

University of Groningen

Radiculopathy and radiating low back pain in general practice

Spijker-Huiges, Antje

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2015

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Spijker-Huiges, A. (2015). *Radiculopathy and radiating low back pain in general practice*. [Thesis fully internal (DIV), University of Groningen]. [S.n.].

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Chapter 4

**Costs and cost-effectiveness of epidural
steroids for acute lumbosacral radicular
syndrome in general practice.
An economic evaluation alongside
a pragmatic RCT**



Authors:

Antje Spijker-Huiges

Karin Vermeulen

Jan C. Winters

Marten van Wijhe

Klaas van der Meer

Spine (Phila Pa 1976). 2014 Nov 15;39(24):2007-12.

Adapted version

ABSTRACT

Background

Lumbosacral radicular syndrome (LRS or radiculopathy) is a benign, generally self-limiting but painful condition caused by a herniated lumbar intervertebral disc which results in an inflammatory process around the nerve root. Segmental epidural steroid injections could lessen pain. Low back pain and sciatica form a large financial burden on national healthcare systems. Improving pain treatment could lower costs to society by diminishing loss of productivity.

Method

We performed a pragmatic, randomized, controlled, single-blinded trial in Dutch general practice. General practitioners included patients with acute LRS. All patients received usual care. Patients in the intervention group received one segmental epidural steroid injection containing 80 mg triamcinolone as well. Follow-up was performed using postal questionnaires at 2, 4, 6, 13, 26 and 52 weeks. Main outcomes were pain, disability and costs. Economic evaluation was performed from a societal perspective with a time horizon of one year.

Results

63 patients were included in the analysis. Mean total costs were €4,414 in the intervention group and €5,121 in the control group. This difference was mostly due to loss of productivity. The point estimate for the incremental cost-effectiveness ratio (ICER) was - €730 (one point diminishment on the NRS back pain score in one patient in the course of one year would save €730). Bootstrapping showed a 95% CI of -€4,476 to €951. The cost-effectiveness acceptability curve (CEAC) showed that without additional investment the probability that epidural corticosteroid injections are cost-effective, is more than 80%.

Conclusion

The effect on pain and disability of epidural corticosteroid injections in LRS is small but significant, and at lower costs with no reported complications or adverse effects. Policy makers could consider segmental epidural steroid injections as an additional treatment option.

INTRODUCTION

Lumbosacral radicular syndrome (LRS, radiculopathy) is pain, radiating from the back to below the knee in one leg (“sciatica”), with Lasègue’s sign and/or neurological symptoms originating from one nerve root. The incidence of LRS in Dutch general practice is 9, and the prevalence 15 per 1,000 per year.¹

LRS is caused by herniation of a lumbar intervertebral disc resulting in a self-limiting inflammatory response around the nerve root, which is the main cause of radicular pain.¹⁻⁶ Anti-inflammatory drugs may lessen the inflammation and the pain, helping patients to profit from the favourable natural prognosis. Segmental epidural steroid injections are a local anti-inflammatory treatment, effective in treating pain on the short term in the acute phase of well-defined radicular syndrome with sciatica.⁶⁻¹⁵ The most common adverse effect of epidural corticosteroid injections (0.82% - 5%) is accidental perforation of the dural sac.¹⁶

In the Netherlands, LRS is treated by general practitioners (GPs) who adhere to the Dutch College of General Practitioner’s Guideline on LRS. According to this guideline, treatment of LRS consists of maintaining normal activities as much as possible, pain treatment with analgesics and referral if necessary. Epidural steroids are applied in LRS in The Netherlands but they are not advised in the guideline as a routine treatment.¹

The medical costs of low-back pain made up 337 million euros in the Netherlands in 2000.¹⁷ The costs of conservatively treated sciatica was \$55,000 per case per 5 years in the US in 1992.¹⁸ Ten per cent of low-back pain patients have radiculopathy; it is most prevalent among working-aged male patients (25 to 64 years). Therefore, LRS is expensive in medical costs as well as loss of productivity. Improving pain treatment in acute LRS could diminish these costs.

In this paper, the costs of adding epidural steroids to the treatment of LRS in general practice, including a cost-effectiveness analysis, will be presented.

METHOD

This study was conducted alongside a randomized, controlled, single-blinded pragmatic trial in 41 general practices in and around the city of Groningen, the Netherlands. Patients were recruited in 2005, 2006 and 2007 and followed for one year. Inclusion criteria were LRS as diagnosed by the including GP, duration of radicular complaints for two to four weeks, and age 18 - 60 years. Exclusion

criteria were a history of spinal surgery or trauma (physical injuries to the spine, caused by external sources, e.g. accidents or violence), maintenance therapy with corticosteroids or anticoagulants, bleeding disorder, cauda equina syndrome, a body mass index of > 35 , mental disability, inadequate mastery of the Dutch language, allergy to corticosteroids, pregnancy or an active wish to conceive and breastfeeding.

Patients with LRS received written information on the study, a baseline questionnaire and an informed consent form from their family physician. Patients completed the forms and sent them to the research centre. Upon receiving the baseline questionnaire and the informed consent, the primary researcher contacted the subjects to check inclusion and exclusion criteria with a pre-written inclusion form. In the absence of exclusion criteria the inclusion form was completed and patients were randomized. Randomization was performed by a GP who was not otherwise involved in the study, using pre-prepared, sequentially numbered, opaque, sealed envelopes containing stickers with either “SESI” (= segmental epidural steroid injection) or “CAU” (= care as usual), balanced after 40 assignments. Upon randomization, the due envelope was opened and the sticker with the allocated treatment was fixed on the completed inclusion form. Inclusion forms were coded and kept separately from coded follow-up questionnaires. Researchers were blinded until after the final analysis of the results.

As demanded by the pragmatic study design, we closely followed daily practice circumstances. All patients received care as usual from their GP. Care as usual was defined, according to the guideline, as pain treatment with analgesics, maintaining normal daily activities as much as possible, and referral if necessary. Patients in the intervention group received a segmental epidural steroid injection in addition. The injections consisted of 80 mgs of triamcinolone in normal saline and were administered at the department of anaesthesiology of the university medical hospital Groningen (UMCG).

The economic evaluation was performed from a societal perspective, which means that all direct medical, and all direct and indirect non-medical costs, including loss of productivity, were taken into account, regardless of who pays for them. The time horizon was one year. Unit prices were drawn from the guidelines for cost-studies (methods and unit-prices for economic evaluations in health care) and online information on medication costs by the Dutch health insurance board.^{19,20}

Follow-up in both groups was performed using postal questionnaires regarding pain, disability, health-related quality of life and costs, measured at 2, 4, 6, 13, 26

and 52 weeks after the start of the treatment. As primary outcome measure, we used the NRS back pain score at four weeks after the start of the treatment.

Statistical Analysis

A difference in back pain score of NRS 1.2 – 2.0 is considered clinically relevant in primary care patients with low back pain. To detect a difference of 1.2 and a common within-group standard deviation of 1.7 with a two-tailed alpha of 0.05 and a power of 0.80, we needed 33 subjects in each group. All analyses were performed using an intention-to-treat basis. Mixed model regression analysis was performed using SAS 9.2 PROC MIXED. Patients were a random factor in the model and treatment a fixed factor. For every outcome variable, treatment and time of measurement as independent variables were tested with sex, age and baseline-values as covariates to account for non-balance in the randomization.

Differences between groups after one year were calculated with 95% confidence intervals based on bootstrap resampling with 5,000 replications. A cost-effectiveness analysis was carried out, in which the incremental cost-effectiveness ratio (ICER) is calculated using the costs and the primary outcome measure.²¹ Bootstrapping also provided information on the uncertainty of the ICERs. Mean annual societal costs were linked to improvement in NRS back pain score. Point estimates for the ICER were computed on complete cost-effect pairs by dividing the incremental societal costs by the incremental effects at 12 months. The simulated values of mean estimates for costs and outcome differences were added to a cost effectiveness plane, in which percentages of patients in each of the four quadrants plane were determined. Finally, a cost-effectiveness acceptability curve (CEAC) was generated. CEACs graphically show the probability of an intervention being cost-effective, depending on the available budget. In our study, the CEAC represents the probability that adding epidural corticosteroid injections to usual care in LRS is cost-effective over a range of thresholds. These thresholds represent the sums that would have to be invested in one patient for one point decrease on the NRS back pain score.

RESULTS

Participants

Eighty-four patients were presented to us by their family physicians, 73 were randomized and 63 were included in the final analysis (figure 4.1).

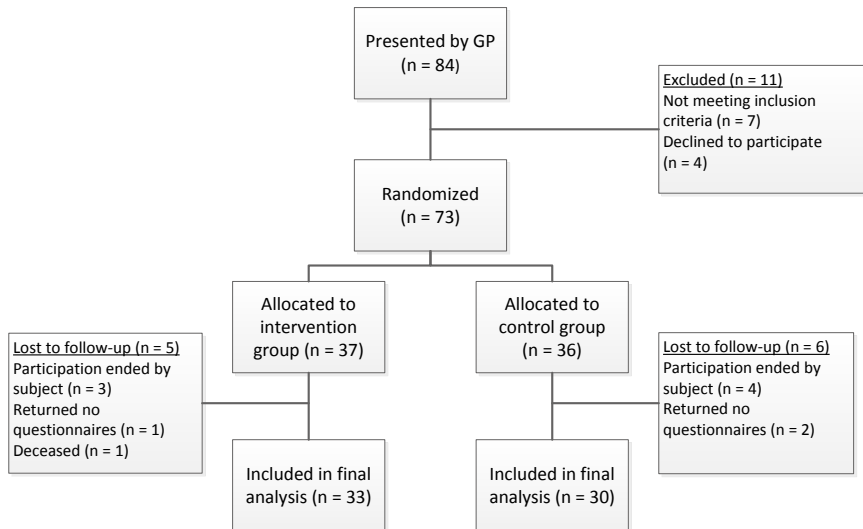


Figure 4.1: Population flow schedule

Summary of clinical effectiveness

The clinical outcomes of this pragmatic trial were published elsewhere and described in chapter 3 of this thesis.²² Patient characteristics including baseline clinical outcomes are shown in table 4.1. The intervention group differed significantly from the control group in all baseline values except for leg pain. In the mixed models regression analysis, these differences were corrected for by including the baseline values as a covariate. Both groups experienced a significant decline over time for all symptoms. The severity of the symptoms, however, remained significantly greater in the control group than in the intervention group for back pain ($p=0.0115$), self-perceived impairment ($p=0.0361$) and the Roland-Morris disability score ($p=0.0173$). There was no significant interaction between the groups in the follow-up period, which means that these differences in severity of symptoms between groups remained constant over the entire follow-up period. No complications or adverse effects of the intervention were reported.

Costs

Costs are presented and compared in table 4.2. Mean total costs for our study period were €4,414 per patient in the intervention group and €5,121 in the control group, with loss of productivity as major contributor. The differences between the groups occurred mainly in the beginning of the treatment period.

Table 4.1: Baseline characteristics and baseline pain scores of the study participants (n=63)

Group	Intervention group (n = 30)	Control group (n = 33)
Men	15	15
Mean age at inclusion (sd)	43.3 (10)	44 (9.6)
Mean NRS back pain (sd)	6.2 (2.6)	4.5 (2.7)
Mean NRS leg pain (sd)	7.8 (1.7)	6.4 (2.3)
Mean NRS pain during the day (sd)	7.7 (1.6)	6.2 (2.1)
Mean NRS pain during the night (sd)	6.4 (2.6)	5.7 (2.7)
Mean NRS total pain (sd)	7.7 (1.2)	6.9 (1.7)
Mean NRS impairment (sd)	7.8 (1.6)	6.7 (2.2)
Mean RMDQ score (sd)	16.5 (4.2)	14.5 (6.1)

NRS: Numerical Rating Scale.

RMDQ: Roland-Morris Disability Questionnaire.

Table 4.2: Mean (SD) costs (in euros) and cost differences between groups during the 1-year follow up

	SESI group n=25 (mean ± SD)	CAU group n=27 (mean ± SD)	Difference (95% CI)
Intervention costs	191 (-)	0 (-)	191 (-)
General Practice care ^a	128 (174)	66 (119)	62 (-10 - 82)
Hospital care ^b	722 (1,939)	719 (1,155)	3 (-399 - 402)
Additional examinations ^c	71 (107)	67 (134)	4 (-40 - 35)
Medication ^d	33 (48)	65 (94)	-32 (-41 - 16)
Physiotherapy	303 (512)	372 (749)	-69 (-246 - 153)
Alternative therapists	8 (34)	51 (183)	-43 (-78 - 5)
Home help visits	6 (28)	45 (188)	-39 (-63 - 6)
Absence from work ^e	2,726 (2,467)	4,278 (6,380)	-1,552 (-2,497 - 430)
Other ^f	263 (1052)	524 (1587)	-261 (-568 - 240)
Total	4,414 (3193)	5,121 (7432)	-695 (-2,424 - 1,129)

Cost-effectiveness

Results of the cost-effectiveness analyses are shown in figures 4.2 and 4.3. The point estimate for the ICER was - €730 (one point improvement in NRS back pain score in one patient in the intervention group would save €730 in the course of one year). Bootstrapping (figure 4.2) showed a 95% CI of -€4476 to €951. The CEAC (figure 4.3) showed that the probability that epidural steroids in acute LRS are cost-effective rises to 100% with an additional investment of about €1200 per patient.

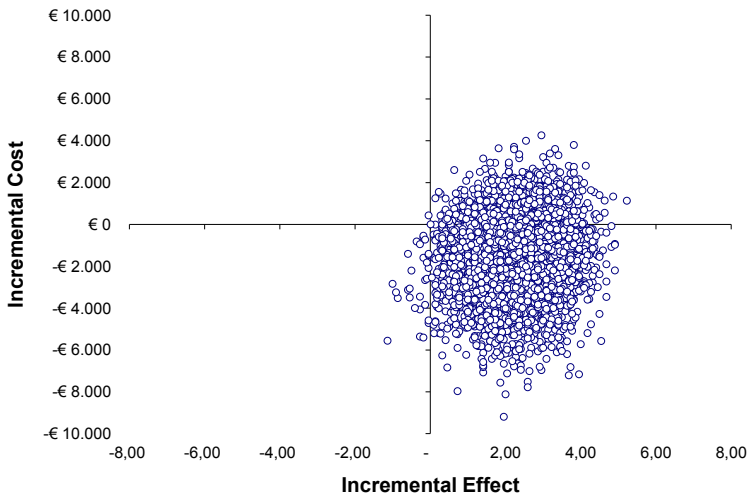


Figure 4.2: Bootstrapped costs and effects.

81% of the cost-effect pairs are located in the south east quadrant, with represents lower costs and more improvement on the primary outcome variable in the intervention group compared to the control group. In other words: more effective, less expensive. 18% of cost-effect pairs are located in the north east quadrant, which represents more improvement in the intervention group than in the control group, but at higher costs: more effective, more expensive.

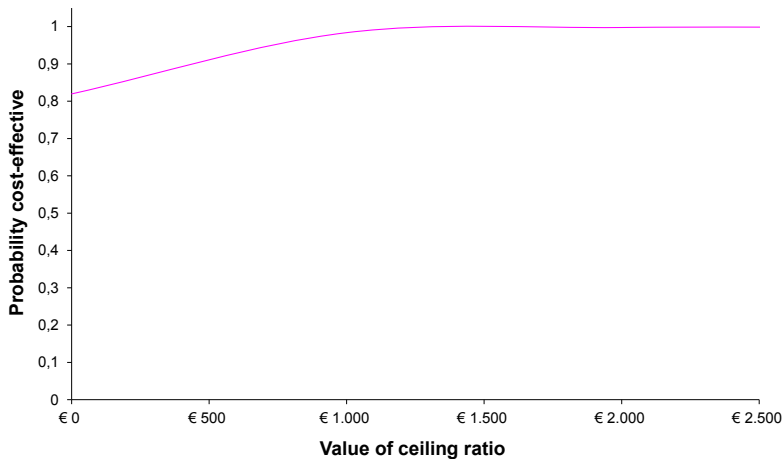


Figure 4.3: Cost-effectiveness acceptability curve (CEAC).

The CEAC graphically shows the probability of whether it would be cost-effective to add segmental epidural steroid injections to care as usual, compared to care as usual alone, at a specific ceiling ratio. This means that the probability that a certain intervention is considered cost-effective, rises with the willingness of decision makers to invest in this intervention. In the current situation, without additional investment, the probability that epidural steroids as an additional treatment are cost-effective is more than 80% (the starting point of the curve). The probability that epidural steroids are cost-effective rises to almost 100% with an additional investment of €1,200 / US \$1,627.

DISCUSSION

Principal findings

In this study, the costs and cost-effectiveness of adding epidural corticosteroid injections to usual care in the treatment of LRS in general practice were assessed. Adding the intervention to usual treatment turned out to be less expensive from a societal perspective than usual care alone. This difference occurred predominantly regarding productivity loss and especially in the first weeks after initiation of treatment. This was also the period in which the intervention had a small significant clinical effect on pain and disability.

Strengths and weaknesses

GPs care for most patients in the acute phase of LRS, yet most clinical trials are conducted in hospital settings. Our study is the first pragmatic trial in general practice investigating costs in LRS from a societal perspective, including productivity loss, which turns out to be a major contributor to costs of illness. A potential problem is the fact that our intervention group differed significantly from the control group in baseline clinical values. We have no explanation for these differences. Incremental cost analyses do not compare absolute values but improvement between groups at each time point compared to baseline. This way, baseline differences are accounted for. In the analyses of the clinical effects, baseline differences were corrected for by including them in the mixed models regression as covariates. Another possible limitation of our study is the fact that we did not take costs of adverse effects of epidural steroids into account. In our study, no adverse effects have been reported. Our study population (n=73) was too small to yield reliable results about adverse effects. Since complications and adverse effects are relatively mild and rare, for example headache, due to liquor loss when the dural sac is accidentally punctured, we expect their costs to be low. Applying (multiple) epidural injections in especially elderly patients may lead to an increased risk in vertebral fractures and additional healthcare costs, as pointed out by Mandel *et al* in a retrospective database study.²³ It is therefore advisable to take caution in elderly patients and/or patients receiving multiple epidural injections.

Other research

A pragmatic, prospective, multicentre, doubleblind, randomized, placebo-controlled trial studying the clinical and cost effectiveness of epidural steroids in

LRS with 12-month follow-up was performed in 2005 by Price *et al.*²⁴ Two-hundred and twenty-eight patients from three centres were included. Epidural corticosteroid injections were found clinically effective on a short-term basis in patients with acute radiculopathy (<6 weeks), but not in chronic radiculopathy (>6 weeks). The most important outcomes were the number needed to treat to realize a 75% improvement in 3 weeks, which was 11, and the cost per QALY for one epidural steroid injection which was £25,746 (€31,904). Since this study made use of providers' and purchasers' perspectives instead of a societal perspective, the results are difficult to compare. Price *et al* did not assess costs of productivity loss, which in our study accounted for the largest difference between groups. Also, Price *et al* assumed that both research groups received a standard package of care including analgesia that did not differ between groups, so costs of pain medication were not explicitly measured, where in our study costs of pain analgesia formed the largest part of direct medical costs in the control group. These differences may explain why Price *et al* concluded that epidural corticosteroid injections are not cost effective.

Meaning and implications

Our study results showed that adding epidural steroids to usual care yields the same or better clinical results than usual care alone, virtually without side-effects, if patients are carefully selected.²⁵⁻²⁸ It is also less expensive than usual care, taking all costs into consideration. Based on the information this study yielded, policymakers in the field could consider implementing epidural corticosteroid injections as an option for pain treatment in the acute phase of LRS, since healthcare and societal costs could be lowered.

REFERENCES

1. Mens JMA, Chavannes AW, Koes BW, Lubbers WJ, Ostelo RWJG, Spinnewijn WEM. [NHG-guideline lumbosacral syndrome] NHG-standaard lumbosacraal radiculair syndroom. *Huisarts en wetenschap*. 2005:171-8.
2. Saal JS. The role of inflammation in lumbar pain. *Spine*. 1995:1821-7.
3. DePalma MJ, Bhargava A, Slipman CW. A critical appraisal of the evidence for selective nerve root injection in the treatment of lumbosacral radiculopathy. *Arch Phys Med Rehabil*. 2005:1477-83.
4. McCarron RF, Wimpee MW, Hudkins PG, Laros GS. The inflammatory effect of nucleus pulposus. A possible element in the pathogenesis of low-back pain. *Spine*. 1987:760-4.
5. Nygaard OP, Mellgren SI, Osterud B. The inflammatory properties of contained and noncontained lumbar disc herniation. *Spine*. 1997:2484-8.
6. Arden NK, Price C, Reading I, Stubbing J, Hazelgrove J, Dunne C, *et al*. A multicentre randomized controlled trial of epidural corticosteroid injections for sciatica: The WEST study. *Rheumatology* (Oxford). 2005:1399-406.
7. Luijsterburg PA, Verhagen AP, Ostelo RW, van Os TA, Peul WC, Koes BW. Effectiveness of conservative treatments for the lumbosacral radicular syndrome: A systematic review. *Eur Spine J*. 2007:881-99.
8. Karpainen J, Malmivaara A, Kurunlahti M, Kyllonen E, Pienimäki T, Nieminen P, *et al*. Periradicular infiltration for sciatica: A randomized controlled trial. *Spine*. 2001:1059-67.
9. Kolsi I, Delecrin J, Berthelot JM, Thomas L, Prost A, Maugars Y. Efficacy of nerve root versus interspinous injections of glucocorticoids in the treatment of disk-related sciatica. A pilot, prospective, randomized, double-blind study. *Joint Bone Spine*. 2000:113-8.
10. Riew KD, Yin Y, Gilula L, Bridwell KH, Lenke LG, Laurysen C, *et al*. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. A prospective, randomized, controlled, double-blind study. *J Bone Joint Surg Am*. 2000:1589-93.
11. Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: A prospective randomized study. *Spine* (Phila Pa 1976). 2002:11-6.
12. Buchner M, Zeifang F, Brocai DR, Schiltenswolf M. Epidural corticosteroid injection in the conservative management of sciatica. *Clin Orthop*. 2000:149-56.
13. Carette S, Leclaire R, Marcoux S, Morin F, Blaise GA, St Pierre A, *et al*. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. *N Engl J Med*. 1997:1634-40.
14. Samanta A, Beardsley J. Sciatica: Which intervention? *BMJ*. 1999:302-3.
15. Valat JP, Genevay S, Marty M, Rozenberg S, Koes B. Sciatica. *Best Pract Res Clin Rheumatol*. 2010:241-52.
16. Lubenow T, Keh-Wong E, Kristof K, Ivankovich O, Ivankovich AD. Inadvertent subdural injection: A complication of an epidural block. *Anesth Analg*. 1988:175-9.
17. Picavet HSJ. Aspecifieke lage rugklachten: Omvang en gevolgen. 2005.
18. Shvartzman L, Weingarten E, Sherry H, Levin S, Persaud A. Cost-effectiveness analysis of extended conservative therapy versus surgical intervention in the management of herniated lumbar intervertebral disc. *Spine*. 1992:176-82.
19. Hakkaart-Van Roijen L., Tan SS, Bouwmans CAM. Guidelines for cost-studies. methods and unit prices for economic evaluations in health care. 2010.
20. Dutch Health Insurance Board [Internet]. Available from: www.medicijnkosten.nl.

21. Drummond M, Manca A, Sculpher M. Increasing the generalizability of economic evaluations: Recommendations for the design, analysis, and reporting of studies. *Int J Technol Assess Health Care*. 2005:165-71.
22. Spijker-Huiges A, Winters JC, van Wijhe M, Groenier K. Steroid injections added to the usual treatment of lumbar radicular syndrome: a pragmatic randomized controlled trial in general practice. *BMC Musculoskelet Disord*. 2014 Oct 11;15:341.
23. Mandel S, Schilling J, Peterson E, Rao S, Sanders W. A retrospective analysis of vertebral body fractures following epidural steroid injections. *J Bone Joint Surg.Am*. 2013;11, 961-964.
24. Price C, Arden N, Coglan L, Rogers P. Cost-effectiveness and safety of epidural steroids in the management of sciatica. *Health Technol Assess*. 2005;1,58, iii.
25. Lauridsen HH, Hartvigsen J, Korsholm L, Grunnet-Nilsson N, Manniche C. Choice of external criteria in back pain research: Does it matter? recommendations based on analysis of responsiveness. *Pain*. 2007:112-20.
26. Roland M, Fairbank J. The roland-morris disability questionnaire and the oswestry disability questionnaire. *Spine*. 2000:3115-24.
27. Peul WC, Van Houwelingen HC, Van den Hout WB, Brand R, Eekhof JA, Tans JT, *et al*. Early surgery or a wait-and-see policy in lumbosacral radicular syndrome: A randomized study. *Ned Tijdschr Geneesk*. 2007:2512-23.
28. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JA, Tans JT, *et al*. Surgery versus prolonged conservative treatment for sciatica. *N Engl J Med*. 2007:2245-56.