2009; 10:39.
7. Hoy D, March L, Woolf A, et al. The global burden of neck pain: Estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014; 73:1309-1315.
8. Manchikanti L, Abdi S, Atluri S, et al. An update of comprehensive evidence-based guidelines for interventional techniques of chronic spinal pain: Part II: Guidance and recommendations. *Pain Physician* 2013; 16:S49-S283.
9. Kaye AD, Manchikanti L, Abdi S, et al. Efficacy of epidural injections in managing chronic spinal pain: A best evidence synthesis. *Pain Physician* 2015; 18:E939-E1004.
10. Manchikanti L, Soin A, Mann DP, Bakshi S, Pampati V, Hirsch JA. Reversal of growth of utilization of interventional techniques in managing chronic pain in Medicare population post Affordable Care Act. *Pain Physician* 2017; 20:551-567.
11. Manchikanti L, Soin A, Mann DP, Bakshi S, Pampati V, Hirsch JA. Comparative analysis of utilization of epidural procedures in managing chronic pain in the Medicare population: Pre and post Affordable Care Act. *Spine (Phila Pa 1976)* 2019; 44:220-232.
12. Verhagen AP, van Middelkoop M, Rubinstein SM, et al. Effect of various kinds of cervical spinal surgery on clinical outcomes: A systematic review and meta-analysis. *Pain* 2013; 154:2388-2396.
13. Oglesby M, Fineberg SJ, Patel AA, Pelton MA, Singh K. Epidemiological trends in cervical spine surgery for degenerative diseases between 2002 and 2009. *Spine (Phila Pa 1976)* 2013; 38:1226-1232.
14. Fineberg SJ, Oglesby M, Patel AA, Pelton MA, Singh K. Outcomes of cervical spine surgery in teaching and non-

teaching hospitals. *Spine (Phila Pa 1976)* 2013; 38:1089-1096.

15. Singh K, Ahmadinia K, Park D, et al. Complications of spinal fusion with utilization of bone morphogenetic protein: A systematic review of the literature. *Spine (Phila Pa 1976)* 2014; 39:91-101.
16. Vaidya R, Carp J, Sethi A, Bartol S, Craig J, Les CM. Complications of anterior cervical discectomy and fusion using recombinant human bone morphogenetic protein-2. *Eur Spine J* 2007; 16:1257-1265.
17. O'Lynnger TM, Zuckerman SL, Morone PJ, Dewan MC, Vasquez-Castellanos RA, Cheng JS. Trends for spine surgery for the elderly: Implications for access to healthcare in North America. *Neurosurgery* 2015; 77:S136-S141.
18. Manchikanti L, Nampiaparampil DE, Manchikanti KN, et al. Comparison of the efficacy of saline, local anesthetics, and steroids in epidural and facet joint injections for the management of spinal pain: A systematic review of randomized controlled trials. *Surg Neurol Int* 2015; 6:S194-S235.
19. Bakhsheshian J, Mehta VA, Liu JC. Current diagnosis and management of cervical spondylotic myelopathy. *Global Spine J* 2017; 7:572-586.
20. Derman PB, Lampe LP, Hughes AP, et al. Demographic, clinical, and operative factors affecting long-term revision rates after cervical spine arthrodesis. *J Bone Joint Surg Am* 2016; 98:1533-1540.
21. Gutman G, Rosenzweig DH, Golan JD. Surgical treatment of cervical radiculopathy: Meta-analysis of randomized controlled trials. *Spine (Phila Pa 1976)* 2018; 43:E365-E372.
22. Tu ZM, Lv GH, Jiang B, Wang B, Li YW, Wu PF. Posterior cervical foraminotomy via full-endoscopic versus microendoscopic approach for radiculopathy: A systematic review and meta-analysis. *Pain Physician* 2019; 22:41-52.
23. Moore A, Wiffen P, Kalso E. Antiepileptic drugs for neuropathic pain and fibromyalgia. *JAMA* 2014; 312:182-183.
24. Manchikanti L, Kaye AM, Knezevic NN, et al. Responsible, safe, and effective prescription of opioids for chronic noncancer pain: American Society of Interventional Pain Physicians (ASIPP) guidelines. *Pain Physician* 2017; 20: S3-S92.
25. Kaye AD, Jones MR, Kaye AM, et al. Prescription opioid abuse in chronic pain: An updated review of opioid abuse predictors and strategies to curb opioid abuse: Part 1. *Pain Physician* 2017; 20:S93-S109.
26. Kaye AD, Jones MR, Kaye AM, et al. Prescription opioid abuse in chronic pain: An updated review of opioid abuse predictors and strategies to curb opioid abuse: Part 2. *Pain Physician* 2017; 20:S111-S133.
27. Manchikanti L, Sanapati J, Benyamin RM, Atluri S, Kaye AD, Hirsch JA. Reframing the prevention strategies of the opioid crisis: Focusing on prescription opioids, fentanyl, and heroin epidemic. *Pain Physician* 2018; 21:309-326.
28. Chakravarthy K, Manchikanti L, Kaye AD, Christo PJ. Reframing the role of neuromodulation therapy in the chronic pain treatment paradigm. *Pain Physician* 2018; 21:507-513.
29. Manchikanti L, Singh V, Benyamin RM, Kaye AD, Pampati V, Hirsch JA. Reframing Medicare physician payment policy for 2019: A look at proposed policy. *Pain Physician* 2018; 21:415-432.
30. Jonan AB, Kaye AD, Urman RD. Buprenorphine formulations: Clinical best practice strategies recommendations for perioperative management of patients undergoing surgical or interventional pain procedures. *Pain Physician* 2018; 21:E1-E12.
31. Fischer B, Jones W, Vojtila L, Kurdyak P. Patterns, changes, and trends in prescription opioid dispensing in Canada, 2005-2016. *Pain Physician* 2018; 21:219-228.
32. Shamji MF, Cook C, Pietrobon R, Tackett S, Brown C, Isaacs RE. Impact of surgical approach on complications and resource utilization of cervical spine fusion: A nationwide perspective to the surgical treatment of diffuse cervical spondylosis. *Spine J* 2009; 9:31-38.
33. Rihn JA, Bhat S, Grauer J, et al. Economic and outcomes analysis of recalcitrant cervical radiculopathy: Is nonsurgical management or surgery more cost-effective? *J Am Acad Orthop Surg* 2019; 27:533-540.
34. Bhatti AB, Kim S. Role of epidural injections to prevent surgical intervention in patients with chronic sciatica: A systematic review and meta-analysis. *Cureus* 2016; 8:e723.
35. Manchikanti L, Falco FJE, Pampati V, Cash KA, Benyamin RM, Hirsch JA. Cost utility analysis of caudal epidural injections in the treatment of lumbar disc herniation, axial or discogenic low back pain, central spinal stenosis, and post lumbar surgery syndrome. *Pain Physician* 2013; 16:E129-E143.
36. Manchikanti L, Pampati V, Benyamin RM, Hirsch JA. Declining utilization of percutaneous epidural adhesiolysis in Medicare population: Evidence-based or over-regulated? *IPM Reports* 2018; 2:9-18.
37. Lee JH, Shin KS, Park SJ, et al. Comparison of clinical efficacy between transforaminal and interlaminar epidural injections in lumbosacral disc herniation: A systematic review and meta-analysis. *Pain Physician* 2018; 21:433-448.
38. Lee JH, Kim DH, Kim DH, et al. Comparison of clinical efficacy of epidural injection with or without steroid in lumbosacral disc herniation: A systematic review and meta-analysis. *Pain Physician* 2018; 21:449-468.
39. Helm S 2nd, Simopoulos TT, Stojanovic MP, Abdi S, El Terany MA. Effectiveness of thermal annular procedures in treating discogenic low back pain. *Pain Physician* 2017; 20:447-470.
40. Manchikanti L, Hirsch JA, Kaye AD, Boswell MV. Cervical zygapophysial (facet) joint pain: Effectiveness of interventional management strategies. *Postgrad Med* 2016; 128:54-68.
41. Manchikanti L, Hirsch JA, Falco FJE, Boswell MF. Management of lumbar zygapophysial (facet) joint pain. *World J Orthop* 2016; 7:315-337.
42. Manchikanti L, Staats PS, Nampiaparampil DE, Hirsch JA. What is the role of epidural injections in the treatment of lumbar discogenic pain: A systematic review of comparative analysis with fusion and disc arthroplasty. *Korean J Pain* 2015; 28:75-87.
43. Shen J, Xu S, Xu S, Ye S, Hao J. Fusion or not for degenerative lumbar spinal stenosis: a meta-analysis and systematic review. *Pain Physician* 2018; 21:1-8.
44. Manchikanti L, Soin A, Boswell MV, Sanapati M, Hirsch JA. Effectiveness of percutaneous adhesiolysis in post lumbar surgery syndrome: A systematic analysis of findings of systematic reviews. *Pain Physician* 2019; 22:307-322.
45. Manchikanti L, Soin A, Benyamin RM, et al. An update of the systematic appraisal of the accuracy and utility of discography in chronic spinal pain. *Pain Physician* 2018; 21:91-110.
46. Hou S, Huh B, Kim HK, Kim KH, Abdi S. Treatment of chemotherapy-induced peripheral neuropathy: systematic review and recommendations. *Pain Physician* 2018; 21:571-592.

47. Salazar AP, Stein C, Marchese RR, Plentz RD, Pagnussat AS. Electric stimulation for pain relief in patients with fibromyalgia: A systematic review and meta-analysis of randomized controlled trials. *Pain Physician* 2017; 20:15-25.
48. Xiang GH, Tong MJ, Lou C, Zhu SP, Guo WJ, Ke CR. The role of unilateral balloon kyphoplasty for the treatment of patients with OVCFS: A systematic review and meta-analysis. *Pain Physician* 2018; 21:209-218.
49. Artemiadis AK, Zis P. Neuropathic pain in acute and subacute neuropathies: a systematic review. *Pain Physician* 2018; 21:111-120.
50. Manchikanti L, Boswell MV, Kaye AD, Helm II S, Hirsch JA. Therapeutic role of placebo: Evolution of a new paradigm in understanding research and clinical practice. *Pain Physician* 2017; 20:363-386.
51. Manchikanti L, Pampati V, Benyamin RM, Hirsch JA. Cost utility analysis of lumbar interlaminar epidural injections in the treatment of lumbar disc herniation, central spinal stenosis, and axial or discogenic low back pain. *Pain Physician* 2017; 20:219-228.
52. Manchikanti L, Pampati V, Kaye AD, Hirsch JA. Therapeutic lumbar facet joint nerve blocks in the treatment of chronic low back pain: cost utility analysis based on a randomized controlled trial. *Korean J Pain* 2018; 31:27-38.
53. Manchikanti L, Pampati V, Kaye AD, Hirsch JA. Cost utility analysis of cervical therapeutic medial branch blocks in managing chronic neck pain. *Int J Med Sci* 2017; 14:1307-1316.
54. Prusova K, Churcher L, Tyler A, Lokugamage U. Royal College of Obstetricians and Gynaecologists guidelines: How evidence-based are they? *J Obstet Gynaecol* 2014; 34:706-711.
55. Clark J, Nijs J, Yeowell G, Goodwin PC. What are the predictors of altered central pain modulation in chronic musculoskeletal pain populations? A systematic review. *Pain Physician* 2017; 20:487-500.
56. Rysavy M. Evidence-based medicine: A science of uncertainty and an art of probability. *Virtual Mentor* 2013; 15:4-8.
57. Hickey S, Roberts H. Evidence based medicine: Neither good evidence nor good medicine. Orthomolecular Medicine News Service, December 7, 2011.
http://orthomolecular.org/resources/omns/v07n15.shtml
58. Schwartz D. Evidence-based medicine is NOT the Holy Grail (Share) – NEW IMPROVED.
https://www.linkedin.com/pulse/evidence-based-medicine-holy-grail-david-schwartz
59. Every-Palmer S, Howick J. How evidence-based medicine is failing due to biased trials and selective publication. *J Eval Clin Pract* 2014; 20:908-914.
60. Cappola AR, FitzGerald GA. Confluence, not conflict of interest: Name change necessary. *JAMA* 2015; 314:1791-1792.
61. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181.
62. Foroutan F, Guyatt G, Alba AC, Ross H. Meta-analysis: Mistake or milestone in medicine? *Heart* 2018; 104:1559-1561.
63. Djulbegovic B, Guyatt G. Evidence vs consensus in clinical practice guidelines. *JAMA* 2019 Jul 19. [Epub ahead of print]
64. Djulbegovic B, Guyatt GH. Progress in evidence-based medicine: A quarter century on. *Lancet* 2017; 390:415-423.
65. Chou R, Hashimoto R, Friedly J, et al. Pain Management Injection Therapies for Low Back Pain. Technology Assessment Report ESIB0813. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. HHSA 290-2012-00014-I.) Rockville, MD: Agency for Healthcare Research and Quality; July 10, 2015.
https://www.cms.gov/medicare/coverage/determinationprocess/downloads/id98ta.pdf
66. Manchikanti L, Knezevic NN, Boswell MV, Kaye AD, Hirsch JA. Epidural injections for lumbar radiculopathy and spinal stenosis: A comparative systematic review and meta-analysis. *Pain Physician* 2016; E365-410.
67. Boswell MV, Manchikanti L. Appropriate design and methodologic quality assessment, clinically relevant outcomes are essential to determine the role of epidural corticosteroid injections. Commentary RE: Chou R, Hashimoto R, Friedly J, Fu R, Bougatsos C, Dana T, Sullivan SD, Jarvik J. Epidural corticosteroid injections for radiculopathy and spinal stenosis: A systematic review and meta-analysis. *Ann Intern Med* 2015; 163:373-381. *Evid Based Med* 2016; 21:89.
68. Rathmell JP, Benzon HT, Dreyfuss P, et al. Safeguards to prevent neurologic complications after epidural steroid injections: Consensus opinions from a multidisciplinary working group and national organizations. *Anesthesiology* 2015; 122:974-984.
69. Racoosin JA, Seymour SM, Cascio L, Gill R. Serious neurologic events after epidural glucocorticoid injection--the FDA's risk assessment. *N Engl J Med* 2015; 373:2299-2301.
70. Manchikanti MV, Manchikanti L, Kaye AD, Pampati V, Hirsch JA. Usage patterns of sacroiliac joint injections - a comparative evaluation of pre and post Affordable Care Act in Medicare population. *IPM Reports* 2018; 2:157-166.
71. Dagenais S, Roffey DM, Wai EK, Haldeman S, Caro J. Can cost utility evaluations inform decision making about interventions for low back pain? *Spine J* 2009; 9:944-957.
72. Kepler CK, Wilkinson SM, Radcliff KE, et al. Cost-utility analysis in spine care: A systematic review. *Spine J* 2012; 12:676-690.
73. Indrakanti SS, Weber MH, Takemoto SK, Hu SS, Polly D, Berven SH. Value-based care in the management of spinal disorders: A systematic review of cost-utility analysis. *Clin Orthop Relat Res* 2012; 470:1106-1023.
74. Furlan AD, Yazdi F, Tsertsvadze A, et al. A systematic review and meta-analysis of efficacy, cost-effectiveness, and safety of selected complementary and alternative medicine for neck and low-back pain. *Evid Based Complement Alternat Med* 2012; 2012:953139.
75. Tosteson AN, Skinner JS, Tosteson TD, et al. The cost effectiveness of surgical versus nonoperative treatment for lumbar disc herniation over two years: Evidence from the Spine Patient Outcomes Research Trial (SPORT). *Spine (Phila Pa 1976)* 2008; 33:2108-2115.
76. Tosteson AN, Lurie JD, Tosteson TD, et al; SPORT Investigators. Surgical treatment of spinal stenosis with and without degenerative spondylolisthesis: Cost-effectiveness after 2 years. *Ann Intern Med* 2008; 149:845-853.
77. Taylor RS, Ryan J, O'Donnelll R, Eldabe S, Kumar K, North RB. The cost-effectiveness of spinal cord stimulation in the treatment of failed back surgery syndrome. *Clin J Pain* 2010; 26:463-469.
78. Carreon LY, Bratcher KR, Ammous F, Glassman SD. Cost-effectiveness of lumbar epidural steroid injections. *Spine (Phila Pa 1976)* 2018; 43:35-40.

79. Alvin MD, Mehta V, Halabi HA, Lubelski D, Benzel EC, Mroz TE. Cost-effectiveness of cervical epidural steroid injections: A 3-month pilot study. *Global Spine J* 2019; 9:143-149.
80. Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. A randomized, double-blind, active control trial of fluoroscopic cervical interlaminar epidural injections in chronic pain of cervical disc herniation: Results of a 2-year follow-up. *Pain Physician* 2013; 16:465-478.
81. Manchikanti L, Cash KA, Pampati V, Malla Y. Two-year follow-up results of fluoroscopic cervical epidural injections in chronic axial or discogenic neck pain: A randomized, double-blind, controlled trial. *Int J Med Sci* 2014; 11:309-320.
82. Manchikanti L, Malla Y, Cash KA, Pampati V, Hirsch JA. Comparison of effectiveness for fluoroscopic cervical interlaminar epidural injections with or without steroid in cervical post-surgery syndrome. *Korean J Pain* 2018; 31:277-288.
83. Whynes DK, McCahon RA, Ravenscroft A, Hardman J. Cost effectiveness of epidural steroid injections to manage chronic lower back pain. *BMC Anesthesiol* 2012; 12:26.
84. Driessen MT, Lin CW, van Tulder MW. Cost-effectiveness of conservative treatments for neck pain: A systematic review on economic evaluations. *Eur Spine J* 2012; 21:1441-1450.
85. Lewis M, James M, Stokes E, et al. An economic evaluation of three physiotherapy treatments for non-specific neck disorders alongside a randomized trial. *Rheumatology (Oxford)* 2007; 46:1701-1708.
86. Leininger B, McDonough C, Evans R, Tosteson T, Tosteson AN, Bronfort G. Cost-effectiveness of spinal manipulative therapy, supervised exercise, and home exercise for older adults with chronic neck pain. *Spine J* 2016; 16:1292-1304.
87. Witiw CD, Tetreault LA, Smieliauskas F, Kopjar B, Massicotte EM, Fehlings MG. Surgery for degenerative cervical myelopathy: A patient-centered quality of life and health economic evaluation. *Spine J* 2017; 17:15-25.
88. Chotai S, Sielatycki JA, Parker SL, et al. Effect of obesity on cost per quality-adjusted life years gained following anterior cervical discectomy and fusion in elective degenerative pathology. *Spine J* 2016; 16:1342-1350.
89. Medvedev G, Wang C, Cyriac M, Amdur R, O'Brien J. Complications, readmissions, and reoperations in posterior cervical fusion. *Spine (Phila Pa 1976)* 2016; 41:1477-1483.
90. Manchikanti L, Helm S 2nd, Benyamin RM, Hirsch JA. A critical analysis of Obamacare: Affordable care or insurance for many and coverage for few? *Pain Physician* 2017; 20:111-138.
91. Manchikanti L, Helm II S, Calodney AK, Hirsch JA. Merit-based incentive payment system: Meaningful changes in the final rule brings cautious optimism. *Pain Physician* 2017; 20:E1-E12.
92. Hirsch JA, Leslie-Mazwi T, Nicola GN, et al. Storm rising! The Obamacare exchanges will catalyze change: Why physicians need to pay attention to the weather. *J Neurointerv Surg* 2019; 11:101-106.
93. Hirsch JA. The pincer movement of cost and quality in neurointerventional care: Resource management as an imperative. *J Neurointerv Surg* 2019; 11:323-325.
94. Manchikanti L, Helm S 2nd, Benyamin RM, Hirsch JA. Evolution of US health care reform. *Pain Physician* 2017; 20:107-110.
95. National Institute for Health and Clinical Excellence. *Guide to the Methods of Technology Appraisal*. NICE, London, 2008.
96. Jarow JP, LaVange L, Woodcock J. Multidimensional evidence generation and FDA regulatory decision making: Defining and using "real-world" data. *JAMA* 2017; 318:703-704.
97. Sherman RE, Anderson SA, Dal Pan GJ, et al. Real-world evidence – What is it and what can it tell us? *N Engl J Med* 2016; 375:2293-2297.
98. Krause JH, Saver RS. Real-world evidence in the real world: Beyond the FDA. *Am J Law Med* 2018;44:161-179.
99. Kirkner RM. FDA, Gottlieb get real about real-world evidence. *Manag Care* 2019; 28:13-16.
100. Manchikanti L, Singh V, Hirsch JA. Facility payments for interventional pain management procedures: Impact of proposed rules. *Pain Physician* 2016; 19 E957-E984.