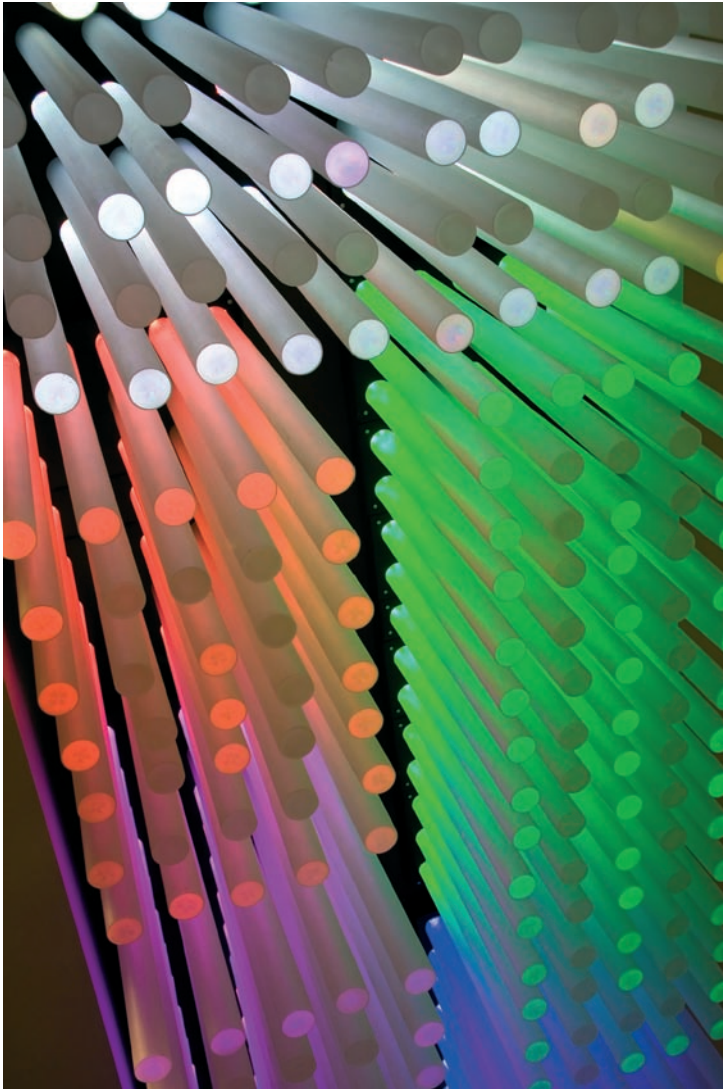# Evidence-based practice regarding the lumbosacral radicular syndrome

Pim Luijsterburg

Stellingen

behorende bij het proefschrift
'Evidence-based practice regarding the lumbosacral radicular syndrome'

1. Nederlandse huisartsen en neurochirurgen volgen goed hun richtlijnen aangaande het lumbosacraal radiculair syndroom. (dit proefschrift)

2. Na operatie vanwege een lumbosacraal radiculair syndroom zijn patiënten (zeer) tevreden over de behandeling. (dit proefschrift)

3. Systematisch doorzoeken van de literatuur (tot mei 2004) levert geen aanwijzingen voor een superieure behandeling bij het lumbosacraal radiculair syndroom. (dit proefschrift)

4. Fysiotherapie bij het lumbosacraal radiculair syndroom levert na een jaar meer herstelde patiënten op dan geen fysiotherapie. (dit proefschrift)

5. Fysiotherapie bij het lumbosacraal radiculair syndroom is geen kosteneffectieve toevoeging aan de huisartsenbehandeling. (dit proefschrift)

6. De heilgymnasten van vroeger en de fysiotherapie van nu, het blijft hoofdzakelijk een kwestie van actief oefenen.

7. Kwaliteit is geen kostenpost maar een investering.

8. Fantasie is belangrijker dan kennis. (Albert Einstein)

9. Iedereen heeft recht op elke medische behandeling, ongeacht wat deze kost.

10. De genezing begint als de huisarts vraagt wat je er zelf aan denkt te gaan doen.

11. Velen klagen over hun uiterlijk maar niemand over zijn verstand.

Evidence-based practice regarding the lumbosacral radicular syndrome

Pim Luijsterburg

Evidence-based practice regarding the lumbosacral radicular syndrome

Evidence-based handelen bij het lumbosacraal radiculair syndroom

Proefschrift

Ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de

rector magnificus
Prof.dr. S.W.J. Lamberts

en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
woensdag 29 november 2006 om 09.45 uur

door

Petrus Antonius Johannes Luijsterburg
geboren te Halsteren

Promotiecommissie

Promotoren   : Prof.dr. B.W. Koes
                          Prof.dr. C.J.J. Avezaat

Overige leden   : Prof.dr.ir. P.M. Bongers
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Contents

General introduction

In general practice the lumbosacral radicular syndrome (LRS) is the most frequently seen specific low-back disorder. LRS is not life threatening, but does cause pain in the leg and disability, often resulting in utilisation of healthcare resources and absenteeism from work. In the literature LRS is also referred to as 'sciatica', 'ischias', or 'ischialgetic pain'. These synonyms are considered to be vague and less specific terms and, if possible, should be avoided.[1] The definition of LRS used in this thesis is as follows: LRS is a disorder with radiating pain in the leg below the knee in one or more lumbar or sacral dermatomes, and can be accompanied by phenomena associated with nerve root tension or neurological deficits.[1-5]

Disc herniations are the most frequent cause of LRS, but other (more rare) causes include spinal or lateral recess stenosis, tumours and radiculitis.[1,5] The incidence of LRS in the Netherlands is estimated at between 60,000 and 75,000 cases per year.[1] The total (direct and indirect) costs of LRS in the Netherlands are estimated at 1.18 billion euro a year.[1]

Most patients seeking medical care in the Netherlands usually first visit a general practitioner (GP), who is regarded as the 'gatekeeper' of the healthcare system. The majority of health problems presented to GPs are treated by the GPs themselves, and these GPs are responsible for most of the referrals to (para)medical specialists. Clinical practice guidelines have been advocated as a means to improve the quality of healthcare services, decrease costs, and/or foster evidence-based decision making.[6-10] In 1996 the Dutch College of General Practitioners published their clinical guideline for LRS[11] and updated it in 2005.[5] In addition, a clinical practice guideline for LRS was issued in 1996 by the Dutch Institute of Quality Health Care;[2] this LRS guideline is a consensus between 12 (para)medical specialties (physical therapists, general practitioners, orthopedic surgeons, anesthesiologists, epidemiologists, neurosurgeons, neurophysiologists, neurologists, radiologists, rehabilitation physicians, physical medical scientists, social medical scientists) involved in treating patients with LRS.

There is consensus that treatment of LRS in the first 6 to 8 weeks should be conservative. Primarily, conservative treatment consists of adequate pain medication, giving information about the natural course of LRS (which generally is favourable), and stimulating the patient to continue normal daily activities. Many conservative treatments are available for treating LRS, and many patients are referred to physical therapy.[1]

According to the guidelines for LRS, surgery can be recommended for patients with objective evidence of a disc herniation who have not responded to conservative treatment.[5,11,12] If this is the case, the patient is usually referred to a neurologist or a neurosurgeon. In the Netherlands the neurosurgeon generally performs surgery in those patients with LRS caused by a disc herniation.

In 1999 the Health Council of the Netherlands published recommendations for research to determine to what extent the current knowledge on LRS is utilised by the (para)medical specialties involved.[1] In particular, the efficacy of guidance in the case of physical therapy needed to be investigated.[1]

The overall objective of the research described in this thesis was to establish the GPs' and neurosurgeons' current management of patients with LRS compared with the guidelines, and to assess the effectiveness of physical therapy in addition to the GP's care in patients with acute LRS.

This thesis consists of eight chapters; because each chapter has been written as a separate article there may be some overlap in content between the chapters.

The study presented in Chapter 1 is based on 63 GPs and 136 of their patients with LRS, and aimed to establish the GPs' current policy in the diagnosis and treatment of LRS compared with their clinical guideline. Chapter 2 presents data compiled from 66 neurosurgeons in the Netherlands and investigated to what extent neurosurgeons endorse the content of the LRS guideline. In Chapter 3 data are presented of the same 66 neurosurgeons and 163 patients who had undergone surgery because of a herniated disc in the lumbar spine; this study evaluated the neurosurgeons' current management of LRS patients who had undergone surgery in comparison with the LRS guideline. Chapter 4 presents the 19-month follow-up data of these 163 LRS patients who had undergone surgery, and aimed to investigate the mid-long-term outcomes after surgery and to identify prognostic factors for persisting LRS complaints.

Chapter 5 presents the results of our systematic review that was conducted to assess the effectiveness of conservative treatments in LRS when compared to placebo, inactive or no treatment, or compared to other forms of conservative care or surgery. Chapter 6 presents the design of a randomised clinical trial of conservative treatment (GP care and additional physical therapy) in patients with acute LRS. Chapter 7 presents the 1-year follow-up data of this trial which included 135 patients with LRS from 112 GPs (note: these are not the same GPs and patients presented in Chapter 1); this study aimed to assess the effectiveness of physical therapy in addition to GP care compared to GP care alone, in patients with acute LRS. Data on our economic evaluation are presented in Chapter 8 that aimed to assess the cost-effectiveness of physical therapy and GP care for patients with acute LRS.

Finally, the General Discussion addresses the most important results of the studies, the study limitations and their implications.

Chapter 1

General practitioners' management of the lumbosacral radicular syndrome compared with a clinical guideline

Pim A.J. Luijsterburg, Arianne P. Verhagen, Sigrid Braak, Anushka Oemraw, Cees J.J. Avezaat, Bart W. Koes.

Abstract

Objective To investigate the current treatment policy of general practitioners (GPs) in patients with a lumbosacral radicular syndrome (LRS) compared with their clinical guideline.

Design A cross sectional survey.

Methods Sixty-three GPs completed questionnaires about their treatment policy in individual LRS patients at baseline and at six months follow-up. Simultaneously, 136 LRS patients of these GPs were interviewed at baseline, and at three and six month's follow-up.

Results Of the 12 recommendations in the guideline related to history taking, four were not adhered to by the GPs in about 25% of the patients. Of the ten recommended physical examinations, three are not frequently carried out by the GPs. Almost 40% of the patients were referred to physiotherapy and 27% received muscle relaxants.

Conclusion The majority of the GPs support the content of the LRS guideline. Overall, there was a good adherence with the guideline for history taking and physical examination, and a moderate adherence for treatment policy.

Introduction

Practice guidelines have been advocated as a means to improve quality, decrease costs, reduce variation, and/or foster evidence-based decision making.[6-10] Guideline recommendations must be implemented to achieve the desired outcomes. To evaluate the implementation it is important to establish whether a profession, in general, accepts the guideline.[9] Furthermore, insight in the current adherence of the professions is needed.[13] Reported rates of adherence with guidelines are extremely variable, ranging from 20% to nearly 100%, depending on the guideline and the definition of adherence.[8,14,15]

In 1996 the Dutch College of General Practitioners published their evidence based clinical guideline for the lumbosacral radicular syndrome (LRS).[2] Appendix A shows the summary of this guideline. Most patients seeking medical care in the Netherlands will first visit a general practitioner (GP), who is regarded as the 'gatekeeper' of the health care system. The majority of health problems presented to GPs are treated by the GPs themselves and they are responsible for most referrals to (para)medical specialists.

The lumbosacral radicular syndrome, also called sciatica, is a disorder with radiating pain and/or neurological deficits in one or more lumbar or sacral dermatomes, often associated with back pain.[2,4,16] LRS is mostly caused by a prolapsed disc, but other causes include spinal or lateral recess stenosis, tumours or radiculitis.[1,2,4] The incidence of LRS in general practice in the Netherlands is estimated between 60,000 and 75,000 a year.[1]

This study was aimed to establish GPs' current policy in the diagnosis and treatment of LRS compared with their clinical guideline.

Methods

General practitioners
GPs were recruited in the Rotterdam area from July to October 2001. After agreeing to participate the GPs were visited and helped to search their electronic medical records (EMD) for appropriate patients with LRS.

Patients
Patients with LRS were identified in the EMDs of the participating general practices based on the following inclusion criteria: diagnosed with LRS (ICPC-code L86) by their GP (see Appendix A) in the previous four months, age between 18 and 65 years, contactable by telephone, able to speak Dutch, and providing written informed consent. Patients with LRS complaints in the preceding six months were excluded. Also excluded were patients with a specific cause for leg pain other than LRS, or with a suspected prolapsed disc in the upper region of the spine.

Questionnaires
From the participating GPs data were collected concerning age, gender, working experience in years, type of general practice (solo practice or group practice) and to what extent they agree with the content of the guideline (almost entirely, partially and almost not). A questionnaire was developed to determine GPs' current management of each participating LRS patient at baseline (study entry) and at six months follow-up. This questionnaire asked the GPs: 1) whether they had asked the patient the 12 questions related to history taking (yes or no), 2) whether the ten recommended physical examinations had been performed (yes or no), and 3) for a description of the prescribed treatment(s) e.g. medication, bed rest and referrals to (para)medical specialists. In both questionnaires GPs had the possibility to give additional explanations if considered necessary.

After obtaining informed consent, the patients were interviewed by telephone at baseline, and at three and six month's follow-up. The interviews established the patients' characteristics, their types of complaints, and the treatment(s) prescribed by the GP.

Statistical analysis
Descriptive statistics were used to present the frequencies of the GPs subscribing to the content of the guideline and their current management of LRS patients compared with the guideline.

We arbitrarily decided that there was no deviation from the LRS guideline when 60% or more of the GPs had answered '(almost) always' to any item in the questionnaire that addressed their global opinion of the guideline.
To establish to what extent the GPs adhere with the guideline, the following cut-off points were used for history taking, physical examination and prescribed treatment(s):
- GPs' adherence with the guideline for history taking was considered good, when at least 50% of the patients was asked more than eight of the 12 questions, moderate when five to eight of the questions were asked, and adherence was considered weak when the GPs asked four or less questions.

- GPs' adherence with the guideline for physical examination was considered good when six or more of the ten examinations were performed in at least 50% of the patients, moderate when four to six examinations were performed, and adherence was considered weak when the GPs carried out three or less of the examinations.
- GPs' adherence with the guideline for treatment was considered good, when there was only one or no deviation from the four types of recommendations (i.e. medication, bed rest, referral to (para) medical specialist), moderate when there was a deviation from two or three types of recommendations, and was considered weak when GPs deviated from all four types of recommendations. A deviation was considered present when treatment did not conform to the guideline in at least 25% of the patients.

All data were coded and analysed using the statistical package SPSS for Windows (version 10.0.7).

Ethics
The procedures of this study were in accordance with the ethical standards of the revised Helsinki declaration of 1983 and were approved by the Erasmus Medical Center ethics committee.

Results

GPs' characteristics
Of the 366 invited GPs, 63 GPs agreed to participate. Figure 1 summarizes GP and patient flow through the study. Reasons for not participating were: lack of time (30%), participating in another study (4%), no financial allowance for participating (2%), and various other reasons (30%), or reasons unknown (34%). The mean age of the participating GPs was 46 (SD 7.6) years, 14% were female, and the mean work experience was 16 (SD 8.7) years. Twenty-seven of the 63 participating GPs agreed entirely with the content of the guideline, 25 GPs partially and 11 GPs had not answered this question.

Patients' characteristics
We identified 292 patients in the GPs' EMDs (range 1 to 9 patients per GP) who were diagnosed with LRS during the previous four months. After applying the inclusion criteria, 229 patients were invited to participate in the study. The reasons for exclusion were: diagnosed with LRS in the previous six months (43%), not speaking Dutch (16%), over 65 years of age (14%), another specific cause for leg pain (14%) and being a patient of another GP in a group practice who did not participate in the study (13%).

Finally, 136 patients gave written consent, their mean age was 47 (SD 13.4) years and 51% was female. No information was available about the non-participating patients.
During the telephone interview, the patients reported that before they first consulted their GP the LRS complaints had persisted for (median) two weeks (IQR 7.2), and the time between the first consultation with their GP and the interview was (median) 14.6 weeks (IQR 16.1).

Figure 1: Flow chart of GPs and patients**.**
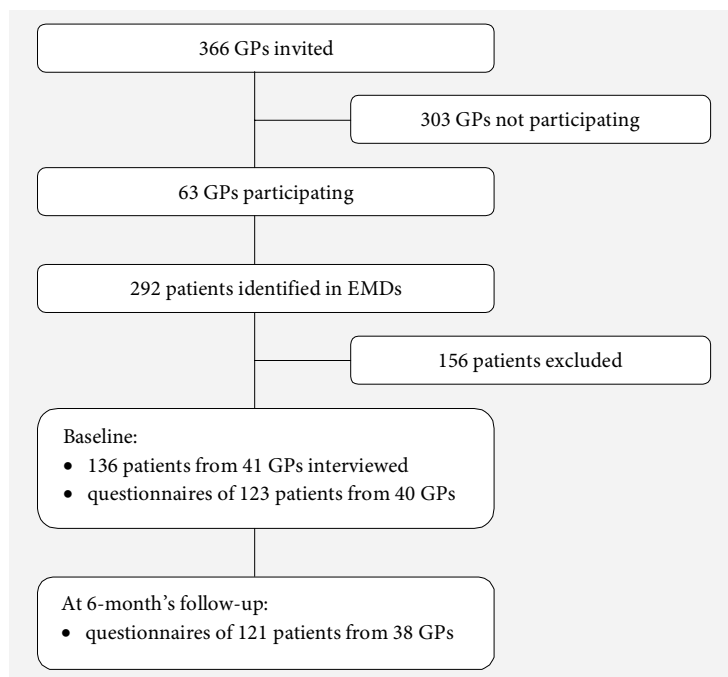
Table 1 lists the patients' complaints at the first consultation with their GP, as reported by the patients during the baseline interview.

Table 1: Complaints of the patients (n=136) at their first consultation with the GP, as reported by the patients at the baseline telephone interview.

	At baseline, n (%)
Back pain with irradiating pain to the leg	112 (82)
Pain below the knee	110 (81)
Sensory deficits in the leg	90 (66)
Decreased muscle strength in the leg	87 (64)
Decreased pain on rest	62 (46)
Increased pain with daily activities	75 (55)
Specific body position with more or less pain	109 (80)
Reported a cause of the complaints	70 (52)
Increased pain on coughing, sneezing or straining	67 (49)
Urinary problems	13 (10)
Saddle anaesthesia	52 (38)

n= number (and percentage) of patients per complaint.

Management of LRS patients
At baseline, 40 GPs completed the questionnaire about the current management of 123 patients (90%), and at six months follow-up 38 GPs completed this questionnaire about 121 patients (89%).

Table 2 lists the questions asked at history taking and the physical examinations performed by the participating patients, as reported by the GPs at baseline based on their medical records (missing data ranges from 1-13%).

Table 2: Questions asked at history taking and physical examinations performed by GPs in 123 patients (baseline data).

	Asked / performed, n (%)	Not asked / not performed, n (%)
History characteristics:		
Back pain with irradiating pain to the leg	123 (100)	0 (0)
Pain below the knee	122 (99)	1 (1)
Sensory deficits in the leg	120 (97)	3 (3)
Decreased muscle strength in the leg	121 (98)	2 (2)
Duration of complaints before first GP consultation	99 (80)	14 (11)
Pain on rest	73 (59)	35 (28)
Pain on daily activities	82 (67)	28 (23)
Specific body position with more or less pain	89 (72)	30 (24)
Cause of the complaints	114 (92)	5 (4)
Pain on coughing, sneezing or straining	104 (85)	16 (13)
Urinary problems	107 (87)	15 (12)
Saddle anaesthesia	94 (76)	29 (24)
Physical examinations:		
Physical inspection	94 (76)	27 (22)
Active examination	90 (73)	32 (26)
Test of Lasègue	107 (87)	16 (13)
Test of Bragard	34 (28)	85 (69)
Ankle tendon reflex	90 (73)	32 (26)
Knee tendon reflex	88 (72)	33 (27)
Sensory deficits in the foot	69 (56)	52 (42)
Muscular strength of the big toe	48 (39)	72 (59)
Walking on heels and on toes	71 (58)	49 (40)
Crossed test of Lasègue	44 (36)	74 (60)

n= number (and percentage) of patients (not) asked/(not) performed.

In 23-28% of the patients the GPs did not ask four questions related to history taking: i.e. decreased or increased pain on rest, on daily activities, on specific body position, and the presence of saddle anaesthesia. Nevertheless, because these recommended questions were asked by the GPs in more than 50% of the patients, we concluded that the GPs' adherence with the LRS guideline is good for history taking.

Seven of the ten physical examinations were carried out by the GPs in more than 50% of the patients. The examinations for muscular strength of the big toe and the crossed test of Lasègue were performed in 39% and 36% of the patients respectively. Therefore, for the physical examinations we concluded that GPs' adherence with the guideline is good.
Table 3 lists the prescribed treatment(s) as reported by the GPs at baseline and at six-month follow-up.

During the six-month follow-up the GPs prescribed medication for 82% of the patients, mostly NSAIDs (54%). In addition, they prescribed paracetamol for 15% of the patients and muscle relaxants for 27% of the patients.

Table 3: Treatments prescribed treatment(s) by 40 GPs in 123 patients at baseline, and by 38 GPs in 121 patients at the 6-month follow-up.

	At baseline (40 GPs/123 pats.), n (%)	6 months (38 GPs/121 pats.), n (%)
Medication	99 (80)	2 (2)
Bed rest	18 (15)	1 (0.8)
Referral for physiotherapy	45 (37)	14 (12)
Referral for manual therapy	2 (2)	1 (0.8)
Referral for X-rays	2 (2)	0
Referral to orthopedic surgeon	2 (2)	0
Referral to neurologist	30 (24)	7 (6)
Referral to neurosurgeon	1 (1)	0
Other	4 (3)	7 (6)

n= number (and percentage) of patients.

The LRS guideline, however, recommends paracetamol as first choice followed by NSAIDs. Moreover, the guideline claims that there is no indication for prescribing muscle relaxants.
The GPs prescribed bed rest in about 15% of the patients during the six-month follow-up. The guideline still recommends bed rest as treatment for severe LRS complaints. However, recent data indicate that this recommendation may be outdated.[17]
The GPs referred 49% of the patients to physiotherapy during the six-month follow-up. The guideline LRS, however, claims that physiotherapy is (as yet) not a treatment alternative for LRS.
During the six-month follow-up the GPs referred about 35% of the patients to a medical specialist: 40% these referrals (missing 60%) took place after a median period of eight (IQR 11) weeks. The majority of these referrals (65%) were made before eight weeks after the first consultation with the GP. However, due to the high percentage of missing data we were unable to determine whether overall the GPs deviated from the recommendation 'referral to specialist'. Because the GPs deviated from three (i.e. medication, bed rest, and referral to paramedical specialists) of the four types of recommendations, we concluded that the GPs' adherence with the guideline for treatment policy is moderate.

Discussion

Fifty-two of the 63 participating GPs agree (at least partially) with the content of the LRS guideline. GPs' adherence with the guideline is good for history taking and physical examination, and moderate for prescribed treatment. The GPs prescribed muscle relaxation medication and physiotherapy in 27% and 49% of the patients, respectively.

Some limitations of the study need to be discussed. Firstly, simply inviting GPs to participate in this study could have introduced selection bias in that motivated GPs may already largely adhere with the LRS guideline.

Furthermore, because GPs were recruited without consideration of the type of general practice or gender, GPs working in a solo practice are over-represented (71% versus 44% for the entire Netherlands).[18] The percentage of female GPs in this study is slightly under-represented (14% versus 21% for the entire Netherlands).[18] Therefore, it is possible that our results under- or overestimate the acceptance of the GPs' guideline for LRS, but we cannot confirm this.

The LRS patients were identified retrospectively (in the previous four months) using the GPs' EMDs and searching for ICPC-code L86. Some patients with LRS may have been missed because the GPs coded them differently, e.g. as ICPC L02 (back complaints). It is reported that the incidence of LRS in general practice in the Netherlands is three patients in three months.[1] In 45 practices we identified 229 LRS patients, giving an incidence rate of five LRS patients in four months. Therefore we assume that no major patient selection occurred because of the partially retrospective design.

Because the questionnaires used in the present study were specifically developed based on the GPs' LRS guideline, no data on the reliability and validity of these questionnaires are available. Inherent to the retrospective design of this study there are some problems in the data collection from GPs and patients. GPs reports about their management in patients with LRS were based on their medical record and on their memory of the consultation. The patients answers were based on their memory only. But, we do not know in which way this influenced the results.

The clinical guideline LRS evaluated was published in 1996 and is recently updated.[5] However, there are no major changes in the updated guideline except that bed rest is not a treatment option any more. The results of our study show that the GPs did not often prescribe bed rest, already. This means that the results from our study are probably comparable if we compare GPs' management in our study with the updated clinical guideline LRS. Also, in the updated guideline more attention is paid about the information and advice given to the patients with LRS i.e. more positive messages aimed to change beliefs and behavior, this in accordance with the study of Chaudhary et al.[19]

Conclusion

This study shows that GPs adhere to a large extent with the guideline for history taking and physical examination, and to a moderate extent for prescribing treatment(s) for patients with LRS.

Appendix A: Summary of the clinical guideline 'Lumbosacral radicular syndrome' of the Dutch College of General Practitioners (1996)

Definition: The lumbosacral radicular syndrome: radiating pain and/or neurological deficits in one or more lumbar or sacral dermatomes, often associated with back pain; mostly caused by irritation and compression (traction) of the nerve root.

History taking: Ask about: 1) localisation, radiation, intensity and duration of the pain, 2) influence of rest, movement and posture, 3) development of the complaints, 4) interference with daily activities caused by leg pain, 5) decreased muscle strength and sensory deficits, 6) influence of coughing, sneezing or straining, 7) previous history of back complaints, and 8) urinary problems and saddle anaesthesia.

Physical examination: 1) physical inspection (spine and pelvis), 2) active examination (ante-, retro-, lateroflexion), and 3) Lasègue sign and test of Bragard. If there is a positive Lasègue sign, decreased muscle strength or sensory deficits perform: 4) ankle tendon reflex and knee tendon reflex, 5) sensory examination of the lateral and medial side of the foot, 6) muscular strength of the big toe, walking on heels and toes, and 7) crossed test of Lasègue.

Additional examinations: X-rays should only be ordered in case of suspicion on malignancy or a fracture due to osteoporosis.

Evaluation: The lumbosacral radicular syndrome should be diagnosed if there are radiating complaints in the leg below the knee, plus one of the following findings: 1) a positive Lasègue sign (or Bragard), or 2) neurological deficits reducible to a single nerve root.

Information and advice: Explain to the patient that radiating complaints are caused by a prolapsed disc that gives pressure on a nerve in the back. There is a favourable course in 80% of the patients with conservative care. Back pain may persist after the leg pain has gone.

Mild complaints: Advice the patient to perform the usual daily activities but to avoid painful movements. Gradually increase the activities.

Severe complaints: Strict bed rest (washing and toilet visits on bed) for two weeks. When the complaints decrease after a few days or two weeks, less strict bed rest (walking, washing and toilet visits allowed). Gradually increase the activities to normal level in six weeks and to patients' level in six to twelve weeks.

Follow-up: Check the patient with bed rest after two to four days. Evaluate the effect of treatment by checking Lasègue sign and the severity of the complaints. Check patients with severe complaints daily and subsequently at least once a week. Accompany the patient till full resumption of daily activities.

Drug treatment: If desired: paracetamol (4-6 dd, 500mg), ibuprofen (3-4 dd, 400 mg), diclofenac (3-4 dd, 25-50 mg), or naproxen (2-3-dd, 250 mg).

Referral: Refer in an instant: 1) cauda equina syndrome, or 2) progressive paresis within a few days in spite of conservative care. Refer for diagnostics and judgement for indication for surgery: 1) Severe radicular pain in spite of bed rest and adequate medication, 2) Severe paresis or progressive paresis in spite of adequate care (walking on heels and toes is impossible), 3) doubtful diagnosis, or 4) mild complaints with no improvement after six to eight weeks.

Chapter 2

Do neurosurgeons subscribe to the guideline lumbosacral radicular syndrome?

Pim A.J. Luijsterburg, Arianne P. Verhagen, Sigrid Braak, Cees J.J. Avezaat, Bart W. Koes.

Abstract

Background This study presents a survey of the opinion of neurosurgeons on the multidisciplinary clinical guideline 'lumbosacral radicular syndrome'. The aim was to describe to what extent neurosurgeons in the Netherlands endorse the content of this guideline. The guideline was issued in 1996 by the Netherlands Institute of Quality Health Care and this is the first attempt to evaluate the implementation of this guideline.
Methods All active neurosurgeons (n=92) in the Netherlands were invited to complete a questionnaire investigating to what extent they agree with the 26 recommendations in the guideline 'lumbosacral radicular syndrome'. The results are represented in frequencies (%) in order to express the magnitude of their consent or dissent with the recommendations.
Results Overall, 75% of the neurosurgeons responded and, of these, 94% agreed (at least partially) with the content of the guideline. Of the 26 recommendations in the guideline, seven were not fully endorsed by the neurosurgeons. Three of these seven recommendations may need revision based on newly published data.
Conclusion This survey shows that almost all neurosurgeons subscribed (at least partially) to the multidisciplinary LRS guideline. Therefore, one important aspect of the implementation process has been fulfilled, i.e. acceptance of the content of the guideline.

Introduction

The lumbosacral radicular syndrome (LRS), also known as 'sciatica', is a disorder with radiating pain in one or more lumbar or sacral dermatomes, and can be accompanied with phenomena associated with nerve root tension or neurological deficits.[2,4,11,16] LRS is mostly caused by a prolapsed disc, but other causes can include spinal or lateral recess stenosis and tumours or radiculitis.[1,4] The incidence of LRS in the Netherlands is estimated between 60,000 and 75,000.[1] In the Netherlands the neurosurgeon generally performs surgery in patients with LRS caused by a prolapsed disc.

A multidisciplinary clinical practice guideline for LRS was issued in 1996 by the Netherlands Institute of Quality Health Care.[2] This guideline (as far as possible evidence-based) is a consensus between 12 (para)medical professions involved in the management of patients with LRS. The guideline presents 26 recommendations (see Appendix A) which serve to guide physicians in their management of patients with LRS.

Clinical guidelines are developed to improve quality of health care and to foster evidence-based decision making.[6-9] But their recommendations must be implemented to achieve the desired outcomes. In order to evaluate the implementation of a particular guideline, it is important to know whether the profession concerned accepts the content of the guideline.[9] Therefore, this study investigated to what extent neurosurgeons in the Netherlands endorse the content of the LRS guideline.

Materials and methods

In June 2001 a questionnaire about the LRS guideline was mailed to all 92 active neurosurgeons associated with the Netherlands Society of Neurosurgeons, together with a letter of recommendation from the chairman of the Society. Reminders were sent after 1 and 2 months.

The questionnaire addressed the following: (1) neurosurgeons' characteristics including age, gender, years of working experience and their type of neurosurgery centre (i.e. university/non-university); (2) to what extent they are acquainted with the content of the multidisciplinary guideline, with answer options: (almost) entirely, partially, and (almost) not; (3) to what extent they subscribe to the content of the guideline, with answer options: (almost) entirely, partially, and (almost) not; and (4) to what extent they agree with each of the 26 recommendations in the guideline, each recommendation had the answer option: (almost) entirely, partially, and (almost) not. All answers could be explained with an explanation if required. In addition, because two of the 26 recommendations concern general practitioners (GPs) and because GPs have their own LRS guideline[11], neurosurgeons were also asked about their acquaintance with the GPs' guideline for LRS.

Descriptive statistics were used to present the frequencies of the neurosurgeons' agreement/disagreement with the multidisciplinary guideline; all frequencies are based on the total number of neurosurgeons. All variables used to describe the neurosurgeons' characteristics are presented as the mean and standard deviation (SD) if they are normally distributed, and by the median and interquartile range (IQR) if they are not normally distributed. We decided that any of the 26 recommendations in the questionnaire was debatable when 60% or less of the neurosurgeons did not agree (almost) entirely with a particular recommendation. All data were coded and analysed using the statistical package SPSS for Windows (version 10.0.7).

Results

Neurosurgeons' characteristics
Of the 92 invited neurosurgeons, 69 (75%) returned the questionnaire. Because 3 of the responding neurosurgeons stated that they did not treat LRS patients, data from 66 respondents were included in the analysis. Reasons for non-response are unknown because the questionnaires were returned anonymously. The median age of the neurosurgeons was 45 (IQR 15) years, 9% were female, and the median work experience was 12 (IQR 17) years. The neurosurgeons estimated to manage a median of 60 LRS patients (IQR 67) during a 3-month period. The median number of patients with LRS who underwent surgery was estimated to be 30 (IQR 45) patients in a 3-month period.

Subscribing to the LRS guideline
The neurosurgeons were asked if they were acquainted with the content of the multidisciplinary guideline and to what extent they subscribe to the guideline. Table 1 shows that 91% are acquainted (at least partially) with the content of the guideline, and that 94% subscribe (at least partially) to the guideline. In contrast, only 50% were acquainted with the LRS guideline issued by the Dutch College of General Practitioners.

Table 1: Neurosurgeons' responses to questions about the multidisciplenary LRS guideline and the LRS guideline issued by the Dutch College of General Practitioners (GPs' guideline).

	Neurosurgeons, n (%)
Acquainted with the content of the guideline:	
(almost) entirely	42 (63.5)
partially	18 (27.5)
(almost) not at all	6 (9.0)
missing answers	0 (0.0)
Subscribe to the guideline:	
(almost) entirely	24 (36.5)
partially	38 (57.5)
(almost) not at all	0 (0.0)
missing answers	4 (6.0)
Acquainted with the content of the GPs' guideline:	
(almost) entirely	15 (22.5)
partially	18 (27.5)
(almost) not at all	33 (50.0)
missing answers	0 (0.0)

n= number of neurosurgeons.

Recommendations

Appendix A lists the 26 recommendations in the multidisciplinary LRS guideline. Table 2 shows to what extent the neurosurgeons agree/disagree with these recommendations.

Over 60% of the neurosurgeons completely agreed with 19 of the 26 recommendations. The remaining 7 recommendations, which were endorsed by less than 60% of the neurosurgeons, are discussed here.

1. Arguments against recommendation 12 (The GP can perform clinical diagnostics and treatment in most LRS-patients) were: 'depends on the seriousness of the complaints (n=2)', 'expert report by the GP is questionable, knowledge of LRS is often insufficient (n=6)', and 'GPs' referral to a specialist is usually late (n=2)'.
2. Arguments against recommendation 17 (The most important indication for surgery in prolapsed disc is severe radicular pain and not the sensory deficits, except for the cauda equina syndrome) were: 'the presence of neurological deficits can be an additional reason to perform surgery (n=2)', and 'as well as severe suffering an important indication for surgery (n=17)'.
3. Arguments against recommendation 19 (After six weeks the GP should discuss the option of surgery with the patient with LRS when there is no clear improvement of the complaints) were: 'six weeks is too long (n=8)', and 'depending on the seriousness of the complaints and level of neurological deficits surgery must be considered sooner (n=5)'.
4. Arguments against recommendation 20 (There is no evidence that the prognosis of paresis improves by surgical intervention) were: 'experience has shown that muscle strength in the leg does improve after surgery (n=7)', and 'has not yet been evaluated, so it can be an indication (n=5)'.

Table 2: Neurosurgeons' (n=66) level of agreement/disagreement (frequencies) with the 26 recommendations in the multidisciplinary LRS guideline.

Recommendation:	(almost) entirely, %	Partially, %	(almost) not, %	Missing, %
1	96	1	1	2
2	82	17	0	1
3	73	21	5	1
4	89	9	0	2
5	73	21	5	1
6	68	17	11	4
7	70	20	6	4
8	64	20	9	7
9	64	23	9	4
10	35	41	18	6
11	71	21	5	3
12	55	33	12	0
13	53	32	14	1
14	82	9	6	3
15	74	21	2	3
16	83	14	3	0
17	41	39	15	5
18	6	27	59	8
19	58	32	6	4
20	55	26	15	4
21	91	3	2	4
22	76	14	5	5
23	79	18	2	1
24	65	29	6	0
25	86	14	0	0
26	65	30	0	5

Finally, the neurosurgeons reported that new evidence was available that no longer supported 3 of the recommendations:

- Recommendation 10 (Neurophysiological examination can provide additional information about the location and severity of the nerve root damage, when radiological findings are not in accordance with clinical findings) because: 'the additional information from a neurophysiological examination is poor (n=9)'.
- Recommendation 13 (Conservative treatments are not sufficiently investigated to draw conclusions regarding their effectiveness) because: 'bed rest, traction and psychotherapy have been examined and are demonstrated not to be useful (n=16)'.
- Recommendation 18 (chemonucleolysis is proven effective for LRS caused by prolapsed disc; the results after one year correspond with the results of surgery) because: 'indication is limited, chemonucleolysis is not effective (n=8)', 'percentage of patients with complaints after chemonucleolysis is higher than after surgery (n=6)', and 'chemonucleolysis is effective but less effective than surgery (n=3)'.

Indication for and timing of surgery
The questionnaire asked the neurosurgeons: "What, in your opinion, is the indication for surgery in patients with LRS caused by a prolapsed disc?"

The neurosurgeons reported 8 indications: the cauda equina syndrome (68%), long-term and disabling pain (67%), progressive paresis (33%), radiological findings in accordance with clinical signs (15%), patients' wishes (15%), recurrences (11%), acute paresis (9%), and persisting complaints (6%).

They were also asked: "At what point of time after the onset of an LRS episode do you recommend surgery for a patient with LRS caused by a prolapsed disc with pain and no neurological deficits?" Table 3 gives the neurosurgeons' answers (range 2-16 weeks) to this question.

Table 3: Neurosurgeons (n=66) recommended timing of surgery for patients with LRS caused by a prolapsed disc.

Surgery after:	%*
2 to 6 weeks	17
6 weeks	18
6 to 8 weeks	5
8 weeks	14
8 to 12 weeks	9
12 weeks	15
12 to 16 weeks	6

* Missing values 16%.

About half of the neurosurgeons (54%) preferred to wait 2-8 weeks and the remainder preferred to wait 8-16 weeks before performing surgery.

Discussion

An important condition for the implementation of any guideline is the extent to which a profession agrees with the content of the guideline.[9,20] This survey shows that most (94%) of the participating neurosurgeons agrees (at least partially) with the content of the multidisciplinary guideline for the management of LRS. The neurosurgeons endorsed 19 of the 26 recommendations in the guideline; the remaining 7 recommendations were accepted by less than 60% of the neurosurgeons. Recommendations 17, 19 and 20 are still being debated because there are (as yet) no convincing data available. Due to a difference in viewpoint between neurosurgeons and GPs, less than 60% of the neurosurgeons agreed with recommendation 12 (The GP can perform clinical diagnostics and treatment in most LRS patients). This difference may be due to the fact that 50% of the neurosurgeons were not aware of the content of the LRS guideline issued by the Dutch College of General Practitioners. For recommendations 10, 13 and 18 the neurosurgeons reported that new evidence invalidated these three recommendations.

In spite of the high response (75%) to the questionnaire some selection bias may have occurred. For example, because the questionnaire was returned anonymously, we have no way of determining the reasons for non-response. Although it is possible that our results under- or overestimate acceptance of the guideline by neurosurgeons, we cannot confirm this.

Because the questionnaire was specifically developed for this study based on the content of the LRS guideline, no data on the reliability and validity of this questionnaire are available.

Also we arbitrarily selected a cut-off point of 60% or less as a measure of whether or not a recommendation was endorsed.

In the Netherlands, patients with the lumbosacral radicular syndrome are not only operated by neurosurgeons. Also orthopedic surgeons perform this operation, but only in a minority of patients (17%). The results of this study cannot be generalized towards the orthopedic surgeons in the Netherlands.

The timing of sugery for a patient with LRS caused by a prolapsed disc ranged from 2 to 16 weeks (Table 3). Half of the neurosurgeons preferred to wait less than 8 weeks, and the others preferred to wait more than 8 weeks. Recommendation 16 of the guideline indicates a waiting period of 4 to 8 weeks.
The LRS guideline of the Dutch College of General Practitioners recommends referral to a specialist when there is no improvement after 6 to 8 weeks. The literature provides no evidence for the most optimal timing of surgery.

The adherence towards the guideline LRS in neurosurgeons' daily practice was not evaluated in this study. In the Netherlands, we do not know to what extent the neurosurgeons actually follow the recommendations of the guideline LRS. Here we only evaluated their altitude towards the guideline because without a positive attitude, implementation becomes difficult.

Conclusion

This study shows that neurosurgeons largely subscribe to the guideline for the management of LRS. The next important step is to investigate the neurosurgeons' actual management of LRS patients compared with the guideline recommendations. Nevertheless, guidelines need to be regulary updated to remain useful to clinicians. The multidisciplinary clinical guideline for the management of LRS was issued in 1996. The present study, 6 years later, shows that neurosurgeons consider that 3 recommendations need to be updated based on new evidence. Shelleke et al. estimated that guidelines should be reassessed for validity every 3 years.[21] Therefore, more studies are needed on the management of LRS in order to update the guidelines for this syndrome.

Appendix A: Recommendations in the multidisciplinary clinical guideline for the management of LRS.

1. LRS is characterised by radiating pain in one or more lumbo or sacral dermatomes, with or without other radicular symptoms.

2. LRS is often caused by a prolapsed disc, but is also caused by a spinal or resessus stenosis, or a combination of these.

3. LRS cannot be explained by mechanical compression of a nerve root only.

4. Many radiological abnormalities in the lumbar spine are not associated with nerve root compression or pain.

5. The test of Lasègue is the most valid and reliable test in acute LRS due to prolapsed disc. The test of Lasègue is often negative in neurological claudicatio.

6. There is no indication for routine X-rays of the lumbar spine in acute LRS.

7. MRI or CT-scan is only needed when surgery is considered, or if the results could have other therapeutical consequences.

8. MRI and CT-scan both have a high sensitivity for detecting a prolapsed disc and a low specificity: it is often impossible to distinguish between a prolapsed disc that causes the LRS and an accidental finding on the basis of imaging alone.

9. In radiological imaging of LRS, MRI is preferred; CT-scan is a good alternative. If uncertainty of nerve root compression persists caudography is indicated.

10. Neurophysiological examination can provide additional information about the location and severity of the nerve root damage, when radiological findings are not in accordance with clinical findings.

11. LRS is often self-limiting. The results of conservative treatments and surgery are similar in the long term (4-10 years), i.e. for those patients who do not undergo surgery because of progressive paresis or cauda equina syndrome.

12. The GP can perform clinical diagnostics and treatment in most LRS patients. Referral to a specialist is only useful when the GP is not sure about the diagnosis or considers surgical intervention.

13. Conservative treatments (e.g. bed rest, traction, physiotherapy and manipulation) are not sufficiently investigated to draw conclusions regarding their effectiveness.

14. The statement that strict bed rest (toilet visits and showering not permitted) is more effective in LRS due to prolapsed disc than liberal bed rest (toilet visits and showering permitted) is not based on prospective RCTs.

15. Effectiveness of 'back-schools' for LRS has not yet been investigated, neither for treatment, nor for prevention.

16. A severe LRS, persisting for 4 to 8 weeks with no improvement, is an indication for radiological examination possibly followed by surgical intervention. If there is improvement, a longer 'wait and see' policy is possible.

17. The most important indication for surgery in prolapsed disc is severe radicular pain and not the sensory deficits, except for the cauda equina syndrome.

18. Chemonucleolysis is proven effective for LRS caused by a prolapsed disc; the results after one year correspond with the results of surgery.

19. After 6 weeks the GP should discuss the option of surgery with the LRS patient when there is no clear improvement of the complaints.

20. There is no evidence that the prognosis of paresis improves by surgical intervention. Therefore, a light or moderate paresis is not an absolute indication for surgery.

21. Cauda equina syndrome caused by lumbar disc prolapse is an absolute indication for rapid surgery.

22. Percutaneous nucleotomy and percutaneous laser therapy are not evidenced-based treatments for LRS caused by disc prolapse.

23. There are no proven effective programs of treatment for primary or secondary prevention of LRS.

24. Advice not to work during and after the treatment of LRS, even in demanding jobs, should be given cautiously. This could delay rehabilitation.

25. The treating surgeon is responsible for medical care before and after surgery.

26. There are strong indications that psychological, social and financial factors play an important role in the development of persisting LRS (and the related disability).

Chapter 3

Neurosurgeons' management of lumbosacral radicular syndrome evaluated against a clinical guideline

Pim A.J. Luijsterburg, Arianne P. Verhagen, Sigrid Braak, Anushka Oemraw, Cees J.J. Avezaat, Bart W. Koes.

Abstract

Objectives To establish to what extent neurosurgeons subscribe to the lumbosacral radicular Syndrome (LRS) guideline, and to evaluate their current management of patients with LRS against the guideline.

Methods All active neurosurgeons in the Netherlands (n=92) were mailed a questionnaire about the guideline and data from 66 responders were analysed. Patients were recruited via seven of the participating neurosurgeons and were interviewed once by telephone. The medical records of the participating patients (n=163) were also examined.

Results Of the 26 propositions in the LRS guideline, seven are not fully endorsed by the neurosurgeons. Three of these seven propositions may need updating based on 'new evidence'. The time between the onset of the LRS episode and the actual moment of surgery was considerably longer than that recommended in the guideline.

Conclusions Based on their current management of LRS patients, the neurosurgeons largely adhere with the LRS guideline.

Introduction

The use of clinical practice guidelines in health care has grown rapidly and is now widespread.[13] Guidelines can be seen as a tool to improve the quality of health services and to incorporate latest scientific knowledge into daily clinical routines,[6,7] their implementation has been shown to improve clinical practice.[8-10] Rates of adherence with guidelines are extremely variable, ranging from 20% to nearly 100%, depending on the guideline and definition of adherence.[8,14,15]

A clinical practice guideline for the lumbosacral radicular syndrome (LRS) was issued in 1996 by the Dutch Institute of Quality Health Care.[2] This LRS guideline is a consensus between 12 (para)medical specialties (physical therapists, general practitioners, orthopedists, anesthetists, epidemiologists, neurosurgeons, neurophysiologists, neurologists, radiologists, rehabilitation doctors, physical medical sciences, social medical sciences) involved in treating patients with LRS. The guideline presents 26 propositions that (as far as possible) have been evidence-based (see Appendix A). These propositions serve to guide physicians in the management of patients with LRS.

The LRS, also called sciatica, is a disorder with radiating pain in one or more lumbar or sacral dermatomes, and can be accompanied with phenomena associated with nerve root tension or neurological deficits.[2,4,11,16] LRS is mostly caused a prolapsed disc but other causes include spinal or lateral recess stenosis, tumours, or infections.[1,2,4,11]

Patients with LRS usually visit their general practitioner (GP) first, and most are treated by their GP. According to the GPs' own guideline for LRS surgery can be recommended for patients with objective evidence of a prolapsed disc who have not responded to conservative treatment.[11,12] If this is the case, the patient is usually referred to a neurologist or a neurosurgeon. In the Netherlands the neurosurgeon generally performs surgery in those patients with LRS caused by a prolapsed disc. In the Netherlands, no data are available about the adherence of neurosurgeons with the LRS guideline, or on their current management of patients with LRS.[1]

Therefore, the aim of this study is to evaluate the implementation of the LRS guideline by neurosurgeons by exploring to what extent neurosurgeons endorse the content of the guideline, and by evaluating their current management of LRS patients who had undergone surgery because of a prolapsed disc in the lumbar spine, against the guideline.

Materials and methods

Neurosurgeons
All 92 neurosurgeons active in the Netherlands, and associated with the Dutch Society of Neurosurgeons, were invited to participate in this study in June 2001.

Patients
Patients were recruited from the practices of seven of the participating neurosurgeons working in four different hospitals in the southern part of the Netherlands. Invited to participate in the study were consecutive LRS patients who had undergone surgery because of a prolapsed disc in the lumbar spine in the previous six months. Additional inclusion criteria were: age between 18 and 65 years, approachable by telephone, understanding Dutch, and providing written informed consent. Excluded were patients with a prolapsed disc other than at the L4-L5, and L5-S1 levels. Eligible patients gave their written informed consent before they enter in the study.

Neurosurgeons' questionnaire
A questionnaire about the LRS guideline (i.e. asking about neurosurgeons' management of LRS patients in general) was mailed to the neurosurgeons together with by a letter of recommendation from the chairman of the Dutch Society of Neurosurgeons. This questionnaire (to be returned anonymously) contained questions on (1) neurosurgeons' characteristics including age, gender, years of working experience, and their type of neurosurgical center (i.e. university or non-university), (2) to what extent they endorse to the content of the guideline 'in general', with answer options: (almost) entirely, partially, and (almost) not, and (3) to what extent they agree with each of the 26 concrete propositions in the guideline (see Appendix A), with for each proposition the answer options: (almost) entirely, partially, and (almost) not. For each question, respondents could give additional information/explanation as required.

Patients' interview
When written consent was received from the patient, a telephone interview was conducted to establish: 1) patients' characteristics including age, gender, and 2) complaint characteristics at the first consultation with the neurosurgeon, e.g. duration, location, urinary problems, saddle anaesthesia, and influence of rest, specific body position, movement and of coughing/sneezing/straining.

Finally, we searched in the medical record of each patient to establish to what extent (compared with the guideline) the neurosurgeons had reported the complaint characteristics, carried out physical, radiological and neurophysiological examinations, and reported the indication for surgery.

Statistical analysis
Descriptive statistics were used to present the frequencies of neurosurgeons subscribing to the content of the guideline and their adherence with the guideline. All frequencies are based on the total number participating neurosurgeons or patients. All variables used to describe the neurosurgeons' and patients' characteristics are presented as the mean and standard deviation (SD) if they are normally distributed, and as median and interquartile range (IQR) if they are not normally distributed.

We determined that a proposition was accepted when 60% or more of the neurosurgeons gave the answer option: '(almost) entirely' for a particular proposition. After careful consideration with experts (general practitioners, neurosurgeons, epidemiologists) we decided that the adherence towards the guideline should be evaluated against 6 main recommendations from the guideline. We expected, in accordance with the main recommendations that:
1. the straight leg raising test and an MRI or CT-scan would be performed in all patients;
2. X-rays would not routinely be made;
3. neurophysiological examinations would not be performed in all patients (because they offer little additive information);
4. the indication for surgery would be reported in the medical record of all patients;
5. surgery would take place 4-8 weeks after the onset of the LRS episode;
6. the neurosurgeons would follow up patients after surgery.

If 5 or 6 of these main recommendations were followed then the neurosurgeons adherence with the guideline was considered good, adherence was considered moderate when 3 or 4 recommendations were followed, and weak when only 1 or 2 were followed.
The data were coded and analysed using the statistical package SPSS for Windows (release 10.0.7).

Ethics
The procedures of this study were in accordance with the ethical standards of the revised Helsinki declaration of 1983 and were approved by the Erasmus Medical Center ethics committee.

Results

Neurosurgeons' characteristics
Of the 92 invited neurosurgeons, 69 (75%) returned the questionnaire. Because three of these respondents reported that they did not treat patients with LRS, data from 66 neurosurgeons were included in the analysis. Reasons for non-response are unknown because the questionnaires were returned anonymously. The median age of the 66 participating neurosurgeons was 45 (IQR 15) years, 9% were female, and the median work experience was 12 (IQR 17) years. Of the total group, 33% worked in a university neurosurgery center, 35% in a non-university center, and 32% worked in both a university and non-university neurosurgery center.

Endorsement of the LRS guideline?
A total of 37% of the neurosurgeons subscribed entirely to the content of the guideline, 57% subscribed partially and 6% had missing values. Of the 26 propositions in the guideline (see Appendix A), propositions 10, 12, 13, 17-20 were subject to debate. According to the neurosurgeons, 3 of these 7 (i.e. 10, 13 and 18) may need updating. These three propositions concern 1) the additive value of the neurophysiologic examination (EMG), 2) the effectiveness of conservative treatments, and 3) the effectiveness of chemonucleolysis.

Patients' characteristics
In the period October 2001 to January 2002, we invited 250 patients (selected from the practices of seven of the neurosurgeons) to participate in this study. These seven neurosurgeons did not differ from the other neurosurgeons in the Netherlands, except that they were all male (in Dutch neurosurgeons 10% is woman). We received written informed consent from 163 patients. Table 1 lists the complaints characteristics of the participating patients at their first consultation with the neurosurgeon, as recalled and reported during the telephone interview.

Table 1: Complaints of the patients (n=163) at the first consultation with the neurosurgeon and recalled during the telephone interview for this study.

	n (%)
Back pain with irradiating pain into the leg	140 (86)
Pain below the knee	158 (97)
Sensory deficits in the leg	142 (87)
Decreased muscle strength in the leg	134 (82)
Less pain on rest	58 (36)
More pain on daily activities	107 (66)
Specific body position with more or less pain	125 (77)
More pain on coughing, sneezing or straining	112 (69)
Presence of urinary problems	44 (27)
Presence of saddle anaesthesia	88 (54)

n= number (and percentage) of patients.

The mean age of the participating patients was 44 (SD 10) years and 86 patients (53%) were female. Telephone interviews were held with all 163 patients on average of 26 (SD 10) weeks after surgery. The median length of time between the onset of the LRS complaints and the consultation with their GP was 4 (IQR 24) weeks, whereas 17 (IQR 26) weeks elapsed between the first consultation with the neurosurgeon. The median length of time between the first consultation with the neurosurgeon and surgery was 6 (IQR 9) weeks.

Management of LRS patients
Of the initial 163 patients, we were able to trace the medical records of 156 (62%) persons. Table 2 gives the examinations in the medical records that were ordered by the neurosurgeons in these 156 patients.

Table 2: Examinations in the medical records as ordered by the neurosurgeons in 156 of the participating patients.

	n (%)
Physical examinations:	
Physical inspection	55 (35)
Active examination	61 (39)
Straight leg raising test	103 (66)
Test of Bragard	18 (12)
Crossed straight leg raising test	10 (6)
Ankle tendon reflex	74 (47)
Knee tendon reflex	61 (39)
Sensory deficits of the foot	79 (51)
Strength of the big toe	26 (17)
Walking on heels and on toes	27 (17)
Radiological and neurophysiological examinations:	
X-rays	12 (8)
Computed tomography	51 (33)
Magnetic resonance imaging (MRI)	96 (62)
Electromyography (EMG)	4 (3)

n= number (and percentage) of patients.

With the exception of the straight leg raising test and tests for sensory deficits in the foot, all other physical examinations were performed in less than 50% of the patients. Radiological examination (MRI or CT-scan) was performed in almost all patients. According to the medical records, X-rays were rarely made, and EMGs were seldom performed.

The indication for surgery was reported in the medical records of all patients i.e. 1) a prolapsed disc L4-L5 (31%), 2) a prolapsed disc L5-S1 (37%), 3) a prolapsed disc L4-L5 and L5-S1 (5%), 4) a persisting lumbosacral syndrome (21%), and 5) other indications (6%).

Based on the medical records, the median length of time between the onset of the LRS episode and the first consultation with the neurosurgeon was 24 (IQR 24) weeks. The median length of time between the first consultation with the neurosurgeon and surgery was 5 (IQR 7.5) weeks. Thus, the actual length of time between the onset of the LRS episode and the moment of surgery was considerably longer than recommended in the guideline (i.e. 29 weeks versus 4-8 weeks in the guideline) due to the medical system in the Netherlands. According to the medical records, the neurosurgeons followed-up 76% of the patients after surgery only once.
Overall, the neurosurgeons deviated from only one of the six main recommendations (i.e. time to surgery after the of the LRS episode). Therefore, we consider the neurosurgeons' adherence with the guideline to be good.

Discussion

Most of the neurosurgeons (94%) agreed (at least partially) with the content of the multidisciplinary LRS guideline.

They did not fully endorse 7 of the 26 propositions in the guideline. Three of these 7 propositions may need updating based on 'new evidence', i.e. 1) the additive value of the neurophysiologic examination (EMG), 2) the effectiveness of conservative treatments, and 3) the effectiveness of chemonucleolysis.

According to their current management of LRS patients, neurosurgeons' adherence with the guideline is good. However, the length of time between the onset of the LRS episode and the moment of surgery was considerably longer than that recommended in the guideline. Some limitations of this study need to be discussed.

In spite of the high response rate (75%) to the questionnaire, selection bias may have occurred. About 25% of the neurosurgeons working in the Netherlands did not respond, but because of the anonymity we cannot establish the reasons for non-response. The results of this study may under- or overestimate endorsement of the guideline by neurosurgeons, but it is not possible to confirm this.

There were 87 patients (35%) who did not participated in the study. Unfortunately, we could not collect any data from these non respondents. Therefore, we do not know if there was a selective non response or not. The participating LRS patients were invited because of surgery on the basis of a prolapsed disc in the lumbar spine. Patients with LRS caused by a tumour, stenosis or infection were not included in this study, therefore we cannot easily generalize the results of our study to these LRS patients.

Because the questionnaires were specifically developed for this study (based on the LRS guideline), no data are available on the reliability and validity of these questionnaires. Also, we arbitrarily determined a plausible cut-off point of 60% for acceptance of the propositions in the guideline.

We found some differences in history characteristics, radiological and neurophysiological examinations between details reported in the interviews with the patients and those reported in the medical records by the neurosurgeons.

Other studies have reported similar discrepancies.[22] These discrepancies might be due to over-reporting by the patients due to recall bias, or under-reporting by the neurosurgeons due to incomplete registration in the medical records.

Recall bias could occur in the patients, because the interviews took place on average of 26 (SD 10) weeks after surgery. Because some items/values in the medical records were missing, the actual adherence with the guideline might be better if all data had been completed.

All patients were recruited from the practices of seven of the participating neurosurgeons working in four different hospitals in the southern part of the Netherlands. Based on their management of the LRS patients, their adherence with the guideline is good. These results cannot be generalised to all neurosurgeons in the Netherlands. Another study is needed in which more patients are recruited from different neurosurgical centers throughout the Netherlands.

This study shows that the participating neurosurgeons largely subscribe to the multidisciplinary LRS guideline, which is an important condition for the implementation of the guideline. The results also show that the neurosurgeons largely adhered with the guideline in their current management of LRS patients. Future studies to evaluate nationwide implementation of the guideline should recruit patients from different types of neurosurgical centres throughout the Netherlands using a prospective design.

Appendix A: Propositions in the multidisciplinary clinical guideline for the management of LRS.

1. LRS is characterised by radiating pain in one or more lumbo or sacral dermatomes, with or without other radicular symptoms.

2. LRS is often caused by a prolapsed disc, but is also caused by a spinal or resessus stenosis, or a combination of these.

3. LRS cannot be explained by mechanical compression of a nerve root only.

4. Many radiological abnormalities in the lumbar spine are not associated with nerve root compression or pain.

5. The test of Lasègue is the most valid and reliable test in acute LRS due to prolapsed disc. The test of Lasègue is often negative in neurological claudicatio.

6. There is no indication for routine X-rays of the lumbar spine in acute LRS.

7. MRI or CT-scan is only needed when surgery is considered, or if the results could have other therapeutical consequences.

8. MRI and CT-scan both have a high sensitivity for detecting a prolapsed disc and a low specificity: it is often impossible to distinguish between a prolapsed disc that causes the LRS and an accidental finding on the basis of imaging alone.

9. In radiological imaging of LRS, MRI is preferred; CT-scan is a good alternative. If uncertainty of nerve root compression persists caudography is indicated.

10. Neurophysiological examination can provide additional information about the location and severity of the nerve root damage, when radiological findings are not in accordance with clinical findings.

11. LRS is often self-limiting. The results of conservative treatments and surgery are similar in the long term (4-10 years), i.e. for those patients who do not undergo surgery because of progressive paresis or cauda equina syndrome.

12. The GP can perform clinical diagnostics and treatment in most LRS patients. Referral to a specialist is only useful when the GP is not sure about the diagnosis or considers surgical intervention.

13. Conservative treatments (e.g. bed rest, traction, physiotherapy and manipulation) are not sufficiently investigated to draw conclusions regarding their effectiveness.

14. The statement that strict bed rest (toilet visits and showering not permitted) is more effective in LRS due to prolapsed disc than liberal bed rest (toilet visits and showering permitted) is not based on prospective RCTs.

15. Effectiveness of 'back-schools' for LRS has not yet been investigated, neither for treatment, nor for prevention.

16. A severe LRS, persisting for 4 to 8 weeks with no improvement, is an indication for radiological examination possibly followed by surgical intervention. If there is improvement, a longer 'wait and see' policy is possible.

17. The most important indication for surgery in prolapsed disc is severe radicular pain and not the sensory deficits, except for the cauda equina syndrome.

18. Chemonucleolysis is proven effective for LRS caused by a prolapsed disc; the results after one year correspond with the results of surgery.

19. After 6 weeks the GP should discuss the option of surgery with the LRS patient when there is no clear improvement of the complaints.

20. There is no evidence that the prognosis of paresis improves by surgical intervention. Therefore, a light or moderate paresis is not an absolute indication for surgery.

21. Cauda equina syndrome caused by lumbar disc prolapse is an absolute indication for rapid surgery.

22. Percutaneous nucleotomy and percutaneous laser therapy are not evidenced-based treatments for LRS caused by disc prolapse.

23. There are no proven effective programs of treatment for primary or secondary prevention of LRS.

24. Advice not to work during and after the treatment of LRS, even in demanding jobs, should be given cautiously. This could delay rehabilitation.

25. The treating surgeon is responsible for medical care before and after surgery.

26. There are strong indications that psychological, social and financial factors play an important role in the development of persisting LRS (and the related disability).

Chapter 4

High level of satisfaction among patients despite persistent symptoms in the mid-long-term following surgery for the lumbosacral radicular syndrome

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Abstract

Objective To determine the mid-long-term outcomes (complaints/treatment satisfaction) after surgery in patients with lumbosacral radicular syndrome (LRS) and to identify prognostic factors for persisting LRS symptoms.

Design Descriptive retrospective and prospective study.

Method A total of 250 consecutive patients operated by seven neurosurgeons in four hospitals between May and December 2001 were selected from the medical records. Patients were invited to participate in a telephone questionnaire at 6 and 19 months post-surgery. All patients had undergone discectomy for LRS (at L4-L4 or L5-S1) and all were aged between 18 and 65 years.

Results Of the 250 patients, 163 participated in the study: of these, 63% reported that LRS-related complaints persisted 19 months after surgery. However, compared with pre-surgery, severe leg pain had decreased in 83% of the patients. Most patients were satisfied with their treatment. Female gender and an age of 51-65 years appeared to be prognostic factors for persistent LRS symptoms.

Conclusion More than half of the patients reported LRS complaints 19 months after surgery.

Introduction

The lumbosacral radicular syndrome (LRS) is a frequently seen disorder in the Netherlands with an annual incidence of 5 per 1000 patients (i.e. 60,000-75,000 new patients with LRS each year).[1] Hoogendoorn et al.[23] reported that there are about 10,000 operations due to LRS caused by a prolapsed disc each year in the Netherlands; this is 6 times more than in Scotland, 4 times more than in England, and twice as many as reported in Sweden.[24]

To our knowledge only one randomised trial has evaluated the effectiveness of surgery compared to conservative treatment in 126 patients with a prolapsed disc.[25] At 1-year follow-up there was a significant difference between the two groups in favor of surgery, whereas at 4 years and at 10 years follow-up no significant differences were found between the groups.[25]

In addition, some descriptive studies have reported on operated patients.[26-37] The wide range in the reported rate of 'successful' surgery (i.e. from 40% to 90%) is probably due to differences in study design, outcome measures and follow-up periods. However, it remains unclear which factors (such as, for example, age, gender and weight) are indeed prognostic for persisting LRS complaints after surgery.[25,38-43]

Therefore, this study investigated the course of complaints after surgery in patients with LRS due to a prolapsed disc (at level L4-L5 or L5-S1), and the prognostic factors for persisting LRS complaints.

Methods

Design
This was a descriptive retrospective and prospective study in patients with LRS who underwent surgery.

Patients
The study population consisted of 250 consecutive patients whose data were supplied by seven neurosurgeons from four Dutch hospitals (in the provinces of Zuid-Holland, Zeeland and Noord-Brabant). These patients were selected from the electronic medical files in the period May through December 2001. All patients with LRS had undergone surgery due to a prolapsed disc at level L4-L5 or L5-S1, and were aged between 18 and 65 years. These 250 patients were invited by post to participate in the present study. After acceptance they were contacted by telephone to answer a questionnaire at 6 months and 19 months post-surgery.

Questionnaires
In the first questionnaire (at 6 months follow-up) patients were asked about demographic and clinical variables that could influence the course of LRS complaints, e.g. gender, age, height, bodyweight, suffering from diabetes, education level, type of employment, sports activities, smoking behaviour, time between first visit to the neurosurgeon and surgery, severity of pain in the leg, and sensory deficits and/or decreased muscle strength in the leg before surgery.
At 19 months follow-up patients were asked about severity of pain in the leg, and about sensory deficits and/or decreased muscle strength in the leg at the moment of the telephone call. Answers to these questions were scored by the patient on an 11-point numerical rating scale (0 = no pain/no sensory deficits/no decreased muscle strength, to 10 = unbearable pain/ total disturbed sensory/total decreased muscle strength). In addition, the patients' level of satisfaction with the treatment was also scored on an 11-point numerical rating scale (0 = absolutely not satisfied, to 10 = totally satisfied).

Data Analysis
A patient was considered free of LRS complaints when reporting no pain in the leg, no sensory deficits and no decreased muscle strength. Reported pain in the back was not considered to be an LRS complaint. LRS complaints were considered 'severe' when patients scored 7 or higher on the 11-point rating scale, 'moderate' when scored 4-6, and 'mild' when scored 1 to 3. All data were coded and analysed using SPSS for Windows (version 11.0.1). Potential prognostic factors during follow-up were identified using univariate logistic regression (method: Enter, p-value <0.10). The combination of these prognostic factors was tested in a multivariate logistic analysis (method: 'forward stepwise' by Wald).

Results

Patients
Of the 250 patients eligible to join the study, 163 completed the informed consent procedure.

The first measurement took place at (mean) 6 months (SD 2.5) after surgery in these 163 patients. In the second measurement at (mean) 19 months (SD 2.1) after surgery, 157 patients (96%) participated; 1 patient no longer wished to participate and 5 patients could not be traced. Table 1 presents the characteristics of the 163 participating patients.

Table 1: Characteristics of the 163 operated patients.

Female (%)	86 (53)
Mean age in years (SD)	44 (10)
18-40 years (%)	63 (39)
41-50 years (%)	49 (30)
51-65 years (%)	51 (31)
Mean height in cm (SD)	176 (10)
Mean bodyweight in kg (SD)	80 (16)
Time between first visit to neurosurgeon and surgery in weeks (IQR)	6 (9)
Severe pain in the leg before surgery (%)	158 (97)
Severe sensory deficits in the leg before surgery (%)	142 (87)
Severe decreased muscle strength in the leg before surgery (%)	134 (82)
Severe back pain before surgery (%)	140 (86)
Paid work before surgery (%)	133 (82)
Low education level (%)	69 (42)
Active on sports (%)	153 (94)
Smoker (%)	98 (60)
Diabetic (%)	2 (1)

SD: standard deviation, IQR: interquartile range.

Over half of the patients were female (n=86) and the mean age was 44 (SD 10) years.

Follow-up
At 19 months follow-up, 58 patients (37%) reported that they were free of LRS complaints and 99 patients (63%) still had LRS complaints. Table 2 presents patients' reported severity of complaints at 19 months follow-up.

Table 2: Severity of complaints reported by 157 patients at 19 months follow-up.

Complaint	Number of patients (%)
Severe pain in the leg (%)	26 (17)
Moderate pain in the leg (%)	37 (24)
Mild pain in the leg (%)	22 (14)
No pain in the leg (%)	72 (45)
Severe sensory deficits (%)	24 (15)
Moderate sensory deficits (%)	31 (20)
Mild sensory deficits (%)	14 (9)
No sensory deficits (%)	88 (56)
Severe decreased muscle strength (%)	13 (8)
Moderate decreased muscle strength (%)	26 (17)
Mild decreased muscle strength (%)	8 (5)
No decreased muscle strength (%)	110 (70)

Compared with pre-surgery, at 19 months follow-up severe pain in the leg, severe sensory deficits and severe decreased muscle strength had decreased by 80%, 72% and 74%, respectively. During the 19 months follow-up a second operation was required in 21 and a third operation was required in 4 of the 157 patients. Furthermore, 44% of the patients reported that they worked less compared with pre-surgery and 61% reported less sports activities. A median of 8.0 (IQR 3.0) was scored on patients' satisfaction with treatment. Figure 1 shows the frequency of patient satisfaction; 87% of the patients scored >5 on the 11-point rating scale.

Figure 1: Patients' satisfaction (n=157) at 19 months post-surgery: score range 0 (=totally not satisfied) tot 10 (=very satisfied).
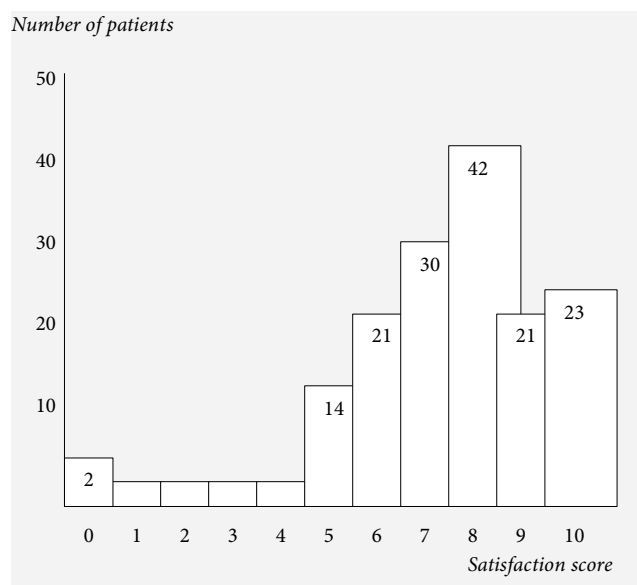
Prognostic factors
Because gender was a confounder for height and bodyweight, the logistic analyses were adjusted for gender. Table 3 gives the prognostic factors for persisting LRS complaints at 19 months post-surgery.

Table 3: Characteristics of the 157 patients with the risk of persisting complaints at 19 months follow-up (univariate logistic analysis).

Characteristic	No complaints (n=58)	Complaints (n=99)	Odds ratio (95% CI)	P
Women versus men	23	60	2.3 (1.2; 4.5)	0.01[$]
Age 18-40 years versus other	29	31	0.5 (0.2; 0.9)	0.21
Age 41-50 years versus other	17	30	1.0 (0.5; 2.1)	0.89
Age 51-65 years versus other	12	38	2.4 (1.1; 5.1)	0.02[$]
Height =< 176 cm versus higher[&]	26	61	1.3 (0.8; 4.7)	0.54
Bodyweight =<80 kg versus heavier[&]	27	62	1.4 (0.7; 3.0)	0.34
Time between neurosurgeon and surgery 0-7 days versus other	33	57	1.0 (0.5; 2.0)	0.96
Time between neurosurgeon and surgery 8-14 days versus other	14	20	0.8 (0.4; 1.7)	0.55
Time between neurosurgeon and surgery 15-30 days versus other	7	12	1.0 (0.4; 2.7)	1.00
Time between neurosurgeon and surgery > 30 days versus other	2	7	2.1 (0.4; 10.6)	0.36
Severe pain in leg before surgery versus other *	55	90	1.8 (0.5; 7.1)	0.38
Severe sensory deficits before surgery versus other *	29	65	0.5 (0.3; 1.0)	0.55
Severe decreased muscle strength before surgery versus other *	29	46	1.1 (0.6; 2.2)	0.67
Severe back pain before surgery versus other **	37	75	1.7 (0.9; 3.6)	0.11
Low education level versus higher level	28	41	0.8 (0.4-; 1.5)	0.40
Paid work before surgery versus no paid work	50	83	0.8 (0.3; 2.1)	0.69
No jogging or running before surgery versus other	50	95	3.8 (1.1; 13.2)	0.04[$]
Smoker before surgery versus no smoker	34	64	1.3 (0.7; 2.5)	0.45

CI Confidence interval

[$] Significant odds ratio.

[&] Adjusted for gender.

* Patients could have reported more than one LRS-related complaint.

** Not considered to be an LRS-related complaint.

Three factors from the univariate logistic analysis had a p-value <0.10. The multivariate logistic analyses showed that female gender (odds ratio; OR 2.3; 95% CI: 1.2; 4.5) and an age of 51-65 years (OR 2.4; 95% CI: 1.1; 5.1) were prognostic factors for persistent LRS complaints after surgery. The percentage of the variance of the model (ideally 100%) was only 11%.

Discussion

At 19 months post-surgery 63% of the patient group reported persisting LRS complaints. Before surgery 97% of the patients reported severe pain in the leg, which decreased to only 17% at 19 months post-surgery. Most of the patients were satisfied with their treatment. Predictive factors for persisting LRS complaints after surgery were female gender and being aged 51-65 years.

Patients operated because of LRS due to a prolapsed disc (at L4-L5 or L5-S1) were retrospectively recruited via seven neurosurgeons. Of the 250 patients who were eligible to participate in the study, 163 participated. The reasons why the remaining 87 patients declined to participate are not known, and it is unknown to what extent this might have biased the results of the study.

The first measurement took place 6 months post-surgery. Because the patients were asked to recall their LRS complaints before surgery, we cannot exclude the possibility of some recall bias.

In 1989 both Habbema et al.[35] and Braakman et al.[36] reported on the health status of patients undergoing surgery due to LRS in the Netherlands. At 1 year post-surgery 35% of the patients (n=361) reported pain in the leg[35], whereas in the present study 55% reported pain in the leg, 44% sensory deficits, and 30% reported decreased muscle strength in the leg. Braakman et al.[36] reported that, compared with the physical examinations, patients underreported decreased muscle strength in the leg. Comparison of the results of our study with those of earlier studies is difficult because of differences in methodology, follow-up periods and outcome measures.

The prognostic factors reported in this study should be interpreted with some caution because the percentage of variance of the model was only 11%. Many studies[28,38,40,41,44] have reported gender as a prognostic factor, but other studies[25,26,30] did not. Jogging has also been mentioned, but mainly as a factor for developing LRS.[45] In the present study being aged 51 to 65 years was found to be a prognostic factor for persisting LRS, whereas in other studies age was not a prognostic factor.[28,41-43]

Conclusion

In the present study over half of the patients reported LRS complaints 19 months after surgery, and most were satisfied with their treatment. However, because we were unable to establish the effectiveness of surgery in patients with LRS, a randomised controlled trial should be performed in a similar group of patients.

Chapter 5

Effectiveness of conservative treatments for the lumbosacral radicular syndrome
A systematic review.

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Submitted.

Abstract

Background Patients with a lumbosacral radicular syndrome are mostly treated conservatively first. The effect of the conservative treatments remains controversial.
Objective To assess the effectiveness of conservative treatments of the lumbosacral radicular syndrome (sciatica).
Search strategy Searched were relevant electronic databases and the reference lists of articles up to May 2004.
Selection criteria Randomised clinical trials of all types of conservative treatments for patients with the lumbosacral radicular syndrome selected by two reviewers.
Data collection and analysis Two reviewers independently assessed the methodological quality and the clinical relevance. Because the trials were considered heterogeneous we decided not to perform a meta-analysis but to summarise the results using the rating system of levels of evidence.
Results Thirty trials were included that evaluated injections, traction, physical therapy, bed rest, manipulation, medication, and acupuncture as a treatment for the lumbosacral radicular syndrome.
Conclusions We do not recommend corticosteroid injections and traction as treatment option because several trials indicated no evidence of an effect. Whether clinicians should prescribe physical therapy, bed rest, manipulation or medication could not be concluded from this review. At present there is no evidence that one type of treatment is clearly superior to others, including no treatment, for patients with a lumbosacral radicular syndrome.

Introduction

The lumbosacral radicular syndrome (LRS), also called sciatica, is a disorder with radiating pain in one or more lumbar or sacral dermatomes, and can be accompanied by phenomena associated with nerve root tension or neurological deficits.[2,4,5,16] A prolapsed disc mostly causes LRS, but other causes include spinal or lateral recess stenosis, tumours or radiculitis.[1,2] The incidence of LRS in general practice in the Netherlands is estimated between 60,000 and 75,000 a year.[1]

Most patients with LRS are treated conservatively in the first 6 to 12 weeks (acute and subacute phase).[2] However, the effectiveness of most of the conservative interventions has not yet been demonstrated beyond doubt. The review of Vroomen et al.[46] about conservative treatment of sciatica showed lacking evidence for or against the efficacy of traction, exercise therapy or drug therapy for the management of LRS.

They reported that epidural steroids may be beneficial for subgroups of nerve root compression. Vroomen et al. searched literature between 1966 and March 1998.
Several new RCT's have been published since, so an updated review on the whole spectrum of conservative management in LRS seems indicated. Also, recent developments in the methodology of systematic reviews are included in the present review and finally more specific physical therapy databases were searched.

The aim of this systematic review was to assess the effectiveness of conservative treatments in the lumbosacral radicular syndrome when compared to placebo, inactive or no treatment, other forms of conservative care or surgery.

Criteria for considering studies for this review

Types of studies
Only randomised clinical trials (RCTs) published in English, Dutch, French and German were included. Excluded were abstracts of which full reports were not available and unpublished studies.

Types of participants
Included were patients with an acute (less than 6 weeks), subacute (6-12 weeks) or chronic (12 weeks or more) lumbosacral radicular syndrome treated in a primary health care or occupational setting. Excluded were patients with LRS, which focus on rarely occurring causes such as tumours and radiculitis.

Types of interventions
All types of conservative treatment such as oral medication (e.g. NSAIDs, muscle relaxants), injections, physical therapy, spinal manipulation, bed rest, traction and acupuncture were included. Comparisons investigated were: (1) conservative treatment versus placebo, inactive or no treatment, (2) conservative treatment versus other type(s) of conservative treatment, and (3) conservative treatment versus surgery.

Types of outcome measures
Studies were included that used at least one of the four primary outcome measures that we considered to be the most important[47], that is an outcome of symptoms (e.g., pain), overall improvement (e.g., proportion of patients recovered, subjective improvement of symptoms), function (e.g., Roland Disability Questionnaire for sciatica, Oswestery Scale), and return to work (e.g., days off work).
Outcomes of physiological or physical examinations (e.g., range of motion, spinal flexibility, degrees of straight leg raising or muscle strength), quality of life (e.g., SF-36, Nottingham Health Profile, Sickness Impact Profile) and psycho-social outcomes (anxiety, depression, pain behaviour) were considered as secondary outcomes. Other outcomes such as medical consumption and side effects were also considered.
The treatment outcomes were assessed at short-term follow-up (less than 3 months after randomisation), at intermediate follow-up (between 3 months and 1 year after randomisation) and at long-term follow-up (1 year or more after randomisation).

Search strategy for identification of studies
We used the search strategy recommended by the Editorial Board of the Cochrane Collaboration Back Review Group.[47]

The highly sensitive search strategies for retrieval of studies of controlled trials[48] was run in conjunction with a specific search for the lumbosacral radicular syndrome and conservative treatments.

All relevant studies meeting our inclusion criteria were identified by: (1) Searches in electronic database: PUBMED-MEDLINE (from 1966 to May 2004), EMBASE (from 1980 to May 2004), Cochrane Central Register of Controlled Trials (CENTRAL, from 1800 to 2004)[49] , Cinahl (from 1982 to May 2004), PsycINFO (psychological interventions from 1984 to May 2004), and PEDro (Physiotherapy Evidence Database to May 2004), and (2) Screening the references of all studies selected from the electronic databases searches and relevant reviews.

Methods

Study selection
One reviewer (PL) performed the search strategy. Two reviewers (PL and TvO) independently selected the studies to be included in the systematic review. First, they screened the title, keywords and abstract for eligibility. Secondly, they assessed the full text papers whether the study met the inclusion criteria regarding design, subjects, and intervention. Disagreements on inclusion are resolved by discussion, or through arbitration by a third reviewer (AV).

Methodological quality assessment
Two reviewers (PL and RO) independently assessed the methodological quality (MQ), using the Delphi list.[50] The Delphi list contains 9 items relevant for the internal validity of each of the assessed articles. Each item was rated as 'yes', 'no', or 'don't know' (insufficient or no information presented). Equal weights were applied that resulted in a total score of each RCT, by adding the 'yes' scores (range 0-9). Disagreements were solved in a consensus meeting. When disagreements persisted a third reviewer (AV) was consulted.

Clinical relevance
Two reviewers (WP and BK) independently assessed the clinical relevance (CR). The Cochrane Collaboration Back Review Group recommends the 5 questions used to judge clinical relevance.[47] Disagreements were solved in a consensus meeting. When disagreements persist a third reviewer (AV) was consulted. A study was considered clinical relevant if the questions 1, 2 and 3 scored 'Yes'.

Data extraction
One reviewer (PL) extracted the data of the included RCTs. In cases of uncertainly about the data extracted from the individual trials a second reviewer (AV) was consulted.

Data analysis
The inter-observer reliability of the quality assessments was calculated using Kappa (< 0.5 means a poor level of agreement between assessors; between 0.5 and 0.7 a moderate level of agreement, and > 0.7 a high level of agreement).[51] A high quality (HQ) RCT was defined as a study that had a positive score (yes) on five or more Delphi criteria (score ranging from 0 to 9).

The data of the effect measurements reported in each study are presented as relative risks (RR) with corresponding 95% confidence intervals for dichotomous data and effect sizes (ES) and 95% confidence intervals for continuous data.

Quantitative analysis
Statistical pooling (meta-analysis) of the study outcomes (using a random effect model) will be performed if the studies are considered clinically homogeneous.

Qualitative analysis
If the studies are considered to be heterogeneous, the factors possibly underlying this phenomenon are considered. The results are summarized using a rating system that consists of five levels of scientific evidence which have been used in previous systematic reviews in the field of back pain, based on the overall quality and the outcome of the studies[47]: 1) strong evidence - consistent findings in multiple high quality RCTs, 2) moderate evidence - consistent findings among multiple low quality RCTs and/or one high quality RCT, 3) limited evidence - one low quality RCT, 4) conflicting evidence - inconsistent findings among multiple RCTs and 5) no evidence - no RCTs.

Results

Description of studies
The search strategy in the electronic databases selected 794 titles to be screened by two reviewers (PL and TvO). Disagreements were discussed and solved; 30 RCTs were included which were published in English and in French. Figure 1 shows the flow chart of the selection process.

Figure 1: Flow chart of the selection process
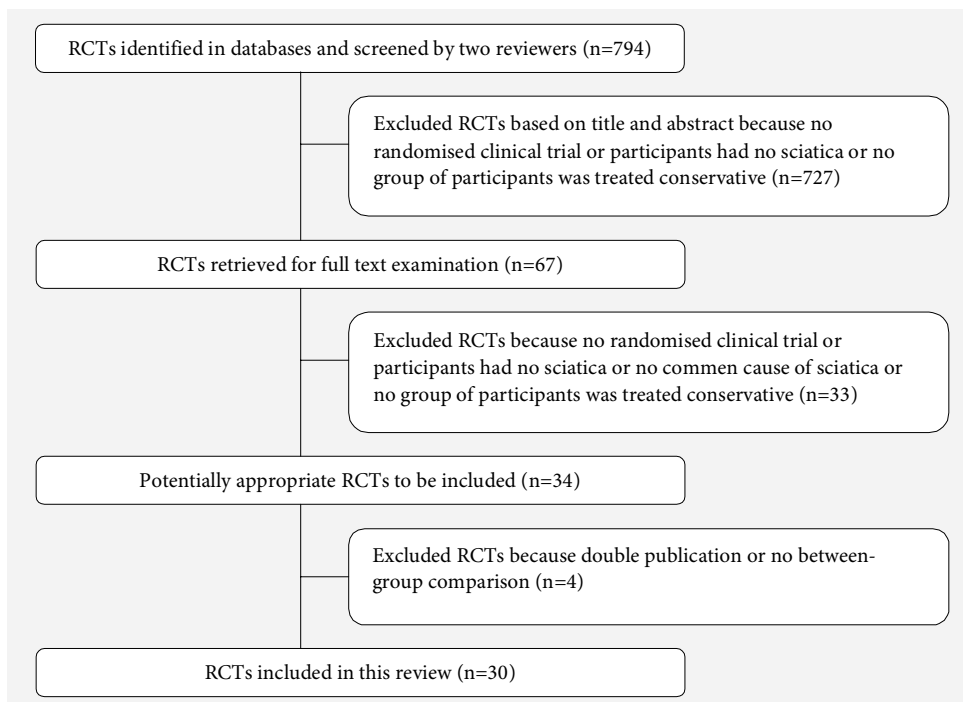
The 30 publications included in total 2780 patients with LRS and evaluated injections (n=14), traction (n=9), physical therapy (n=4), bed rest (n=2), manipulation (n=2), medication (n=2) and acupuncture (n=1). In 18 RCTs the sample size was small, meaning less than 30 patients in one study arm.

Methodological quality of the included studies
The two reviewers (PL and RO) agreed on 230 of the 270 item scores (85.2%). The inter-observer reliability of the MQ assessment (kappa=0.70) was moderate. Disagreements were solved in consensus for most cases, the third reviewer (AV) had to decide 5 times (1.8%). Detailed results of the MQ assessment are presented in tables 1 to 7. Twelve studies (40.0%) of the 30 included RCTs were considered to be of high quality. The overall MQ score ranged from 2 to 9 out of maximal 9 points. The most prevalent shortcomings of the studies concerned: no adequate description of treatment allocation concealment (n=27), no attempt to blind the care provider (n=26) or the analysis did not include an intention-to-treat analysis (n=23).

Clinical relevance
The two reviewers (WP and BK) agreed on 125 of the 150 item scores (83.3%). The inter-observer reliability of the clinical relevance assessment (kappa=0.67) was moderate. Disagreements were solved in consensus for all cases. Detailed results of the clinical relevance assessment are presented in tables 1 to 7. The overall clinical relevance score ranged from 0 to 5 out of maximal 5 points. Ten studies (33.3%) were considered clinical relevant because a 'Yes' was scored on the first 3 questions.
Finally, 6 RCTs[4,52-56] were considered to be of high quality and clinical relevant. Five RCTs[52-56] evaluated injections and 1 RCT[4] medication.

Evidence of effectiveness
Even in subgroups according to the intervention the included RCTs were not considered clinically comparable concerning study population (duration of the LRS), control treatment, duration of follow-up, and outcome measures. Because of this heterogeneity we refrained from statistical pooling and performed a qualitative analysis.

Injections
Table 1 shows the characteristics of fourteen studies that compared injection to placebo (9 RCTs), to no treatment (2 RCTs) and to other injections (4 RCTs).

Versus placebo
Nine studies[52-55,57-61] compared epidural or extradural corticosteroid injection to placebo injection. Six studies were considered high quality[52-55,58,60] of which one study[60] did not provide any data.
In three high quality studies[52,53,55] and one low quality study[59], we found no difference in pain between injection and placebo at short-term. However, in another one high quality[54] and one low quality study[61] we found an effect in pain at short-term, in favor of injection.
In three high quality studies[52,55,58] and one low quality study[57], we found no difference in overall improvement between injection and placebo at short-term. However, in another low quality study[59] we found an effect in improvement, in favor of injection.
Long-term effects for pain and overall improvement were not found in two high quality studies[54] and one low quality study.[61] Also, no short or long-term effects were found for disability and return to work in three high quality studies.[52-54]

In conclusion, when comparing corticosteroid injections to placebo for patients with LRS we found conflicting evidence regarding pain and overall improvement at short-term follow-up and no difference (2 HQ, 1 LQ trials: strong evidence) at long-term follow-up. For disability and return to work we found no difference (3 HQ trials: strong evidence) at short and long-term follow-up.

Versus no treatment
Two studies[57,62] compared epidural corticosteroid injection to no injection. In both studies, one of high quality[62] and one of low quality[57], we found no difference in overall improvement and return to work between groups. Therefore, when comparing corticosteroid injections to no treatment for patients with LRS we found no difference (1 LQ trial: limited evidence) regarding overall improvement at short-term follow-up and no difference (1 HQ trial: moderate evidence) regarding return to work at intermediate follow-up.

Versus other injections
Four studies[56,63-65] compared epidural or intramuscular corticosteroid injection to an injection of a NSAID or an anaesthetic. In one high quality[56] and two low quality studies[63,65] we found no difference in pain and return to work at short-term. However, in another low quality study[64] we found a difference in pain at short-term, in favor of corticosteroid injection. In one high quality study[56] we found a difference in pain at intermediate follow-up, in favor of injection with radioscopic control. In one low quality study[63] we found no difference in pain at long-term.
In one high quality study[56] we found a difference in disability at short-term and intermediate follow-up, in favor of injection with radioscopic control.
Therefore, we conclude there is conflicting evidence for the benefit of corticosteroid injection above an injection with a NSAID or anaesthetic regarding pain at short-term follow-up. There is moderate evidence that an injection with radioscopic control is more effective than injection without radioscopic control regarding pain at intermediate follow-up and regarding disability at short-term and intermediate follow-up for patients with LRS. No difference (2 LQ trials: moderate evidence) between injections was found regarding return to work at short-term follow-up and regarding pain at long-term follow-up.

Traction
Table 2 shows the characteristics of nine studies that compared traction to inactive/sham traction (4 RCTs) and to another conservative treatment (5 RCTs).

Versus inactive/sham traction
Four studies[66-69] compared traction to inactive/sham traction. One low quality study[67] did not report any data.
In one high quality[69] and one low quality study[66] we found no difference in pain between traction and inactive/sham traction at short-term. Also, in one low quality study[68] we found no difference in improvement between groups at short-term.
Therefore, when comparing traction and inactive/sham traction for patients with LRS we found no difference (1 HQ, 2 LQ trials: moderate evidence) regarding pain and disability at short-term follow-up.

Versus other conservative care

Five studies[70-74] compared traction to an other conservative treatment. All five studies were considered of low quality. In one study[70] we found a difference between traction and other conservative care in overall improvement, in favor of traction. However, in three studies[72-74] we found no difference in overall improvement between groups. In one study[72] we found no difference in pain between traction and other treatments, but in another study[71] we found a difference in pain, in favor of traction. In one study[72] we found no difference in return to work between groups.

Therefore, when comparing traction to other conservative treatments for patients with LRS we found conflicting evidence regarding improvement and pain at short-term follow-up. We found no difference (1 LQ trial: limited evidence) regarding return to work at short-term follow-up.

Physical therapy

Table 3 shows the characteristics of four studies that compared physical therapy to inactive treatment (1 RCT), to other conservative care (2 RCTs) and to surgery (1 RCT).

Versus inactive treatment

In one high quality study[75] we found no difference in pain and disability at short and intermediate follow-up between the groups.

Therefore, when comparing physical therapy to inactive treatment for patients with acute LRS we found no difference (1 HQ trial: moderate evidence) regarding pain and disability at short and intermediate follow-up.

Versus other conservative care

Two low quality studies[70,72] compared physical therapy to other conservative treatments. In these studies we found no difference in overall improvement, pain and return to work between groups.

Therefore, when comparing physical therapy to other conservative care for patients with LRS we found no difference (2 LQ trials: moderate evidence) regarding overall improvement, pain and return to work at short-term.

Versus surgery

In one low quality study[25] we found a difference in improvement at 1 year follow-up, in favor of surgery. In the same study we found no difference in improvement at 4 and 10 years follow-up between the two groups.

Therefore, we conclude there is limited evidence that surgery is more effective for patients with LRS regarding overall improvement than physical therapy at 1-year follow-up. At 4 and 10-year follow-up we found no difference (1 LQ trial: limited evidence) regarding overall improvement between surgery and physical therapy.

Bed rest

Table 4 shows the characteristics of two studies that compared bed rest to no treatment. In one low quality study[17] we found no differences in overall improvement, pain, and disability at short-term follow-up between the groups. In one high quality study[75] we found no differences in pain, disability, at short and intermediate follow-up between the groups.

Therefore, when comparing bed rest to no treatment for patients with acute LRS we found no difference (1 HQ, 1 LQ trial: moderate evidence) regarding overall improvement at short-term follow-up and no difference (1 HQ trial: moderate evidence) regarding pain and disability at short and intermediate follow-up.

Manipulation
Table 5 shows the characteristics of two studies that compared manipulation to other conservative care (1 RCT) and to surgery (1 RCT).

Versus other conservative care
In one low quality study[72] we found no difference in overall improvement, pain and return to work between the groups. Therefore, when comparing manipulation to other conservative care for patients with LRS we found no difference (1 LQ trial: limited evidence) regarding overall improvement, pain and return to work at short-term follow-up.

Versus chemonucleolysis
In one low quality study[76] we found no differences in pain and disability between the groups. Therefore, when comparing manipulation to chemonucleolysis for patients with LRS we found no difference (1 LQ trial: limited evidence) regarding pain and disability at short and long-term follow-up.

Medication
Table 6 shows the characteristics of two studies that compared medication to placebo. In one high quality study[4] we found no difference in sick leave between the groups. In one low quality study[77] we found no difference in overall improvement between the groups. Therefore, when comparing piroxicam or tizanidine to placebo for patients with acute LRS we found no difference (1 HQ, 1 LQ trial: moderate evidence) regarding overall improvement and sick leave at short-term follow-up.

Acupuncture
Table 7 shows the characteristics of a high quality study[78] that compared acupuncture to placebo. No data were presented in this article. Therefore, we conclude there is no evidence of the effectiveness of acupuncture for patients with LRS.

Discussion

This systematic review included 30 RCTs with a total of 2780 patients with LRS that evaluated various conservative treatments. Twelve of the 30 included studies were of high methodological quality and 10 studies were considered clinical relevant. Based on the results of this systematic review regarding the conservative treatment of patients with LRS we conclude that:
1) At long-term there is no evidence in favor of corticosteroid injections when compared to placebo, no treatment or NSAID or anaesthetic injection, apart from conflicting evidence for short-term pain relief.
2) At short-term there is no evidence in favor of traction when compared to sham traction or other conservative treatments.
3) At short-term there is no evidence in favor of physical therapy compared to inactive treatment, other conservative treatments or surgery.
4) At short-term there is no evidence in favor of bed rest compared to no treatment.

5) At short-term there is no evidence in favor of manipulation compared to other conservative treatments or chemonucleolysis.
6) At short-term there is no evidence in favor of medication compared to placebo.
7) No evidence was found regarding acupuncture.

In this review, like every review, there are risks of publication and language bias. There are indications that studies with negative results are not easily published as positive studies.[79,80] Furthermore, relevant studies, which are registered in unknown databases may not be included. Because of our extensive search strategy this risk was considered small.

Although efforts were made to find all published RCTs in restricted languages (i.e. English, Dutch, French and German), some relevant studies published in other languages might have been missed. Also, the number of non-English journals indexed in searched electronic databases is limited.

There was an overall clinical heterogeneity of the included studies. There appeared tot be many differences in study populations i.e. the duration of LRS, interventions, duration of follow-up and outcome measures.

It was considered clinically inappropriate to pool the results of the RCTs in the different types of conservative treatments. Therefore a qualitative analysis was performed, using the 5 levels of evidence.[47] Although the levels of evidence used may be considered arbitrary, it seems unlikely that a different rating system would have resulted in different conclusions. But, in this review we included studies that almost all reported no differences in outcomes between intervention and control group. When finding no differences between groups we cannot conclude 'there is evidence that the intervention is not effective or not different from the control treatment'.[81] Recommended by the Cochrane Collaboration than is to conclude that there is 'no evidence for an effect'. The analyses according the 5 levels of evidence are useful when significant differences are reported between treatment groups. But, when no differences between groups are reported in the majority of the included studies we found it problematic to use the levels, because we cannot conclude for example: 'there is strong evidence for no evidence of an effect'. Therefore, we have chosen to conclude with statements such as: 'we found no differences between groups'. The question remains how many trials are needed or how strong must the evidence be, to conclude that a treatment is not effective.

The methodological quality of the majority of the included studies, although improving over the past several years, was not high. Only 12 of the 30 included studies were regarded of high methodological quality. There is, however, a difficulty in blinding the patients and care provider during most conservative treatments that cannot be compared with placebo (i.e. bed rest, physical therapy, manipulation and traction).

There were studies with small sample sizes available for inclusion in this review. The number of patients in the groups was often too small to reach an adequate statistical power; only 12 studies had groups, that each consisted of over 30 patients, included.

The methodological quality might have been misclassified. Relying on the information in reported RCTs may create bias due to underreporting. But the risk of misclassification is considered small because a valid and reliable criteria list was used.[82]

The conclusions of this review that included 30 trials are not all in accordance with the conclusions of the review of Vroomen et al.[46] that included 19 trials.

We included more trials that evaluated corticosteroid injections and found no evidence of effect at short or at long-term follow-up. Also regarding traction we found more trials with no evidence of effect at short-term follow-up. Therefore, we do not recommend these two treatment options for patients with LRS. For the other conservative treatment options (physical therapy, bed rest, manipulation and medication) no evidence of effect was found at short-term follow-up, and long-term effects are unknown. At present there is no evidence that one type of treatment is clearly superior for patients with a lumbosacral radicular syndrome.

Conclusions

Implications for practice
In the conservative treatment of patients with LRS we do not recommend clinicians to use corticosteroid injections and traction because several trials indicated no evidence of an effect. Whether clinicians should prescribe physical therapy, bed rest, manipulation or medication could not be concluded from this review. For acupuncture no evidence was found.

Implications for research.
There is no knowledge whether corticosteroid injection could play a role in short-term pain relief. Also unknown are the long-term effects of traction, physical therapy, bed rest, manipulation or medication. We recommend high quality RCTs of sufficient sample size with long-term follow-up concerning physical therapy, manipulation or medication for patients with LRS. The outcome measures should include overall improvement, patients' satisfaction, severity of pain in the leg, functional health status, quality of health status, return to work and side effects.

Table 1: Characteristics of 14 included studies evaluating injections.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Borms, 1988[64] MQ 2 (1,8) # CR 2 (1,2) $	40 patients with acute, subacute or chronic complaints. 12 women. Mean age in years: I 36.7, C 41.6.	I Intramuscular injection. N=20. Tiaprofenic 200 mg. C Intramuscular injection. N=20. Ketoprofen 100 mg.	At 1, 2, 3 and 4 days follow-up evaluated were: 1) Pain (VAS 0-100) 2) Straight leg raising test 3) Finger to floor distance (cm) 4) Schöber 5) Spinal stiffness (0-4)	Pain: D1: ES 0.1 (-0.6; 0.7)& D2: ES 0.3 (-0.3; 0.9) D3: ES 0.6 (0.0; 1.3) D4: ES 0.6 (0.0; 1.3) Side effects: stomach pain (5) and skin reaction (3)	Dropouts: not described. Other treatments were allowed.
Buchner et al, 2000[62] MQ 5 (1,3,4,8,9) CR 2 (1,3)	36 patients with acute, subacute or chronic complaints. 13 women. Age range: 20-50 years.	I Epidural injection. N=17. Methylprednisolone 100mg/10ml bupivacaine (0.25%). C No injection. N=19.	At 2 and 6 weeks and 6 months follow-up evaluated were: 1) Pain (VAS 0-100) 2) Disability (HFAQ 0-100) 3) Straight leg raising test 4) Return to work 5) Surgery	Pain: W2: (I) 30.8 vs (C) 37.1 W6: (I) 32.9 vs (C) 38.1 M6: (I) 32.9 vs (C) 39.2 Disability: W2: (I) 63.7 vs (C) 57.5 W6: (I) 61.5 vs (C) 78.8 M6: (I) 80.9 vs (C) 73.4 Return to work: M6: RR 0.5 (0.1; 2.0) Surgery: M6: RR 0.6 (0.1; 2.7) Side effects: none.	Dropouts: 0.
Bush and Hillier, 1991[61] MQ 4 (1,4,5,7) CR 4 (1,2,3,4)	23 patients with acute, subacute or chronic complaints. 8 women. Mean age in years: 37.7.	I Epidural injection. N= 12. Triamcinolone acetonide 80mg/25ml. C Placebo injection. N=11. Normal saline 25 ml.	At 4 weeks and 1 year follow-up evaluated were: 1) Pain (VAS 0-100) 2) Patients' lifestyle (Grogono and Woodgate 6-18) 3) Straight leg raising test	Pain: W4: ES 1.2 (0.2; 2.0) Y1: ES 0.4 (-0.4; 1.3) Side effects: none	Dropouts: I 4, C 1. Bed rest, analgesics, corsets and manipulation were allowed.

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Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Carette et al, 1997[52] MQ 9 (1,2,3,4,5,6,7,8,9) CR 3 (1,2,3)	158 patients with acute, subacute or chronic complaint. 55 women. Mean age in years: I 39.0, C 40.6.	I Epidural injection. N=78. Methylprednisolone acetate 2 ml mixed by 8 ml of isotonic saline. C Placebo injection. N=80. Isotonic saline 1 ml	At 3 weeks and 3 months follow-up evaluated were: 1) Disability (OLBPQ 0-100 and SIP) 2) Improvement (7 item scale) 3) Pain in leg (VAS 0-100) 4) Pain (MGPQ) 5) Physical examinations	Disability (OLBPQ): W3: TE: -2.5 (-7.1; 2.2) M3: TE: -1.9 (-9.3; 5.4) Improvement: W3: TE: 3.4 (-11.4; 18.2) M3: TE: -0.4 (-16.5; 15.7) Pain in leg: W3: TE: -8.6 (-17.5; 0.3) M3: TE: -4.0 (-15.2; 7.2) Side effects: dura punctured: 2 times reported headache: 37 times reported	Dropouts: I 4, C 1.
Cuckler et al, 1985[58] MQ 8 (1,3,4,5,6,7,8,9) CR 2 (1,2)	73 patients with subacute or chronic complaints in hospital. 36 women. Mean age in years: I 48.5, C 49.5.	I Epidural injection. N=42. Two ml of sterile water containing 80 mg of methylprednisolone acetate and 5 ml of 1% procaine. C Placebo injection. N=31. Two ml of saline with 5 ml 1% procaine.	1) Success (no. of patients) 2) Surgery (no. of patients)	Success: H24: RR: 1.0 (0.7; 1.3) M13-M30: RR: 0.9 (0.7; 1.1) Surgery: M13-M30: RR: 0.8 (0.6; 1.1)	Dropouts: 0. No side effects reported in article.
Dilke et al, 1973[53] MQ 5 (1,3,4,5,7) CR 5 (1,2,3,4,5)	100 patients with acute, subacute or chronic complaints. 44 women. Age range in years: 18-75.	I Extradural injection. N=51. Methylprednisolone 80mg/10 ml normal saline. C Placebo injection. N=48.	At 3 months follow-up were evaluated: 1) Pain (no. of patients) 2) Return to work 3) Surgery (no. of patients) 4) Analgesic consumption	No pain: M3: RR: 0.8 (0.7; 1.0) Return to work: M3: RR: 0.2 (0.1; 0.7) Surgery: M3: RR: 0.7 (0.3; 1.6) Side effects: none	Dropouts: not described.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Helliwell et al, 1985[59] MQ 4 (1,4,5,7) CR 4 (1,2,4,5)	39 patients with subacute or chronic complaints. 30 women. Mean age in years: I 44.6, C 47.4.	I Extradural injection. N=20. Methylprednisolone 80mg/10 ml normal saline. C Placebo injection. N=19.	At 3 months follow-up evaluated were: 1) Pain (no pain) 2) Improvement (no. of patients) 3) Straight leg raising 4) Lumbar movement	No pain: M3: RR: 2.1 (0.8; 5.3) Improvement: M3: RR: 2.7 (1.2; 6.0) Side effects: 0	Dropouts: not described.
Karpinnen et al, 2001[54] MQ 8 (1,2,3,4,5,6,7,8) CR 3 (1,2,3)	160 patients with acute, subacute or chronic complaint. 38 women. Mean age in years: I 43.8, C 43.7.	I Epidural injection. N=80. Methylprednisolone 40mg/ml - bupivacaine 5 mg/ml injection. C Placebo injection. N=80. Isotomic (0.9%) sodium chloride solution injection.	At 2 and 4 weeks, at 3, 6, and 12 months follow-up evaluated were: 1) Pain in leg (VAS 0-100) 2) Disability (OLBPQ 0-100) 3) Sick leave (days per month) 4) Lumbar flexion (Schöber) 5) Quality of life (NHP) 6) Straight leg raising	Pain in leg: W2: TE 12.5 (1.6; 23.4) W4: TE 2.3 (-8.7; 13.4) M3: TE -0.5 (-12.0; 11.0) M6: TE -16.2 (-26.8; -5.6) M12: TE -5.3 (-15.7; 5.0) Disability OLBPQ: W2: TE 5.1 (-0.3; 10.4) W4: TE 1.5 (-4.4; 7.3) M3: TE -1.3 (-8.6; 6.1) M6: TE -5.9 (-12.4; 0.7) M12: TE -0.4 (-7.0; 6.2) Sick leave: W4: TE -0.5 (-4.9; 3.9) M3: TE 0.2 (-3.9; 4.4) M6: TE -1.7 (-5.1; 1.7) M12: TE 0.6 (-1.2; 2.4) Side effects: retroperitoneal hematoma: 1 time	Dropouts: I 2, C 0.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Klenerman et al, 1984[57] MQ 2 (1,4) CR 2 (1,2)	74 patients with acute, subacute or chronic complaints.	I1 Epidural injection. N=16. Depomedrone 80 mg/20 ml normal saline. I2 Epidural injection. N=19. Bupivacaine solution 20 ml 0.25%. C1 Placebo injection. N=16. Normal saline 20 ml. C2 No injection. N=12.	At 2 weeks and 2 months follow-up evaluated were: 1) Pain (VAS 100 mm) 2) Clinician opinion of patient 3) Lumbar flexion (Schöber) 3) Straight leg raising 4) Failed or not failed	Clinician opinion patient failed: I1 vs C1: RR 0.7 (0.2; 2.6) I2 vs C1: RR 1.0 (0.4; 2.8) I1 vs C2: RR 1.3 (0.3; 5.9) I2 vs C2: RR 1.9 (0.4; 8.1) Side effects: 0	Dropouts: 11
Mathews et al, 1987[63] MQ 3 (1,3,4) CR 1 (2)	57 patients with acute or subacute complaints. 14 women. Age range in years: 22-59.	I Epidural injection. N=23. Bupivacaine 20 ml (0.125%) and 2 ml methylprednisolone acetate. C Control injection. N=34. Lignocaine 2 ml over the sacral hiatus.	At 1, 3, 6, and 12 months follow-up evaluated were: 1) Improvement 2) Range of movement 3) Straight leg raising 4) Neurological examination	Improvement (pain score 5 or 6 on 6-point VAS): M1: RR 1.2 (0.7; 1.8) M12: RR 1.0 (0.5; 1.8)	Dropouts: I 5, C 14. No data reported at 3 and 6 months follow-up. No side effects reported in article.
Ridley et al, 1988[60] MQ 5 (1,3,4,5,8) CR 3 (1,2,4)	39 patients with acute, subacute or chronic complaints. 20 women. Mean age in years: I 40, C 39.	I Epidural injection. N=19. Methylprednisolone 2ml with 10 ml saline. C Placebo injection. N=16. Saline 2 ml.	At 1 and 2 weeks follow-up evaluated were: 1) Rest pain (VAS) 2) Walking pain (VAS) 3) Straight leg raising test	Side effects: Headache: 2 times reported	Dropouts: 4. Data not clear presented and at 4, 12, and 24 weeks only I was measured. In C 14 received a steroid injection (crossover).
Rogers et al, 1992[65] MQ 4 (1,3,5,7) CR 3 (1,2,3)	30 patients with acute, subacute or chronic complaints. 16 women. Mean age in years: I 42, C 41.	I Epidural injection. N=15. Methylprednisolone 80 mg/2 ml, 14 ml lignocaine 2% and saline 4 ml. C Epidural injection. N=15. Lignocaine 14 ml 2% saline 6 ml.	At 1 month follow-up evaluated were: 1) Pain (5-point scale) 2) Work status (3-point scale) 3) Straight leg raising test 4) Drug intake	No pain: M1: RR 3.0 (0.3; 25.7) Full work status: M1: RR 1.6 (0.7; 3.8)	Dropouts: 0. No side effects reported in article.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Snoek et al, 1977[55] MQ 5 (1,3,4,5,7) CR 3 (1,2,3)	51 patients with acute, subacute or chronic complaints. 25 women. Age range in years: 26-67.	I Extradural injection. N= 27. Methylprednisolone 80 mg/2 ml. C Placebo injection. N= 24. Saline 2 ml.	After treatment and at 14 months follow-up evaluated were: 1) Improvement by patient 2) Improvement by physical therapist 3) Radiating pain 3) Mobility of the lumbar spine 4) Straight leg raising test 5) Analgesic consumption	Improvement by patient: AF: RR 1.6 (0.9; 2.8) Improvement by physical therapist: AF: RR 1.7 (1.0; 2.9) Relief of radiating pain: AF: RR 2.1 (0.6; 7.1) Side effects: 0	Dropouts: not described.
Thomas et al, 2003[56] MQ 7 (1,2,3,4,5,7,8) CR 5 (1,2,3,4,5)	31 patients with acute or subacute complaints. 18 women. Mean age in years: 50.5.	I Transforaminal epidural corticosteroid injection with radioscopic control. N=15. C Interspinous epidural corticosteroid injection with no epidurographic control. N=16.	At 6, 30 days and 6 months follow-up evaluated were: 1) Pain (VAS) 2) Disability (RDQ) 3) Schöber's index (cm) 4) Finger floor distance (cm) 5) Straight leg raising test	Pain: D6: ES 0.5 (-0.3; 1.2) D30: ES 0.5 (-0.2; 1.3) M6: ES 0.9 (0.2; 1.7) Disability: D6: ES 0.97 (0.3; 1.8) D30: ES 0.3 (-0.4; 1.0) M6: ES 0.7 (0.1; 1.5) Side effects: 0	Dropouts: 0.

#: Total score of the MQ (items that scored 'Yes'), $: Total score of the CR (questions that scored 'Yes'), &: 95% Confidence Interval I: Intervention group, C: Control group, RR: Relative Risk, ES: Effect Size, TE: Treatment Effect (the difference between the change in the intervention group and the change in the control group; negative values indicate a positive treatment effect), H: Hour, D: Day, W: Week, M: Month, AF: After treatment, HFAQ: Hannover functional ability questionnaire, MGPQ: McGill pain questionnaire, OLBPQ: Oswestry low back disability questionnaire, NHP: Nottingham Health Profile, SIP: Sickness impact profile, VAS: Visual analogue scale, RDQ: Roland disability questionnaire.

Table 2: Characteristics of 9 included studies evaluating traction.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Coxhead et al, 1981[72] MQ 2 (1,4) # CR 1 (3) $	334 patients with acute, subacute or chronic complaints.149 women. Mean age in years: 41.9.	Factorial design. I1 Traction. n=143. C1 No traction. n=149. I2 Manipulation. n=155. C2 No manipulation. n=137. I3 Exercises. n=150. C3 No exercises. n=142. I4 Corset. n=124. C4 No corset. n=168.	1) Improvement (no. of patients) 2) Pain (score range -100 to +100) 3) Return to work (no. of patients)	Improvement: W4: I1 vs C1, RR: 0.7 (0.5; 1.1) & W4: I2 vs C2, RR: 0.7 (0.4; 1.0) W4: I3 vs C3, RR: 0.8 (0.5; 1.3) W4: I4 vs C4, RR: 0.8 (0.5; 1.2) M4: I1 vs C1, RR: 1.0 (0.7; 1.5) M4: I2 vs C2, RR: 0.8 (0.6; 1.3) M4: I3 vs C3, RR: 1.3 (0.9; 2.0) M4: I4 vs C4, RR: 1.1 (0.7; 1.7) Pain: W4: I1 vs C1, ES: 0.1 (-0.1; 0.4) W4: I2 vs C2, ES: 0.3 (0.0; 0.5) W4: I3 vs C3, ES: 0.1 (-0.2; 0.3) W4: I4 vs C4, ES: 0.1 (-0.1; 0.3) Return to work: W4: I1 vs C1, RR: 0.9 (0.7; 1.2) W4: I2 vs C2, RR: 0.9 (0.7; 1.2) W4: I3 vs C3, RR: 1.0 (0.8; 1.3) W4: I4 vs C4, RR: 1.0 (0.7; 1.3)	Dropouts: 66. No data presented at 16 months follow-up. No side effects reported in article.
Larsson et al, 1980[71] MQ 3 (1,3,4) CR 3 (1,2,4)	82 patients with acute or subacute complaints. 31 women. Mean age in years: 37.	I Auto traction. N=41. Traction force performed by patient. C N=41. Corset and rest.	At 1 and 3 weeks, at 3 months follow-up: 1) Pain in leg (no pain), 2) Free of symptoms (no. of patients), 3) Surgery (no. of patients), 4) Straight leg raising	No pain in leg: W1: RR 8.0 (1.1; 61.1) W3: RR 2.3 (0.8; 6.7) Free of symptoms: M3: RR 1.1 (0.7; 1.8) Surgery: M3: RR 0.7 (0.2; 2.2)	Dropouts: 3 No side effects reported in article.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Lidström and Zachrisson, 1970[70] MQ 3 (1,4,5) CR 3 (1,2,4)	62 patients with acute, subacute or chronic complaints. 33 women. Age range in years: 21-61.	I1 Physical therapy. N=21. Hot packs, massage, mobilizing and strengthening exercises for the spine. I2 Traction. N=20. Tru-Trac traction. C Control. N=21. Hot packs and rest.	After treatment evaluated were: 1) Improvement by patient 2) Improvement by clinician	Improvement by patient: I1 vs C: RR 0.7 (0.4; 1.2) I2 vs C: RR 1.4 (1.0; 1.9) Improvement by clinician: I1 vs C: RR 0.8 (0.4; 1.4) I2 vs C: RR 1.4 (1.0; 2.3)	Dropouts: not described. No side effects reported in article.
Ljunggren et al, 1984[73] MQ 2 (1,4) CR 2 (1,2)	49 patients subacute or chronic complaints. 17 women. Mean age in years: 39.	I Traction. N=26. Traction is performed by patient. C Traction. N=23. Traction is performed by physical therapist.	After treatment and at 2 weeks follow-up evaluated were: 1) Pain (VAS) 2) Effect by clinician 2) Physical examination	Good effect by clinician: AF: RR 0.7 (0.2; 2.7) W2: RR 1.2 (0.3; 4.7)	Dropouts: not described. No data reported at 3 months, and at 1 to 2 years follow-up. No side effects reported in article.
Ljunggren et al, 1992[74] MQ 4 (1,4,5,9) CR 2 (1,2)	50 patients with subacute or chronic complaints. 23 women. Age range in years: 19-62.	I Traction. N=24. Traction is performed by physical therapist. C Exercises. N=26. Isometric exercises for the abdominal, back, hip and thigh muscles.	After treatment evaluated were: 1) Pain (VAS) 2) Improvement (by clinician) 2) Disability (RDQ) 3) Mobility lumbar spine 4) Straight leg raising test	Improved by clinician or free of pain: AF: RR 1.1 (0.6; 2.1)	Dropouts: not described. No side effects reported in article.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Mathews and Hickling, 1975[67] MQ 2 (1,4) CR 1 (2)	27 patients with acute, subacute or chronic complaints. 9 women. Mean age in years: 44.	I Traction. N=13. Force between 36 and 61 kg. C Inactive traction. N=14. Traction force did not exceed 9 kg.	At 3, 6 weeks and 3 months follow-up evaluated were: 1) Pain 2) Finger floor distance 3) Straight leg raising test.	--	Dropouts: not described. No data reported. No side effects reported in article.
Reust et al, 1988[69] MQ 6 (1,3,4,5,8,9) CR 2 (1,2)	60 patients. 25 women. Mean age in years: I1 51.6, I2 45.7, C 55.3.	I1 Light traction. N=22. First day 5 kg, second day 10 kg, other days 15 kg traction force. I2 Normal traction. N=18. First day 5 kg, second day 10 kg, other days increasing with 5 kg till max of 50 kg traction force. C Inactive traction. N=20. Traction force of 5 kg a day.	After treatment evaluated were: 1) Pain (VAS 0-100) 2) Straight leg raising test 3) Finger floor distance	Pain: AF: I1 vs C: ES 0.02 (-0.6; 0.6) AF: I2 vs C: ES 0.13 (-0.5; 0.8)	Dropouts: 0. No side effects reported in article.
Weber, 1973[66] MQ 2 (1,4) CR 2 (1,2)	86 patients with acute, subacute or chronic complaints. 30 women. Age range in years: 30-60.	I Tru-Trac traction. N= 37. Force 1/3 of patient's body weight. C Inactive traction. N=35. Same as in I, but force up to 7 kp.	After treatment evaluated were: 1) Pain (no. of patients) 2) Mobility of the lumbar spine 3) Neurological signs	Pain improved: AF: RR 1.1 (0.7; 1.8) Side effects: 0	Dropouts: I 6, C 8.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Weber et al, 1984[68] MQ 3 (1,4,9) CR 2 (1,2)	215 patients with subacute or chronic complaints. 91 women.	I1 Tru-Trac traction. N=37. I2 Spina-Trac. N=21. Patient performed traction force. I3 Auto-traction. N=26. Patient performed traction force. I4 Manual traction. N=24. Traction force performed by physical therapist. C1 Simulated Tru-Trac. N=35. C2 Simulated Spina-trac. N=23. C3 Manual traction. N=23. C4 Isometrec exercises. N=26.	After treatment, 2 weeks and 3 months follow-up evaluated were: 1) Improvement 2) Pain 3) Mobility of lumbar spine 4) Straight leg raising test 5) Motor and sensory function 6) Need for analgesics	Improvement: I1 vs C1: RR 1.1 (0.7; 1.8) I2 vs C2: RR 1.1 (0.4; 3.3) I3 vs C3: RR 0.6 (0.2; 1.5) I4 vs C4: RR 1.1 (0.6; 2.1)	Dropouts: 28. No side effects reported in article.

[#]: Total score of the MQ (items that scored 'Yes'), [$]: Total score of the CR (questions that scored 'Yes'), [&]: 95% Confidence Interval I: Intervention group, C: Control group, RR: Relative Risk, ES: Effect Size, W: Week, M: Month, AF: After treatment, VAS: Visual analogue scale, RDQ: Roland disability questionnaire.

Table 3: Characteristics of 4 included studies evaluating physical therapy.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Coxhead et al, 1981[72] MQ 2 (1,4)[#] CR 1 (3)[$]	334 patients with acute, subacute or chronic complaints. 149 women. Mean age in years: 41.9.	Factorial design. I1 Traction. n=143. C1 No traction. n=149. I2 Manipulation. n=155. C2 No manipulation. n=137. I3 Exercises. n=150. C3 No exercises. n=142. I4 Corset. n=124. C4 No corset. n=168.	1) Improvement (no. of patients) 2) Pain (score range -100 to +100) 3) Return to work (no. of patients)	Improvement: W4: I1 vs C1, RR: 0.7 (0.5; 1.1)[&] W4: I2 vs C2, RR: 0.7 (0.4; 1.0) W4: I3 vs C3, RR: 0.8 (0.5; 1.3) W4: I4 vs C4, RR: 0.8 (0.5; 1.2) M4: I1 vs C1, RR: 1.0 (0.7; 1.5) M4: I2 vs C2, RR: 0.8 (0.6; 1.3) M4: I3 vs C3, RR: 1.3 (0.9; 2.0) M4: I4 vs C4, RR: 1.1 (0.7; 1.7) Pain: W4: I1 vs C1, ES: 0.1 (-0.1; 0.4) W4: I2 vs C2, ES: 0.3 (0.0; 0.5) W4: I3 vs C3, ES: 0.1 (-0.2; 0.3) W4: I4 vs C4, ES: 0.1 (-0.1; 0.3) Return to work: W4: I1 vs C1, RR: 0.9 (0.7; 1.2) W4: I2 vs C2, RR: 0.9 (0.7; 1.2) W4: I3 vs C3, RR: 1.0 (0.8; 1.3) W4: I4 vs C4, RR: 1.0 (0.7; 1.3)	Dropouts: 66. No data presented at 16 months follow-up. No side effects reported in article.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Hofstee et al, 2002[75] MQ 5 (1,3,4,8,9) CR 2 (1,3)	250 patients with acute complaints. 100 women. Mean age in years: 39.0.	I1 Bed rest. N=84; 43 at home and 41 in hospital. Stay in bed for 7 days. Only out of bed for bathroom and shower. I2 Physical therapy. N=83. Instructions and advice, segmental mobilisation, disc unloading and loading exercises depending on patient's condition and hydrotherapy. Twice a week for at least 4, at most, 8 weeks. C Continuation of ADL. N=83.	At 1, 2 and 6 months follow-up evaluated were: 1) Pain in leg (VAS 0-100) 2) Disability (QDS 0-100) 3) Surgery (no. of patients)	Pain: M1: I1 vs C, MD: 2.5 (-6.4; 11.4) M1: I2 vs C, MD: 0.8 (-8.2; 9.8) M2: I1 vs C, MD: 0.9 (-8.7; 10.4) M2: I2 vs C, MD: -0.3 (-9.4; 10.0) M6: I1 vs C, MD: 0.5 (-8.4; 9.3) M6: I2 vs C, MD: -1.0 (-10.0; 8.0) Disability: M1: I1 vs C, MD: -4.8 (-10.6; 0.9) M1: I2 vs C, MD: -0.5 (-6.3; 5.3) M2: I1 vs C, MD: -2.7 (-9.9; 4.4) M2: I2 vs C, MD: 0.0 (-7.2; 7.3) M6: I1 vs C, MD: -2.7 (-10.2; 4.8) M6: I2 vs C, MD: -0.7 (-8.4; 6.9) Surgery: M6: I1 vs C, RR: 1.4 (0.7; 2.9) M6: I2 vs C, RR: 1.2 (0.6; 2.5) Side effects: cauda equina syndrome: 1 time pulmonary embolism: 1 time	Dropouts: I1 6, I2 11, C 8.
Lidström and Zachrisson, 1970[70] MQ 3 (1,4,5) CR 3 (1,2,4)	62 patients with acute, subacute or chronic complaints. 33 women. Age range in years: 21-61.	I1 Physical therapy. N=21. Hot packs, massage, mobilizing and strengthening exercises for the spine. I2 Traction. N=20. Tru-Trac traction. C Control. N=21. Hot packs/rest.	After treatment evaluated were: 1) Improvement by patient 2) Improvement by clinician	Improvement by patient: I1 vs C: RR 0.7 (0.4; 1.2) I2 vs C: RR 1.4 (1.0; 1.9) Improvement by clinician: I1 vs C: RR 0.8 (0.4; 1.4) I2 vs C: RR 1.4 (1.0; 2.3)	Dropouts: not described. No side effects reported in article.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Weber, 1983[25] MQ 2 (1,4) CR 3 (1,2,4)	126 patients with acute, subacute or chronic complaints. 58 women. Mean age in years: I 40.0, C 41.7.	I Surgery. N=60. C Conservative treatment. N=66. Continued physical therapy in other hospital for six weeks.	At 3, 6, 9 months and at 1, 4, and 10 years follow-up evaluated were: 1) Pain 2) Improvement by patient 3) Neurological deficits 4) Mobility of the lumbar spine	Improvement by patient: Y1: RR 1.8 (1.2; 2.6) Y4: RR 1.3 (1.0; 1.7) Y10: RR 1.0 (0.8; 1.4)	Dropouts: 5. No data presented at 3, 6 and 9 months follow-up. No side effects reported in article.

#: Total score of the MQ (items that scored 'Yes'), $: Total score of the CR (questions that scored 'Yes'), &: 95% Confidence Interval I: Intervention group. C: Control group, RR: Relative Risk, ES: Effect Size, MD: Mean differences, W: Week, M: Month, QDS: Quebec disability scale, VAS: Visual analogue scale.

Table 4: Characteristics of 2 included studies evaluating bed rest.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Hofstee et al, 2002[75] MQ 5 (1,3,4,8,9) # CR 2 (1,3) $	250 patients with acute complaints. 100 women. Mean age in years: 39.0.	I1 Bed rest. N=84; 43 at home and 41 in hospital. Stay in bed for 7 days. Only out of bed for bathroom and shower. I2 Physical therapy. N=83. Instructions and advice, segmental mobilisation, disc unloading and loading exercises depending on patient's condition and hydrotherapy. Twice a week for at least 4, at most, 8 weeks. C Continuation of ADL. N=83.	At 1, 2 and 6 months follow-up evaluated were: 1) Pain in leg (VAS 0-100) 2) Disability (QDS 0-100) 3) Surgery (no. of patients)	Pain: M1: I1 vs C, MD: 2.5 (-6.4; 11.4) & M1: I2 vs C, MD: 0.8 (-8.2; 9.8) M2: I1 vs C, MD: 0.9 (-8.7; 10.4) M2: I2 vs C, MD: -0.3 (-9.4; 10.0) M6: I1 vs C, MD: 0.5 (-8.4; 9.3) M6: I2 vs C, MD: -1.0 (-10.0; 8.0) Disability: M1: I1 vs C, MD: -4.8 (-10.6; 0.9) M1: I2 vs C, MD: -0.5 (-6.3; 5.3) M2: I1 vs C, MD: -2.7 (-9.9; 4.4) M2: I2 vs C, MD: 0.0 (-7.2; 7.3) M6: I1 vs C, MD: -2.7 (-10.2; 4.8) M6: I2 vs C, MD: -0.7 (-8.4; 6.9) Surgery: M6: I1 vs C, RR: 1.4 (0.7; 2.9) M6: I2 vs C, RR: 1.2 (0.6; 2.5) Side effects: cauda equina syndrome: 1 time pulmonary embolism: 1 time	Dropouts: I1 6, I2 11, C 8.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Vroomen et al, 1999[17] MQ 4 (1,3,4,8) CR 3 (1,2,3)	183 patients with acute complaints. 80 women. Mean age in years: I 44, C 48.	I Bed rest. N=92. Only out of bed to use toilet and to bathe. C Watchful-waiting. N=91.	At 2, 3 and 12 weeks follow-up evaluated were: 1) Improvement by patients 2) Improvement by investigator 3) Pain in leg (VAS 0-100) 4) Disability (RDQ) 5) Satisfaction (11-point) 6) Days off work	Improvement by patients: W2: adj OR: 1.1 (0.6; 2.0) W12: adj OR: 1.0 (0.4; 2.9) Improvement by investigator: W2: adj OR: 0.7 (0.3; 2.0) W12: adj OR: 0.6 (0.2; 1.7) Pain in leg: W3: ES 0.3 (0.0; 0.6) W12: ES 0.1 (-0.2; 0.4) Disability: W3: ES 0.2 (-0.1; 0.5) W12: ES 0.1 (-0.2; 0.4) Days off work: W12: median I 46, C 47	Dropouts: I 7, C 7. No side effects reported in article.

#: Total score of the MQ (items that scored 'Yes'), $: Total score of the CR (questions that scored 'Yes'), &: 95% Confidence Interval I: Intervention group, C: Control group, RR: Relative Risk, ES: Effect Size, MD: Mean differences, W: Week, M: Month, adj OR: adjusted odds ratio, VAS: Visual analogue scale, RDQ: Roland disability questionnaire, QDS: Quebec disability scale.

Table 5: Characteristics of 2 included studies evaluating manipulation.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Burton et al, 2000[76] MQ 4 (1,3,4,8) [#] CR 3 (1,2,3) [$]	40 patients with acute, subacute or chronic complaints. 21 women. Mean age in years: 41.9.	I Manipulation. N=20. C Chemonucleolysis. N=20.	At 2 and 6 weeks and 12 months follow-up evaluated were: 1) Pain in leg (7-point rating scale) 2) Disability (RDQ) 3) Pain in back	Pain: W2: ES 0.0 (-0.6; 0.7) [&] W6: ES 0.0 (-0.6; 0.6) M12: ES 0.1 (-0.6; 0.7) Disability: W2: ES 0.7 (0.1; 1.3) W6: ES 0.5 (-0.1; 1.1) M12: ES 0.2 (-0.4; 0.8) Side effects: 0	Dropouts: I 5, C 5.
Coxhead et al, 1981[72] MQ 2 (1,4) CR 1 (3)	334 patients with acute, subacute or chronic complaints.149 women. Mean age in years: 41.9.	Factorial design. I1 Traction. n=143. C1 No traction. n=149. I2 Manipulation. n=155. C2 No manipulation. n=137. I3 Exercises. n=150. C3 No exercises. n=142. I4 Corset. n=124. C4 No corset. n=168.	1) Improvement (no. of patients) 2) Pain (score range -100 to +100) 3) Return to work (no. of patients)	Improvement: W4: I1 vs C1, RR: 0.7 (0.5; 1.1) W4: I2 vs C2, RR: 0.7 (0.4; 1.0) W4: I3 vs C3, RR: 0.8 (0.5; 1.3) W4: I4 vs C4, RR: 0.8 (0.5; 1.2) M4: I1 vs C1, RR: 1.0 (0.7; 1.5) M4: I2 vs C2, RR: 0.8 (0.6; 1.3) M4: I3 vs C3, RR: 1.3 (0.9; 2.0) M4: I4 vs C4, RR: 1.1 (0.7; 1.7) Pain: W4: I1 vs C1, ES: 0.1 (-0.1; 0.4) W4: I2 vs C2, ES: 0.3 (0.0; 0.5) W4: I3 vs C3, ES: 0.1 (-0.2; 0.3) W4: I4 vs C4, ES: 0.1 (-0.1; 0.3)	Dropouts: 66. No data presented at 16 months follow-up. No side effects reported in article.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
				Return to work:	
				W4: I1 vs C1, RR: 0.9 (0.7; 1.2)	
				W4: I2 vs C2, RR: 0.9 (0.7; 1.2)	
				W4: I3 vs C3, RR: 1.0 (0.8; 1.3)	
				W4: I4 vs C4, RR: 1.0 (0.7; 1.3)	

[#]: Total score of the MQ (items that scored 'Yes'), [$]: Total score of the CR (questions that scored 'Yes'), [&]: 95% Confidence Interval I: Intervention group, C: Control group, RR: Relative Risk, ES: Effect Size, W: Week, M: Month, VAS: Visual analogue scale, RDQ: Roland disability questionnaire.

Table 6: Characteristics of 2 included studies evaluating medication.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Berry and Hutchinson, 1988[77] MQ 4 (1,3,4,8)[#] CR 1 (2)[$]	59 patients with acute complaints. Age range: 18-70 years.	I Tizanidine (muscle relaxant). N=28. Tablets 4 mg, 3 times daily. C Placebo tablets. N=31.	At 3 and 7 days follow-up evaluated were: 1) Improvement 2) Pain on movement, at rest, at night (VAS 0-100) 3) Restriction of movement 4) Consumption of aspirin tablets	Improvement: D3: RR 0.9 (0.3; 3.0)[&] D7: RR 0.8 (0.5; 1.2)	Dropouts: not described. The 59 patients were a subgroup from 112 patients with acute low back pain. No side effects reported in article.
Weber et al, 1993[4] MQ 5 (1,4,5,6,7) CR 3 (1,2,3)	214 patients with acute complaints. Mean age in years: 48.	I Piroxicam (NSAID). N=120. C Placebo medication. N=94.	At 1, 2, 3, 4 weeks and 3 and 12 months follow-up evaluated were: 1) Pain in leg (VAS 0-100) 2) Disability (RDQ) 3) Sick leave	Sick leave: W4: RR 1.0 (0.8; 1.3)	Dropouts: 36. Data not clear presented. No side effects reported in article.

[#]: Total score of the MQ (items that scored 'Yes'), [$]: Total score of the CR (questions that scored 'Yes'), [&]: 95% Confidence Interval I: Intervention group, C: control group, RR: Relative risk, D: Day, W: Week, VAS: Visual analogue scale, RDQ: Roland disability questionnaire.

Table 7: Characteristics of included study evaluating acupuncture.

Study	Participants	Interventions	Outcomes	Results and side effects	Notes
Duplan et al, 1983[78] MQ 5 (1,3,4,5,7) [#] CR 0 (-) [$]	30 patients with acute complaints. 9 women. Mean age in years: 40.	I Acupuncture on electrically detected points. N=15. C Acupuncture on placebo points. N=15.	After 5 sessions evaluated were: 1) Duration of improvement 2) Improvement in decubitis 3) Improvement after 10 minutes standing 4) Use of analgesics	--	Dropouts: not described. No data presented. No side effects reported in article.

[#]: Total score of the MQ (items that scored 'Yes'), [$]: Total score of the CR (questions that scored 'Yes'), I: Intervention group, C: control group.

Chapter 6

Conservative treatment in patients with an acute lumbosacral radicular syndrome: design of a randomised clinical trial [ISRCTN68857256]

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Abstract

Background The objective is to present the design of randomised clinical trial (RCT) on the effectiveness of physical therapy added to general practitioners' management compared to general practitioners' management only in patients with an acute lumbosacral radicular syndrome (also called sciatica).
Methods/Design Patients in general practice diagnosed with an acute (less than 6 weeks) lumbosacral radicular syndrome and an age above 18 years are eligible for participation. The general practitioners' treatment follows their clinical guideline. The physical therapy treatment will consist of patient education and exercise therapy. The primary outcome measure is patients reported global perceived effect. Secondary outcome measures are severity of complaints, functional status, health status, fear of movement, medical consumption, sickness absence, costs and treatment preference. The follow-up is 52 weeks.
Discussion Treatment by general practitioners and physical therapists in this study will be transparent and not a complete "black box". The results of this trial will contribute to the decision of the general practitioner regarding referral to physical therapy in patients with an acute lumbosacral radicular syndrome.

Background

Why a design article?
Publishing the design of the trial has several advantages. It may prevent publication bias.[83] A study producing positive results seems more likely to be published than a study that reports no or negative results.[79,80] Also, the study can be included in systematic reviews because data can be retrieved from the researcher.[79] Publishing the design of a study before the results are available provides an opportunity to reflect critically on the design of the study, irrespective of the results. Also, a design article provides detailed information about the intervention within the trial to care givers.

The lumbosacral radicular syndrome (LRS) is a complex of symptoms related to the lumbosacral nerve roots. The LRS is a disorder with radiating pain in the leg below the knee in one or more lumbar or sacral dermatomes, and can be accompanied by phenomena associated with nerve root tension or neurological deficits (i.e. sensory deficits in the leg, decreased muscle strength in the leg, decreased reflexes, urinary problems).[2,4,11,16] A prolapsed disc is a frequent cause of LRS, but other causes include spinal or lateral recess stenosis, tumours and radiculitis.[1,2,4,11] The incidence of LRS in the Netherlands is estimated at 5 per 1000 persons a year.[1]

Most patients seeking medical care in the Netherlands will first visit a general practitioner (GP), who is regarded as the 'gatekeeper' of the health care system. The majority of health problems presented to GPs are treated by the GPs themselves and they are responsible for most referrals to (para) medical specialists. In 1996 the Dutch College of General Practitioners published their clinical guideline for LRS.[11] There is consensus that treatment of LRS in the first six to eight weeks should be conservative. The exact content of the conservative treatment is yet not clear.[46] Since the study of Vroomen et al.[17] bed rest is not regarded a treatment option for LRS anymore.

Primarily, treatment consists of adequate pain medication, giving information about the natural course of LRS, which in general is favourable, and stimulating to continue the normal daily activities of the patient. GPs in the Netherlands largely comply with the recommendations stated in the clinical guideline regarding management in patients with LRS.[84] However, they deviated regarding the referral to physical therapy (PT), almost half of patients with LRS were referred, whereas this was not recommended in the guideline. No specific patients characteristics could be found for the prescription of physical therapy. So, in general practice referral to PT in patients with LRS is common. However, there is a lack of knowledge of the effectiveness of PT in LRS. Therefore, the aim of this article is to present the design of a randomised clinical trial of conservative treatment (general practitioners and physical therapy) in patients with acute LRS.

Methods/Design

Aim
The LRS trial aims to assess the effectiveness of PTs' management added to GPs' management compared to GPs' management only in patients with acute LRS. We will use a multicentre, randomised clinical trial as study design. Figure 1 shows the flow chart of the proposed design of the LRS trial. The procedures and design of this study are approved by the Erasmus Medical Center Ethics Committee.

Study population
Participating GPs in and around Rotterdam, the Netherlands, will invite patients with suspected acute LRS to participate in the trial. GPs will invite patients from May 2003 till November 2004 if they have radiating (pain) complaints in the leg below the knee; duration of the (pain)complaints is less than 6 weeks, the age is above 18 years and they present one of the following symptoms: more pain on coughing, sneezing or straining, decreased muscle strength in the leg, sensory deficits in the leg, decreased reflex activity in the leg or a positive straight leg raising test. Patients will receive a letter of information about the LRS trial from their GP. Patients' name and telephone number will be faxed to the research institute.
Subsequently, a researcher (PL) will screen eligible patients by telephone and make an appointment to check inclusion and exclusion criteria, to complete the informed consent procedure and to perform the baseline measurement.
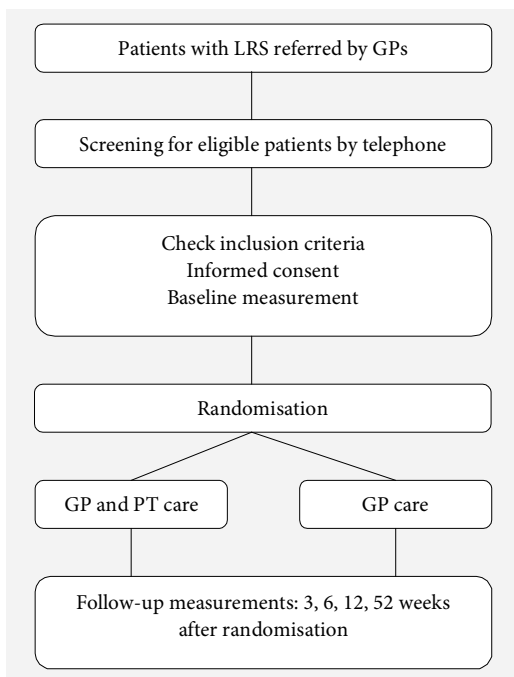
Figure 1: Flow chart of the LRS trial

Figure 2 shows the criteria that must be fulfilled to participate in the LRS trial. A research assistant will check these criteria during patients first visit. The informed consent procedure is completed when patients meet the criteria, are willing to participate and give their written consent. Hereafter, the baseline measurement will take place.

Figure 2: Selection criteria for trial eligibility

Inclusion:
Radiating (pain) complaints in the leg below the knee
Severity of complaints scored above 3 on a 10 point VAS (0= no complaints; 10= maximum complaints)
Duration of the (pain) complaints less than 6 weeks
Age above 18 years
Able to speak and read Dutch
Presents of one of the following symptoms:
More pain on coughing, sneezing or straining
Decreased muscle strength in the leg
Sensory deficits in the leg
Decreased reflex activity in the leg
Positive straight leg raising test

Exclusion:
Radiating (pain) complaints in the preceding 6 months
Back surgery in the past 3 years
Treated with epidural injections

Exclusion:
Pregnancy
Co-morbidity that primary determines overall well being
Direct indication for surgery (unbearable pain, fast progression of paresis or cauda equina syndrome
Expected loss to follow-up (i.e. moving towards other part of the country, long lasting foreign holiday)

Randomisation

Randomisation will take place after baseline measurement by the research assistant. We use a concealed randomisation procedure using a computer generated randomisation list developed by an independent person. Patients' specific and unique trial number will be typed in a special developed database (i.e. not editable for research assistant and a second randomisation action using the same trial number is not possible) and the random allocation will appear on screen. In order to prevent unequal treatment group sizes, block randomisation will be used with blocks of 10 patients.[85] This means that after every 10th patient the number of patients allocated to both treatment groups is equal. Towards every randomised patient will be explained that the management of their complaint by his or her GP will be continued. Patients who are allocated to physical therapy will be shown a list of participating physical therapists of which he or she can make a choice. The research assistant makes the first appointment with the physical therapist most easily accessible by the patient.

Blinding

For obvious reasons GPs and PTs are not blinded for treatment allocation. But they are not involved with treatment effect measurements. The patients cannot be blinded because of the ethical reasons as stated by the Medical Ethical Committee. The researcher is involved in the statistical analysis, but the analysis and interpretation of the findings will be audited and verified by an independent and not involved statistician. In this trial the primary outcome measurement and most of the secondary outcome measurements will be scored by the patients. Studies from Ostelo et al[86] and Scholten-Peeters et al[87] mentioned that in this type of study patients are blinded to a certain extent because they are unaware of the exact content of both treatments or may be called naive to the content of the treatment not received. Other more or less similar designed trials from Vroomen et al[17] and Hofstee et al[75] reported that it is not possible to blind participating patients for allocated treatment. Therefore, we think it is important to know any treatment preference of the patients at baseline. Supplementary analysis may show to what extent this effects the scores on outcome measurements of the patients.

GP intervention

All patients will be treated by the GP according to their clinical guideline (see Figure 3). GPs will give information and advice about LRS. If necessary they prescribe adequate pain medication. We asked the GPs not to refer patients to paramedical specialists (i.e. manual therapist, physical therapist, exercise therapist, etc.). Referral to PT is based on randomisation and performed by the research assistant.

Figure 3: Summary of the clinical guideline 'Lumbosacral radicular syndrome' of the Dutch College of General Practitioners (1996)

Definition: The lumbosacral radicular syndrome: radiating pain and/or neurological deficits in one or more lumbar or sacral dermatomes, often associated with back pain; mostly caused by irritation and compression (traction) of the nerve root.

History taking: Ask about: 1) localisation, radiation, intensity and duration of the pain, 2) influence of rest, movement and posture, 3) development of the complaints, 4) interference with daily activities caused by leg pain, 5) decreased muscle strength and sensory deficits, 6) influence of coughing, sneezing or straining, 7) previous history of back complaints, and 8) urinary problems and saddle anaesthesia.

Physical examination: 1) physical inspection (spine and pelvis), 2) active examination (ante-, retro-, lateroflexion), and 3) Lasègue sign and test of Bragard. If there is a positive Lasègue sign, decreased muscle strength or sensory deficits perform: 4) ankle tendon reflex and knee tendon reflex, 5) sensory examination of the lateral and medial side of the foot, 6) muscular strength of the big toe, walking on heels and toes, and 7) crossed test of Lasègue.

Additional examinations: X-rays should only be ordered in case of suspicion on malignancy or a fracture due to osteoporosis.

Evaluation: The lumbosacral radicular syndrome should be diagnosed if there are radiating complaints in the leg below the knee, plus one of the following findings: 1) a positive Lasègue sign (or Bragard), or 2) neurological deficits reducible to a single nerve root.

Information and advice: Explain to the patient that radiating complaints are caused by a prolapsed disc that gives pressure on a nerve in the back. There is a favourable course in 80% of the patients with conservative care. Back pain may persist after the leg pain has gone.

Mild complaints: Advice the patient to perform the usual daily activities but to avoid painful movements. Gradually increase the activities.

Severe complaints: Strict bed rest (washing and toilet visits on bed) for two weeks. When the complaints decrease after a few days or two weeks, less strict bed rest (walking, washing and toilet visits allowed). Gradually increase the activities to normal level in six weeks and to patients' level in six to twelve weeks.

Follow-up: Check the patient with bed rest after two to four days. Evaluate the effect of treatment by checking Lasègue sign and the severity of the complaints. Check patients with severe complaints daily and subsequently at least once a week. Accompany the patient till full resumption of daily activities.

Drug treatment: If desired: paracetamol (4-6 dd, 500mg), ibuprofen (3-4 dd, 400 mg), diclofenac (3-4 dd, 25-50 mg), or naproxen (2-3 dd, 250 mg).

Referral: Refer in an instant: 1) cauda equina syndrome, or 2) progressive paresis within a few days in spite of conservative care. Refer for diagnostics and judgement for indication for surgery: 1) Severe radicular pain in spite of bed rest and adequate medication, 2) Severe paresis or progressive paresis in spite of adequate care (walking on heels and toes is impossible), 3) doubtful diagnosis, or 4) mild complaints with no improvement after six to eight weeks.

PT intervention

PT treatment will imply information and advice about LRS and exercise therapy. Passive modalities such as massage, manipulation techniques or applying applications (e.g. ultra sound or current waves) are not allowed in the PT treatment. This PT treatment protocol was accomplished in a consensus meeting with participating PTs. The PT will report what kind of information/ advice and what type of exercise the patient receives in each session. Both GP and PT intervention will be restricted to a maximum of 9 treatments/ consultations in the first 6 weeks after randomisation.

Theoretical background
In the Netherlands, PTs are mainly taught the biomechanic model.[86] This model focuses on somatic issues; it assumes a causal relation between tissue damage and pain. PT could be of additional value in the management of patients with LRS because PTs are 'the experts' in treating musculoskeletal disorders with exercises and advice/ information. The pain reported by a patient is used as guidance to determine the intensity of the exercises and the advice about resuming normal daily activities and work. This study assumes that focussing on (pain) complaints with exercises and advice is the optimal PT treatment in the acute phase (0 to 6 weeks) of LRS. It is possible that patients may suffer from a fear of movement because of pain.[88] Good advice/ information will reassure these patients and exercises will show them that movement is possible. So, the secondary treatment goal of the PT is to decrease the possibly present fear of movement in these patients.

Sample size
This trial attempts to enrol 182 patients with LRS, 91 patients in both treatment groups. This sample size is regarded sufficient to detect a difference of 20% (with a α of 0.05 and a power of 80%) in the primary outcome (GPE) between the two treatment groups. A difference of 20% is considered to be clinically relevant.[89]

Measurements
Figure 4 shows the outcome measures and the points of time they are collected. At baseline we will collect patients characteristics such as gender, date of birth, height and body weight. In standardised history taking there will be established whether patients are familiar with LRS in the past, report more pain in the leg on coughing/ sneezing or straining, on sitting, standing, walking and lying down, and if patients report a decreased muscle strength and sensory deficits in the leg. The physical examination consists of the straight leg raising test, the crossed straight leg raising test, test of Bragard, finger-floor distance, standing on toes and heels, knee tendon reflex, ankle tendon reflex, strength of m. extensor hallicus longus, sensory tests (touch, sharp and blunt) in the dermatomes L5/ S1 in the feet.

Figure 4: Data collection and outcome measures

	Baseline	3 weeks	6 weeks	12 weeks	52 weeks
Inclusion/ exclusion	X				
Patient characteristics	X				
History taking	X		X	X	
Physical examination	X		X	X	
Global perceived effect (7-points scale)	X	X	X	X	X
Severity of complaints (VAS)	X	X	X	X	X
Functional status (RDQ)	X		X	X	X
Health status (SF-36/ EQ-5D)	X		X	X	X
Fear of movement (TSK)	X				X
Medical consumption	X	X	X	X	X
Sickness absence	X	X	X	X	X
Costs	X	X	X	X	X
Treatment preference	X	X	X	X	X

VAS=visual analogue scale; RDQ=Roland Morris disability questionnaire for sciatica; SF-36=Short form 36 questionnaire; EQ-5D=Euroqol, TSK=Tampa scale for kinesiophobia.

Primary outcome measure
The primary outcome measure is the Global Perceived Effect (GPE), measured on a 7 points scale ranging from 1=completely recovered to 7=vastly worsened. It is regarded a clinical relevant outcome measure and is regarded valid and responsive to measure the patients' perceived benefit.[90-92]

Secondary outcome measures
Pain severity of the leg and the back will be scored on a 11 points Visual Analogue Scale (VAS) ranging from 0=no pain to 10=unbearable pain. Reliability, validity and responsiveness of the VAS have been shown.[93-95]
The functional status will be measured with the Roland Morris Disability Questionnaire (RDQ) for sciatica.[96] The scoring of the RDQ is achieved by counting the number of positive responses: a patient individual score can vary from 0 (no disability) to 24 (severe disability). The RDQ has proved to be a valid instrument and appears to be responsive for clinical relevant changes.[92,97-100]
Health status will be measured by the 36-item short form (SF-36)[101] and the Euroqol (EQ-5D) instrument.[102,103] Validity and responsiveness on both SF-36[104-106] and EQ-5D[107-109] proved to be sufficient.
Fear of movement will be measured by the Tampa scale for kinesiophobia (TSK).[110,111] The TSK consists of 17 items; each rated on a 4-point likert scale. The TSK has been shown to be a valid and responsive instrument.[112,113]
Costs will be calculated and include LRS related sickness absence from work, medical consumption (i.e. medication use, additional therapies, visits to health care providers), out-of-pocket expenses and paid help. Patients' treatment preference will be evaluated at baseline and at 4 follow-up measurements.

Statistical analysis
Baseline comparability will be investigated by descriptive statistics to examine whether randomisation was successful. If necessary, adjustments for baseline variables will be performed in the analysis. Group differences and 95% confidence intervals will be calculated for all outcome measures. The statistical analysis will be performed according tot the intention-to-treat principle, analysing the patients in the treatment group to which they were randomly allocated. Between group differences will be calculated using the Student t-test for continuous variables or Chi-Square for dichotomous variables. In addition a per-protocol analysis will be performed, analysing only those patients with no serious protocol deviations. Comparing the results of the intention-to-treat and the per-protocol analysis will indicate if and to what extent protocol deviations might have biased the results. Multivariate regression analysis will be conducted to examine the influence of baseline variables on outcome.

Discussion

This article introduces a design of a RCT to evaluate the additional effectiveness of PTs' management added to GPs' management in patients with LRS. The study is designed in a way that GP and PT treatment is transparent (according a guideline and a consensus meeting) and not a complete "black box". The results of this trial will contribute to the decision of the GP regarding referral of patients with LRS to PT. The inclusion of patients will run until the end of the year 2004. The follow-up measurements will be completed in the end of the year 2005.

Chapter 7

Effectiveness of physical therapy plus general practitioners' care versus general practitioners' care alone for sciatica. A randomised clinical trial with 1-year follow-up.

Pim A.J. Luijsterburg, Arianne P. Verhagen, Raymond W.J.G. Ostelo, Hans J.M.M. van den Hoogen, Wilco C. Peul, Cees J.J. Avezaat, Bart W. Koes.
Submitted

Abstract

Objective To assess the effectiveness of physical therapy additional to general practitioners' care compared to general practitioners' care alone, in patients with acute sciatica.

Design, setting and patients A randomised clinical trial in primary care with a 12-months follow-up period. 135 patients with acute sciatica (recruited from May 2003 to November 2004) were randomised in two groups: 1) the intervention group received physical therapy added to the general practitioners' care, and 2) the control group with general practitioners' care only.

Intervention Physical therapy consisting of active exercises added to general practitioners' care.

Main outcome measures The primary outcome was patients' global perceived effect. Secondary outcomes were severity of leg and back pain, severity of disability, general health and absence from work. The outcomes were measured at 3, 6, 12 and 52 weeks after randomisation.

Results At 3 months follow-up, 70% of the intervention group and 62% of the control group reported improvement (RR 1.1; 95% CI 0.9; 1.5). At 12 months follow-up, 79% of the intervention group and 56% of the control group reported improvement (RR 1.4; 95% CI 1.1; 1.8). No significant differences in secondary outcomes were found at short-term or long-term follow-up.

Conclusions At 12 months follow-up, evidence was found that physical therapy added to general practitioners' care is more effective in the treatment of patients with acute sciatica than general practitioners' care alone. There are indications that physical therapy is especially effective in patients reporting severe disability at presentation.

Trial registration An International Standard Randomised Controlled Trial Number was assigned to this trial (ISRCTN68857256) at www.controlled-trials.com.

Introduction

The lumbosacral radicular syndrome (LRS), also called sciatica, is a disorder with radiating pain in the leg below the knee in one or more lumbar or sacral dermatomes, and can be accompanied by phenomena associated with nerve root tension or neurological deficits.[2-4,11] A prolapsed disc is a frequent cause of LRS, but other causes include spinal or lateral recess stenosis, tumours and radiculitis.[1,2,4,11] The incidence of LRS in the Netherlands is estimated at 5 per 1000 persons a year.[1] Most patients seeking medical care in the Netherlands will first visit a general practitioner (GP).

In 1996 the Dutch College of General Practitioners published their clinical guideline for LRS[11] and updated it in 2005.[5] There is consensus that treatment of LRS in the first 6 to 8 weeks should be conservative.

The exact content of the conservative treatment is, however not yet clear.[46] After the study of Vroomen et al.[17] bed rest is no longer regarded as a treatment option for LRS.[5]

GPs in the Netherlands largely comply with the recommendations stated in the clinical guideline regarding the management of patients with LRS.[84] However, in our previous observational study it was shown that GPs did not adhere to the guideline regarding the referral to physical therapy (PT); almost half of patients with LRS were referred for PT, although this was not recommended in the guideline. No specific characteristic could be identified to explain this referral to PT.[84] However, there is a lack of knowledge concerning the effectiveness of PT in LRS. Therefore, this study aimed to assess the effectiveness of PT management additional to GP management compared to GP management alone, in patients with acute LRS.

Methods

More detailed information about the methods of the LRS trial is presented elsewhere.[114] The Erasmus Medical Center Ethics Committee approved the procedures and design of this trial.

Study population
Participating GPs in Rotterdam and the surrounding area invited patients with acute LRS to participate in the trial from May 2003 to November 2004. Table 1 shows the eligibility criteria.

Table 1: Selection criteria for trial eligibility

Inclusion:
Radiating (pain) complaints in the leg below the knee
Severity of complaints scored above 3 on an 11-point NRS (0= no complaints; 10= maximum complaints)
Duration of the (pain) complaints less than 6 weeks
Age between 18 and 65 years
Able to speak and read Dutch
Presence of one of the following symptoms:
More pain on coughing, sneezing or straining
Decreased muscle strength in the leg
Sensory deficits in the leg
Decreased reflex activity in the leg
Positive straight leg raising test
Exclusion:
Radiating (pain) complaints in the preceding 6 months
Back surgery in the past 3 years
Treated with epidural injections
Pregnancy
Co-morbidity that determines overall well-being
Direct indication for surgery (unbearable pain, fast progression of paresis or cauda equina syndrome)
Expected loss to follow-up (i.e. moving to another part of the country, long-lasting foreign holiday)

NRS: Numerical rating scale.

Randomisation

A concealed randomisation procedure[10] was used, which was based on a computer-generated randomisation list developed by an independent person. In order to prevent unequal treatment group sizes, block randomisation was used with blocks of 10 patients.[85] The research assistant performed the randomisation after baseline measurement.

Blinding

For obvious reasons the GPs, physical therapists and patients were not blinded for treatment allocation. The statistical analysis and interpretation of the findings was audited and verified by an independent and independent statistician.

GP care

All patients were treated by the GP according to their clinical guideline.[11] GPs gave information and advice about LRS and, if necessary, prescribed (pain) medication.

Physical therapy

PT treatment consists of exercise therapy as well as giving information and advice about LRS. Passive modalities such as massage and manipulation techniques, or applications such as ultrasound therapy or electrotherapy were not allowed. The treatment protocol was developed in a consensus meeting with participating physical therapists. They acted as coaches and guided the patient in order to stimulate return to activity, despite the pain experience. Both GP and PT interventions were restricted to a maximum of 9 treatments/consultations in the first 6 weeks after randomisation.

Measurements

Collected at baseline were patients' characteristics such as gender and date of birth. Standardised history taking was used to establish whether patients were familiar with LRS in the past, reported more pain in the leg on coughing/sneezing or straining, on sitting, standing, walking and lying down, and whether patients reported decreased muscle strength and sensory deficits in the leg. The physical examination included amongst others the straight leg raising test and the test of Bragard.

Primary outcome measure

The primary outcome measure was the Global Perceived Effect (GPE), measured on a 7-point scale ranging from 1=completely recovered to 7=vastly worsened.[90-92] These ratings were dichotomised as improved ("completely recovered" and "much improved"), versus not improved ("slightly improved", "not changed", "slightly worsened", "much worsened" and "worse than ever").

Secondary outcome measures

Pain severity of the leg and the back was scored separately on an 11-point numerical rating scale (NRS) ranging from 0=no pain to 10=unbearable pain.[115] The functional status was measured with the Roland Morris Disability Questionnaire (RDQ) for sciatica.[96]
Health status was measured by the 36-item short form (SF-36)[101] and the Euroqol (EQ-5D) instrument.[102,103] Fear of movement was measured by the Tampa scale for kinesiophobia (TSK).[110,111] LRS-related absence from work (in days) and medical consumption were measured by means of a questionnaire.

Statistical analysis
The statistical analysis was performed according to the intention-to-treat principle, analysing all patients in the treatment group to which they were randomly allocated. Baseline comparability was investigated by descriptive statistics to examine whether randomisation was successful. Missing (item) values were assigned the last available score. Group differences and 95% confidence intervals (CI) were calculated for all outcome measures with a baseline value. Between group differences were calculated using the Student's t-test for continuous variables and the Chi-square test for dichotomous variables. Results are presented as relative risks (RR) or effect sizes (ES) with corresponding 95% CI. There was a statistical significant difference if the p-value was smaller than 0.05, and a clinically relevant difference when a 20% difference appeared in one of the outcome measurements between both groups. In addition a per-protocol analysis was performed, analysing only those patients with no serious treatment protocol deviations, e.g. received the allocated treatment. Pre-determined subgroup analyses were performed for patients with severe disability (RDQ >= 17).

Results

Study population
In total 112 GPs participated in the trial and referred 170 patients for eligibility check. Excluded from the trial were 35 patients for one or more of the following reasons; 16 patients did not want to participate, 1 patient was older than 65 years, 7 patients had (pain) complaints for more than 6 weeks, 3 patients had no radiating (pain) complaints in the leg below the knee, 5 patients were not available for follow-up measurements, 3 patients had back surgery in the past 3 years, 1 patient had received an epidural injection, 7 patients were already treated by a PT, and 2 patients were pregnant.

Included and randomised were 135 patients, 67 patients received GP plus PT care (the intervention group), and 68 patients received GP care only (the control group). Four patients dropped-out immediately after randomisation because they no longer wished to participate, 1 in the intervention group and 3 in the control group. Figure 1 shows the flow chart of the trial.
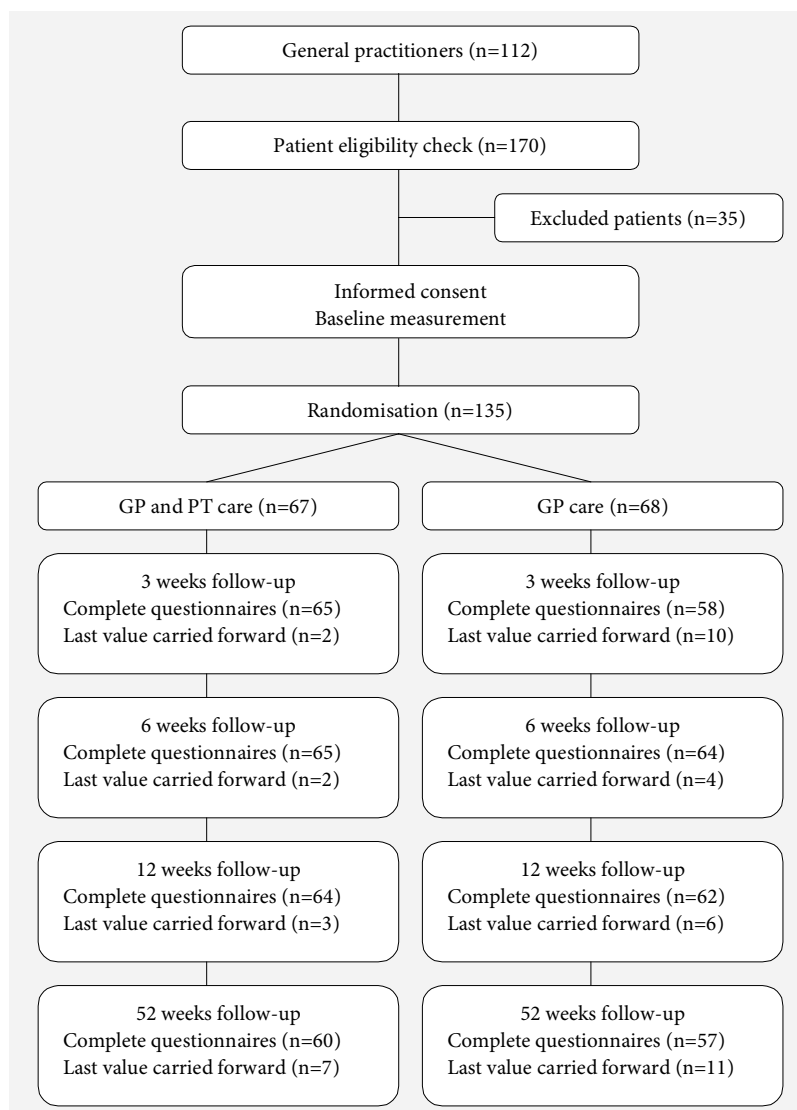
Characteristics of the study population
Table 2 gives the demographic and clinical characteristics of the randomised patients. The two groups were considered comparable for all measured baseline characteristics.

Interventions
At 6 weeks follow-up, the 67 patients of the intervention group and 68 patients of the control group reported a mean GP consult of respectively 1.1 (SD: 1.5) and 1.7 (SD: 1.8), since baseline. The mean GP consult at 12 weeks and 52 weeks follow-up was respectively 1.6 (SD: 1.4) and 1.8 (SD 1.9) in the intervention group and respectively 1.9 (SD: 2.1) and 2.2 (SD 2.7) in the control group. These differences were not significant. At baseline, the GPs had prescribed NSAIDs, opioids, and muscle relaxants for respectively 47, 8 and 23 patients in the intervention group, and for respectively 40, 10 and 15 patients in the control group.

Figure 1: Flow chart of the trial


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                  │  General practitioners (n=112)    │
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                                 │
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                  │  Patient eligibility check (n=170)│
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                                 │        ┌────────────────────────┐
                                 ├────────│ Excluded patients (n=35)│
                                 │        └────────────────────────┘
                  ┌──────────────────────────────────┐
                  │        Informed consent           │
                  │      Baseline measurement         │
                  └──────────────────────────────────┘
                                 │
                  ┌──────────────────────────────────┐
                  │      Randomisation (n=135)        │
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GP and PT care (n=67)	GP care (n=68)
3 weeks follow-up Complete questionnaires (n=65) Last value carried forward (n=2)	3 weeks follow-up Complete questionnaires (n=58) Last value carried forward (n=10)
6 weeks follow-up Complete questionnaires (n=65) Last value carried forward (n=2)	6 weeks follow-up Complete questionnaires (n=64) Last value carried forward (n=4)
12 weeks follow-up Complete questionnaires (n=64) Last value carried forward (n=3)	12 weeks follow-up Complete questionnaires (n=62) Last value carried forward (n=6)
52 weeks follow-up Complete questionnaires (n=60) Last value carried forward (n=7)	52 weeks follow-up Complete questionnaires (n=57) Last value carried forward (n=11)

Patients in the intervention group were treated by 33 different physical therapists. The number of treated patients per physical therapist ranged from 1 to 9. Patients in the intervention group reported a mean of 6.7 (SD: 2.9) PT treatments of at 6 weeks follow-up, and 9.7 (SD: 4.7) at 12 weeks follow-up. The mean time between randomisation and the first PT treatment was 4.6 days (SD: 3.1). The physical therapists reported that during the first treatment 60% (range: 10-100%) of the time was spent on history taking and physical examination, 30% (range: 0-60%) on giving information and advice about LRS, and 10% (range: 0-40%) on active exercise therapy (duration of one treatment session was 30 minutes).

Table 2: Baseline characteristics of the 135 patients randomised in two treatment groups.

Characteristics	GP + PT care (n=67)	GP care only (n=68)
Female gender, n (%)	38 (57)	27 (40)
Age in years, mean (SD)	42 (10)	43 (12)
Paid job, n (%)	48 (72)	50 (74)
Reporting sickness absence, n (%)	34 (51)	32 (47)
Sickness absence from onset in days, mean (SD)	3.1 (4.9)	4.2 (6.8)
Time between onset LRS and baseline in days, mean (SD)	12.1 (10.1)	14.2 (10.2)
Never LRS in past, n (%)	49 (73)	54 (79)
More pain in leg on coughing, sneezing or straining, n (%)	40 (60)	37 (54)
Decreased muscle strength in the leg, n (%)	48 (72)	44 (65)
Sensory deficits in the leg, n (%)	54 (81)	53 (78)
Positive straight leg raising test, n (%)	37 (55)	35 (52)
Positive test of Bragard, n (%)	25 (37)	23 (34)
Taking medication, n (%)	58 (87)	48 (71)
Leg pain on NRS[&], mean (SD)	6.3 (2.2)	6.3 (2.2)
Back pain on NRS, mean (SD)	5.8 (2.8)	5.7 (2.5)
RDQ[ε] score, mean (SD)	15.9 (4.1)	15.4 (5.0)
TSK[¥] score, mean (SD)	39.0 (5.8)	41.0 (7.1)

[&] NRS=Numerical Rating Scale. Score range from 0 (no pain) to 10 (unbearable pain).

[ε] RDQ=Roland disability questionnaire. Score range from 0 (no disability) to 24 (severe disability).

[¥] TSK=Tampa scale for kinesiophobia. Scores range from 17 to 68 points; higher score indicates more kinesiophobia.

During the second through ninth treatment, 33% (range: 0-100%) of the time was spent on giving information and advice, and 67% (range: 0-100%) on active exercise therapy.

Outcomes
In both groups patients improved over time. At 3, 6 and 12 weeks after baseline there was no significant difference between the two groups on the primary outcome: GPE (Table 3). However, at these follow-up moments the intervention group showed a higher proportion of 'improved' patients.

Table 3: Data on treatment results at 3, 6, 12 and 52 weeks after baseline: primary outcome.

Global perceived effect[*]	GP + PT care Improved n=67 (%)	GP care only Improved n=68 (%)	RR (95% CI)	NNT
3 weeks after baseline	30 (45)	22 (32)	1.4 (0.9; 2.1)	8
6 weeks after baseline	38 (60)	30 (44)	1.3 (0.9; 1.8)	8
12 weeks after baseline	47 (70)	42 (62)	1.1 (0.9; 1.5)	12
52 weeks after baseline	53 (79)	38 (56)	1.4 (1.1; 1.8)	4

[*]: Ratings on patient's globally perceived effect on a 7-point scale were dichotomised (see Methods section).

RR: Relative risk.

CI: Confidence interval.

NNT: Number needed to treat.

At 52 weeks after baseline there was a significant and a clinical difference between the groups on the primary outcome measure global perceived effect, in favor of the intervention group (Table 3). 53 patients (79%) in the intervention group versus 38 patients (56%) in the control group reported to be 'improved' (RR, 1.4; 95% CI: 1.1; 1.8). There were no significant differences between the groups in most of the secondary outcomes at 3, 6, 12 and 52 weeks after baseline (Table 4).

Table 4: Data on treatment results at 3, 6, 12 and 52 weeks after baseline: secondary outcomes.

	GP + PT care Improvement n=67	GP care only Improvement n=68	Mean difference [GP+PT] - [GP] (95% CI)	Effect size (95% CI)
3 weeks after baseline				
Leg pain on NRS [&][#]	-2.3 (2.4)	-1.9 (2.4)	-0.4 (-1.2; 0.4)	0.17 (-0.2; 0.5)
Back pain on NRS [&][#]	-2.0 (2.8)	-1.7 (2.4)	-0.3 (-1.2; 0.6)	0.12 (-0.2; 0.5)
6 weeks after baseline				
Leg pain on NRS [&][#]	-3.0 (2.7)	-3.3 (2.8)	0.3 (-0.6; 1.2)	0.11 (-0.2; 0.5)
Back pain on NRS [&][#]	-2.3 (3.1)	-2.6 (2.7)	0.3 (-0.7; 1.3)	0.19 (-0.2; 0.5)
RDQ score [ϲ][#]	-5.3 (7.0)	-6.6 (6.1)	1.3 (-0.9; 3.6)	0.22 (-0.1; 0.5)
General health [£][#]	2.2 (16.4)	-2.8 (13.9)	5.0 (0.2; 10.1)	0.36 (-0.0; 0.7)
12 weeks after baseline				
Leg pain on NRS [&][#]	-3.9 (2.8)	-3.7 (3.1)	-0.2 (-1.2; 0.8)	0.05 (-0.3; 0.4)
Back pain on NRS [&][#]	-2.7 (3.2)	-2.6 (2.9)	-0.1 (-1.2; 0.9)	0.04 (-0.3; 0.4)
RDQ score [ϲ][#]	-7.7 (7.3)	-8.5 (6.7)	0.8 (-1.6; 3.2)	0.12 (-0.2; 0.5)
General health [£][#]	-1.2 (18.4)	-4.7 (16.4)	3.5 (-2.4; 9.5)	0.22 (-0.1; 0.5)
52 weeks after baseline				
Leg pain on NRS [&][#]	-4.4 (2.7)	-3.7 (2.7)	-0.7 (-1.7; 0.2)	0.26 (-0.1; 0.6)
Back pain on NRS [&][#]	-3.0 (3.1)	-2.3 (2.9)	-0.7 (-1.7; 0.4)	0.23 (-0.1; 0.6)
RDQ score [ϲ][#]	-10.0 (6.5)	-9.1 (6.1)	-0.9 (-3.0; 1.3)	0.14 (-0.2; 0.5)
TSK score [¥][#]	-3.3 (7.3)	-4.5 (6.6)	1.2 (-1.2; 3.6)	0.17 (-0.2; 0.5)
General health [£][#]	-3.1 (15.7)	-4.1 (16.7)	1.0 (-4.5; 6.5)	0.06 (-0.3; 0.4)

All outcome measures are presented in in means and standard deviation, unless otherwise stated.

[&] NRS=Numerical Rating Scale. Score range from 0 (no pain) to 10 (unbearable pain).

[#] Negative results denote positive results for patients.

[ϲ] RDQ=Roland disability questionnaire. Score range from 0 (no disability) to 24 (severe disability).

[£] Dimension of the SF-36=Short form 36 questionnaire. Score range each dimension 0-100; higher score indicates a better health state.

[¥] TSK=Tampa scale for kinesiophobia. Scores range from 17 to 68 points; higher score indicates more kinesiophobia.

At 12 and 52 weeks follow-up the mean improvement on leg pain was clinically relevant in both groups; respectively 3.9 and 4.4 points for the intervention group and respectively 3.7 and 3.7 points for the control group. The mean improvement on disability (RDQ) was also clinically relevant at 12 and 52 weeks follow-up in both groups; respectively 7.7 and 10.0 points for the intervention group and respectively 8.5 and 9.1 points for the control group.

There were no significant differences between both groups in the number of patients reporting absence from work or reported days absence from work.

At 12 weeks follow-up, 36 patients (54%) in the intervention group and 25 patients (37%) in the control group reported a mean of respectively 16.2 days (SD 21.3) and 13.1 days (SD 24.1) absence from work. At 52 weeks follow-up, 30 patients (45%) in the intervention group and 25 patients (37%) in the control group reported, over the whole year, a mean of respectively 29.2 days (SD 48.4) and 28.9 days (SD 72.3) absence from work.

Co-interventions
In the 52 weeks after baseline 11 patiënts (16%) in the intervention group and 6 patients (9%) in the control group visited a neurologist. In the intervention group 4 patients visited a neurosurgeon, 1 patient a orthopedist, and 4 patients (6%) received surgery due to LRS.
In the control group 6 patients visited a neurosurgeon, 2 patients a orthopedist, and 3 patients (4%) received surgery. There were a few co-interventions (i.e. occupational physician) in both groups, but there were no significant differences between the two groups.

Per-protocol analysis
The per-protocol analysis (the patients that received the allocated treatment according randomisation) was restricted to 66 patients in the intervention group and 55 patients in the control group. Restricting the analysis to the 'per protocol' patients did not change the within group and between group differences in any substantial way.

Subgroup analysis
The subgroup with severe disability (RDQ >=17) consisted of 67 patients. The intervention group (n=37) and the control group (n=30) were considered comparable for all measured baseline characteristics. At 12 and 52 weeks follow-up, respectively 29 (78%) and 31 (84%) patients with severe disability in the intervention group and 15 (50%) and 16 (53%) patients in the control group reported to be 'improved' (12 weeks and 52 weeks: RR, 1.6; 95% CI, 1.1; 2.3); indicating a significant and a clinically relevant difference.

Discussion

At 12 weeks after baseline there was no significant difference between both groups on the primary outcome, but most of the patients (70% in the intervention group and 62% in the control group) reported to be 'improved'. At 52 weeks follow-up there was a significant (RR, 1.4; 95% CI, 1.1; 1.8) and clinically relevant difference (23%) between both groups, in favor of the intervention group.
Therefore, adding PT care to GP care is more effective than GP care alone in the long-term, for the average patient with (sub) acute sciatica. Moreover, PT care added to GP care seemed to be especially effective in the subgroup with patients reporting more severe disability at presentation.

Although the control group had 3 dropouts compared with only 1 in the intervention group, this did not appear to bias the results because all dropped-out immediately after randomisation, and results of both the per-protocol analysis and the intention-to-treat analysis were similar. Also, there are no indications that not blinding GPs, physical therapists and patients biased the results; at 12 weeks follow-up the within-group improvement of both groups was considerable for GPE, the leg pain on NRS and the RDQ.

At long-term follow-up a clinically relevant change was found on the primary outcome measure (GPE) between the two groups, in favor of the intervention group; the difference was 23%. A priori was stated that a clinically relevant difference had to be at least 20%.[114] However, recent work of Ostelo and De Vet shows the need for more research on the exact value for the minimal clinically important difference between two groups in this type of study.[116]

A few randomised clinical trials have evaluated physical therapy as a treatment for the LRS. Hofstee et al. focused on bed rest, physical therapy and continuation of activities of daily living[75]; their trial included 250 patients with acute sciatica, and the authors concluded after a 6-month follow-up period that bed rest and physical therapy are no more effective than continuation of the activities of daily living.[75] Coxhead et al. compared four methods of physical therapy (traction, exercises, manipulation and corset therapy) in 322 participating patients with sciatica[72]; the authors concluded that although active physical therapy appeared to be of short-term value, it did not seem to confer any long-term benefit.[72] Lidström and Zachrisson compared three methods of physical therapy (massage/exercises, traction and hot packs) in 62 patients with sciatica[70]; after treatment (one month after randomisation) they concluded that the traction group showed better results than the other two groups.[70] The results of our study are not in concordance with the earlier studies, because we found that in the long-term PT care added to GP care is effective. The previous studies did not measure the absence from work (or did not report on this outcome). In the present study, there were no significant differences in absence from work between groups at short or long-term follow-up.

The results of our study indicate that PT added to GP care was better for the average patient with a LRS than GP care alone in the long-term. Moreover, for patients with severe disability at presentation, PT care added to GP care seemed to be especially effective. Future trials are necessary to evaluate the effectiveness of physical therapy in patients with severe disability.

Chapter 8

Cost effectiveness of physical therapy and general practitioner care for sciatica. An economic evaluation alongside a randomised controlled trial.

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Submitted

Abstract

Objective To evaluate the cost-effectiveness of physical therapy and general practitioner care for patients with an acute lumbosacral radicular syndrome (LRS; also called sciatica)

Design, setting and patients An economic evaluation alongside a randomised clinical trial in primary care. 135 patients were randomly allocated to physical therapy added to general practitioners' care (n=67) or to general practitioners' care alone (n=68).

Main outcome measures The clinical outcomes were global perceived effect and quality of life. The direct and indirect costs were measured by means of questionnaires. The follow-up period was one year. The Incremental Cost Effectiveness Ratio (ICER) between both study arms was constructed. Confidence intervals for the ICER were calculated using Fieller's method and using bootstrapping.

Results There was a significant difference on perceived recovery at 1-year follow-up in favor of the physical therapy group. The additional physical therapy did not have an incremental effect on quality of life. At 1-year follow-up, the ICER for the total costs was € 6224 (95% CI: -10419; 27551) per improved patient gained. For direct costs only, the ICER was € 837 (95% CI: -731; 3186).

Conclusions Physical therapy provided no cost effective addition to care in general practice, for patients with LRS. Although, adding physical therapy resulted in more perceived recovery.

Introduction

The lumbosacral radicular syndrome (LRS), also called sciatica, is a disorder with radiating pain in the leg below the knee in one or more lumbar or sacral dermatomes, and can be accompanied by phenomena associated with nerve root tension or neurological deficits.[2-5] A prolapsed disc is a frequent cause of LRS, but other causes include spinal or lateral recess stenosis, tumours and radiculitis.[1,5] The incidence of LRS in the Netherlands is estimated at 5 per 1000 persons a year.[1] LRS is not life threatening, but it causes pain in the leg and disability, often resulting in utilisation of healthcare resources and absenteeism from work.[1] The total, direct and indirect, costs of LRS in the Netherlands are estimated at 1.18 billion euro a year.[1] Therefore, there is a need to determine the most cost effective intervention for LRS.

Most patients seeking medical care in the Netherlands will first visit a general practitioner (GP). In 1996 the Dutch College of General Practitioners published their first clinical guideline for LRS[11] and updated it in 2005.[5] There is consensus that treatment of LRS in the first 6 to 8 weeks should be conservative.

Many conservative treatments are available for treating LRS, but most patients are referred to physical therapy.[84] The effectiveness of conservative treatments is however not yet clear.[117] A randomised controlled trial was performed to evaluate the effectiveness of physical therapy added to general practitioner care compared to general practitioner care alone in patients with acute LRS.[114] The clinical effects at 1-year follow-up has been reported elsewhere.[118] This study aimed to assess the cost-effectiveness of physical therapy and general practitioner care for patients with acute LRS.

Methods

More detailed information about the methods of the LRS trial is presented elsewhere.[114] The Erasmus Medical Center Ethics Committee approved the procedures and design of this trial.

Study population
Participating GPs (n=112) in Rotterdam and the surrounding area invited patients with acute LRS to participate in the trial from May 2003 to November 2004. Table 1 shows the eligibility criteria.

Table 1: Selection criteria for trial eligibility

Inclusion:
Radiating (pain) complaints in the leg below the knee
Severity of complaints scored above 3 on an 11-point NRS (0= no complaints; 10= maximum complaints)
Duration of the (pain) complaints less than 6 weeks
Age between 18 and 65 years
Able to speak and read Dutch
Presence of one of the following symptoms:
More pain on coughing, sneezing or straining
Decreased muscle strength in the leg
Sensory deficits in the leg
Decreased reflex activity in the leg
Positive straight leg raising test
Exclusion:
Radiating (pain) complaints in the preceding 6 months
Back surgery in the past 3 years
Treated with epidural injections
Pregnancy
Co-morbidity that determines overall well-being
Direct indication for surgery (unbearable pain, fast progression of paresis or cauda equina syndrome)
Expected loss to follow-up (i.e. moving to another part of the country, long-lasting foreign holiday)

NRS: Numerical rating scale.

Randomisation
A concealed randomisation procedure was used, which was based on a computer-generated randomisation list developed by an independent person.

In order to prevent unequal treatment group sizes, block randomisation was used with blocks of 10 patients.[85] The research assistant performed the randomisation after baseline measurement.

Blinding
For obvious reasons the GPs, physical therapists and patients were not blinded for treatment allocation. The statistical analysis and interpretation of the findings was audited and verified by an independent and uninvolved statistician.

GP care
All patients were treated by the GP according to their clinical guideline.[11] GPs gave information and advice about LRS and, if necessary, they prescribed (pain) medication.

Physical therapy
The treatment consists of exercise therapy as well as giving information and advice about LRS. Passive modalities such as massage and manipulation techniques, or applications such as ultrasound therapy or electrotherapy were not allowed. The treatment protocol was developed in a consensus meeting with participating physical therapists (n=61). They acted as coaches and guided the patient in order to stimulate return to activity. Both GP and physical therapy interventions were restricted to a maximum of 9 treatments or consultations in the first 6 weeks after randomisation.

Measurements
The primary outcome measure was global perceived effect (GPE), measured on a 7-point scale ranging from 1=completely recovered to 7=vastly worsened.[90-92] These ratings were dichotomised as improved ("completely recovered" and "much improved"), versus not improved ("slightly improved", "not changed", "slightly worsened", "much worsened" and "worse than ever"). GPE was rated as the percentage of patients that reported to be 'improved'. The Euroqol (EQ-5D) instrument was used to calculate utilities.[119,120] The outcome measures and costs were assessed at baseline and cumulative at 3, 6, 12, 52 weeks after randomisation using questionnaires. The economic evaluation was performed from a societal perspective, meaning that all relevant costs and effects are measured regardless of who pays the costs and who benefits from the effects. Table 2 shows an overview of the costs used in the economic evaluation.

Table 2: Overview unit costs in the economic evaluation.

Costs	Cost (€) [#]
Direct health care costs:	
Physical therapy (per visit)	22.75
General practitioner (per visit)	20.20
Manual therapy (per visit)	25.90
Cesar or Mensendieck therapy (per visit)	23.00
Consultation specialist in hospital (per visit)	56.00
Hospitalisation (per day)	337.00
Surgery due to sciatica (laminectomie)	1149.94
Direct nonhealth care costs:	
Help in housekeeping (per hour)	8.30
Indirect costs:	
Absence from paid work (per hour) [&]	34.98

[#]: Price according to Dutch guidelines[121] or according to professional association (2005).

[&]: Because we were only interested in the extent of productivity costs, used was an overall mean income per hour regardless age or gender.

The direct health care costs were: costs of physical therapy, general practitioners care, medication, addition visits to other healthcare providers and hospitalisation. Direct nonhealth care costs were: costs of devices, out of pocket expenses and costs of help in housekeeping. Indirect costs outside the health care system were the costs of production losses caused by absence from work. The costs for paid work were calculated by using the friction cost approach (friction period 154 days) based on the overall mean income of the Dutch population.[121]

Statistical analysis
The statistical analysis was performed according to the intention-to-treat principle, analysing all patients in the treatment group to which they were randomly allocated. Missing (item) values were assigned the last available score.

Differences in resource utilization between the two arms were assessed. Costs were calculated by multiplication of each unit of resource use by its unit price. A comparison in resource use between the arms will provide insight in major cost drivers. Dealing with the nonnormality of the cost data a nonparametric test (Mann-Whitney/Wilcoxon) can be used.[122] The Incremental Cost Effectiveness Ratio (ICER) on total costs and direct costs only between both study arms was constructed. Confidence intervals for the ICER were calculated using Fieller's method[123] (parametric approach) and using bootstrapping (nonparametric approach) and graphically presented on the cost effectiveness plane. Furthermore, a cost effectiveness acceptability curve was constructed.[124] The acceptability curve shows the probability that a treatment is cost effective at a specific ceiling ratio.[122] No sensitivity analysis was undertaken, as most variations in cost or health effect were included in the bootstrap estimates of the ICER.

Results

Included and randomised were 135 patients, 67 patients received GP care plus physical therapy (the intervention group), and 68 patients received GP care only (the control group). Figure 1 shows the flow chart of the trial.

Four patients dropped-out immediately after randomisation because they no longer wished to participate, 1 in the intervention group and 3 in the control group. At 1 year follow-up 117 patients (87%) completed their questionnaire, which included the cost data. Table 3 shows the baseline characteristics of the randomised patients.

Figure 1: Flow chart of the trial.
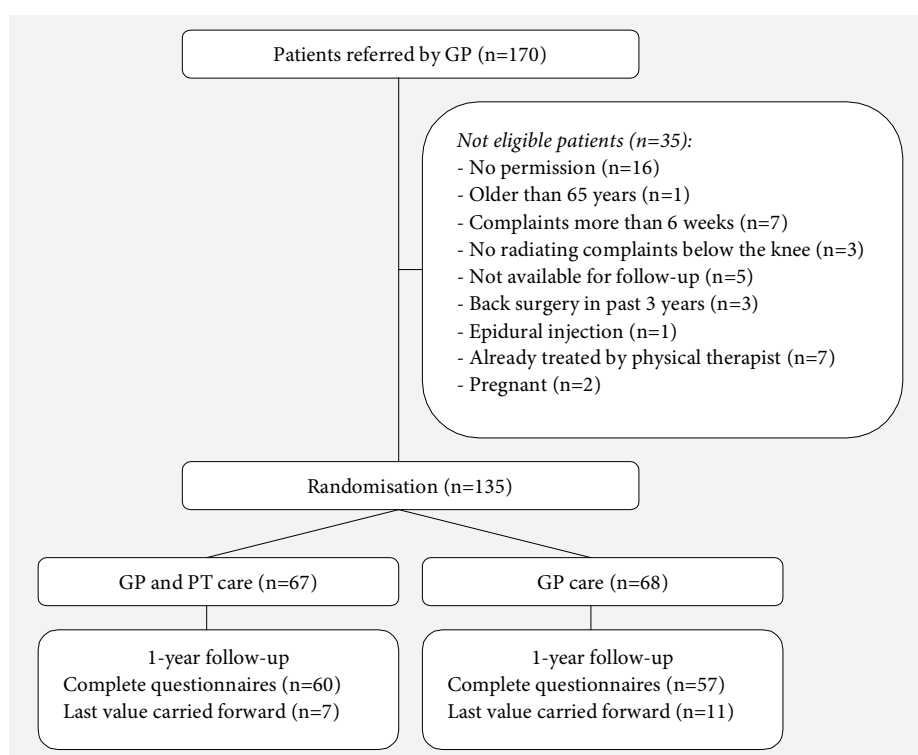
The two groups were considered similar for all measured baseline characteristics. Therefore, presented are only the unadjusted differences between the intervention and control group.[118]

Table 3: Baseline characteristics of the 135 patients randomised in two treatment groups.

Characteristics	GP + PT care (n=67)	GP care only (n=68)
Female gender (n, %)	38 (57)	27 (40)
Age in years (mean, SD):	42 (10)	43 (12)
Paid job (n, %)	48 (72)	50 (74)
Reporting sickness absence (n, %)	34 (51)	32 (47)
Sickness absence from onset in days (mean, SD) $	3.1 (4.9)	4.2 (6.8)
Time between onset LRS and baseline in days (mean, SD)	12.1 (10.1)	14.2 (10.2)
Never LRS in past (n, %)	49 (73)	54 (79)
Taking medication for LRS(n, %)	58 (87)	48 (71)
EQ-5D index score (mean, SD)	0.39 (0.35)	0.41 (0.35)

$: Before randomisation.

Health effect of additional physical therapy
After 1 year, there was a significant and a clinically relevant difference between the groups, on primary outcome (GPE) in favor of the intervention group.[118] Table 4 shows that in the intervention group 53 of 67 patients (79%) and 38 of 68 patients (56%) in the control group reported to be 'improved' (RR, 1.4; 95% CI: 1.1; 1.8).

Table 4: Data on GPE and utility at 3, 6, 12 and 52 weeks follow-up.

	Baseline	*3 weeks*	*6 weeks*	*12 weeks*	*52 weeks*
GP + PT care (n=67)					
Perceived effect [*]: Improved (%)	--	n=30 (45)	n=38 (60)	n=47 (70)	n=53 (79)
Utility [&], mean (SD)	0.39 (0.35)	--	0.59 (0.34)[+]	0.65 (0.33)	0.76 (0.25)
GP care only (n=68)					
Perceived effect [*]: Improved (%)	--	n=22 (32)	n=30 (44)	n=42 (62)	n=38 (56)
Utility [&], mean (SD)	0.41 (0.35)	--	0.70 (0.26)[+]	0.73 (0.30)	0.73 (0.27)

[*]: Ratings on patient's globally perceived effect on a 7-point scale were dichotomised (see Methods section).

[&]: Utility measured with Euroqol: EQ-5D index score; not measured at 3 weeks follow-up.

[+]: Statistically significant difference in favor of GP care only group (P = 0.049)

At baseline and at 6 and 12 weeks follow-up, the mean of the utility was higher in the control group and at 6 weeks follow-up statistically significant different, in favor of the control group (Table 4). At 1-year follow-up, the utility in the intervention group was higher. Figure 2 shows the mean utility for the intervention and control group at baseline and at 6, 12 and 52 weeks follow-up.

Figure 2: Mean utility at baseline and at 6, 12 and 52 weeks follow-up.

Utility (mean)
Weeks follow-up
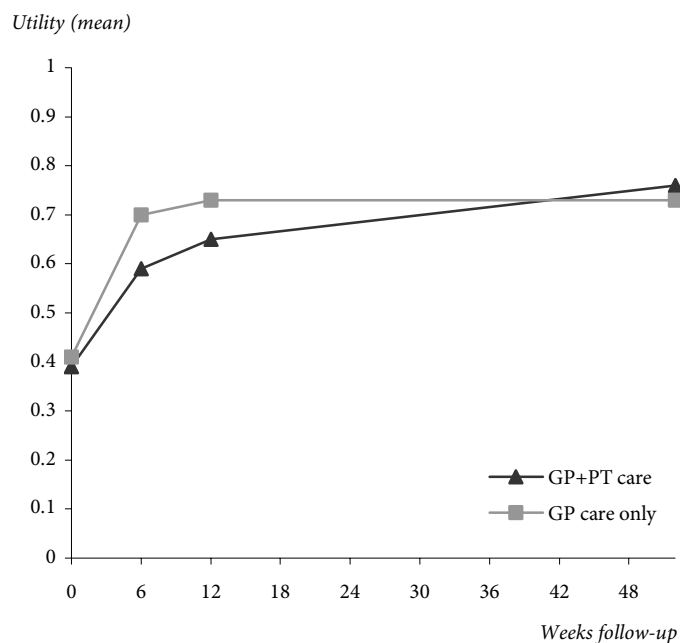
Calculating QALYs for the groups, showed more QALYs for the control group (mean 0.70, SD 0.25) than the intervention group (mean 0.67, SD 0.26), but this was no statistically significant difference.

Healthcare utilisation and absence from work
During the 1-year follow-up 11 patients (16%) in the intervention group and 6 patients (9%) in the control group visited a neurologist. In the intervention group 4 patients (6%) visited a neurosurgeon, 1 patient (2%) an orthopedic surgeon, and 4 patients (6%) received surgery due to LRS. In the control group 5 patients (7%) visited a neurosurgeon, 2 patients (3%) an orthopedic surgeon, and 3 patients (4%) received surgery. At 1-year follow-up, 30 patients (45%) in the intervention group reported a mean of 29.2 days (SD 48.4) absence from work and 25 patients (37%) in the control group reported a mean of 28.9 days (SD 72.3). These were not statistically significant differences.

Costs
Table 5 shows the direct and indirect costs from the intervention and control group at 1-year follow-up. The total direct and indirect costs consisted mainly of production losses. At 3, 6, 12 and 52 weeks follow-up there were significant differences between groups on costs for physical therapy visits, in favor of the control group. The total direct and indirect costs were also statistically significant different at the 4 follow-up moments, in favor of the control group.

Economic evaluation
Because the additional PT resulted in a statistically significant higher proportion of patient recovered a cost effectiveness analysis with GPE, the primary outcome measure, was performed. The cost effectiveness analysis was conducted twice, one time taking only the direct costs into account and one time using total costs, i.e. including direct and productivity costs.

Table 5:Cumulative mean direct and indirect costs per patient in euro (€) at 3, 6, 12 and 52 weeks follow-up.

	3 weeks	*6 weeks*	*12 weeks*	*52 weeks*
GP + PT care (n=67)				
Direct costs				
General practitioner	13.6 (18.1)	23.2 (30.5)	33.2 (28.3)	36.2 (37.3)
Physical therapy	87.3 (52.2)[+]	139.6 (77.6)[+]	191.8 (125.2)[+]	241.4 (328.4)[+]
Manual therapy	2.7 (15.7)	3.5 (20.1)	10.8 (57.4)	35.2 (128.8)
Cesar or Mensendieck therapy	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	14.1 (83.8)
Neurologist in hospital	4.2 (14.8)	6.7 (26.7)	9.2 (26.9)	26.7 (77.0)
Neurosurgeon in hospital	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	7.5 (32.2)
Orthopedic surgeon in hospital	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	1.7 (13.7)
Hospitalisation	5.0 (41.2)	5.0 (41.2)	5.0 (41.2)	135.8 (531.4)
Surgery due to sciatica	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	68.7 (274.5)
Medication for sciatica	13.3 (13.2)	31.0 (30.1)	50.7 (50.9)	74.9 (73.7)
Nonhealth care	4.1 (17.1)	5.3 (20.8)	8.5 (39.3)	12.3 (51.7)
Total direct costs	**127.5 (90.7)**[+]	**210.7 (132.2)**[+]	**293.3 (165.9)**[+]	**619.3 (899.3)**[+]
Indirect costs				
Production losses	1281.4 (1590.9)	2127.1 (2577.2)	3245.9 (4252.5)	5629.6 (9048.9)
Total direct and indirect costs	**1408.9 (1616.8)**[+]	**2337.8 (2616.9)**[+]	**3539.2 (4320.8)**[+]	**6248.9 (9602.5)**[+]

	3 weeks	6 weeks	12 weeks	52 weeks
GP care only (n=68)				
Direct costs				
General practitioner	25.0 (22.6)	33.9 (36.3)	38.9 (43.2)	44.6 (54.1)
Physical therapy	9.4 (28.4) [+]	18.1 (45.4) [+]	30.8 (80.1) [+]	76.9 (187.6) [+]
Manual therapy	1.9 (11.2)	1.5 (8.8)	12.2 (85.5)	10.7 (47.0)
Cesar or Mensendieck therapy	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	12.5 (65.8)
Neurologist in hospital	2.5 (11.6)	5.8 (19.7)	5.8 (21.9)	13.2 (44.5)
Neurosurgeon in hospital	0.0 (0.0)	0.8 (6.8)	3.3 (21.4)	3.3 (13.3)
Orthopedic surgeon in hospital	0.0 (0.0)	0.0 (0.0)	1.6 (9.5)	2.5 (15.1)
Hospitalisation	0.0 (0.0)	54.5 (410.1)	74.3 (454.2)	148.7 (718.7)
Surgery due to sciatica	0.0 (0.0)	0.0 (0.0)	16.9 (139.5)	50.7 (237.9))
Medication for sciatica	11.4 (16.2)	24.9 (34.0)	40.9 (54.1)	62.0 (81.2)
Nonhealth care	5.3 (16.8)	5.5 (19.4)	7.2 (29.9)	10.7 (55.6)
Total direct costs	**53.4 (45.4)** [+]	**143.5 (435.4)** [+]	**219.7 (616.8)** [+]	**425.1 (1043.3)** [+]
Indirect costs				
Production losses	1196.4 (1756.4)	1728.4 (2696.8)	2613.2 (4826.1)	4379.8 (9060.1)
Total direct and indirect costs	**1249.8 (1772.8)** [+]	**1871.9 (2846.5)** [+]	**2832.9 (5179.8)** [+]	**4804.9 (9803.2)** [+]

All costs presented in in means and standard deviation,

[+]: Statistically significant difference in favor of GP care only group (Mann-whitney test; P < 0.05)

In table 6, point estimates for the ICERs are shown. The health effect was expressed in patient improved (GPE) gained. Confidence intervals for the ICER were calculated using Fieller's method.[123]

Table 6: ICER and 95% confidence interval (parametric approach).

	ICER	95% confidence interval (Fieller method)
Additional costs (€) per patient improved gained (direct costs)	837	-732; 3186
Additional costs (€) per patient improved gained (total costs)	6224	-10419; 27551

The ICER for the direct costs only was € 837 per improved patient gained. This means that for every extra patient in the intervention group that reported to be 'improved' the extra direct costs were € 837. The ICER for the total costs was € 6224 per patient improved gained.

In the statistical analysis, besides the calculation of parametric confidence intervals, a bootstrap procedure was performed. In such procedure, a random sample with replacement is taken from the original sample of patients, for both groups, with a size equal to the original sample size. For such bootstrap sample, again additional costs and effects and the ICER may be calculated. By repeating this procedure many times (here 2,500), the uncertainty around the ICER can be assessed. For instance, each pair of additional costs and additional effects, can be displayed in a scatter diagram (Figure 3). The ICER and 95% confidence interval estimated with the bootstrap procedure were similar to the results of the parametric approach presented in table 6.

Figure 3: Scatter diagram of bootstrapped additional direct costs and effects.
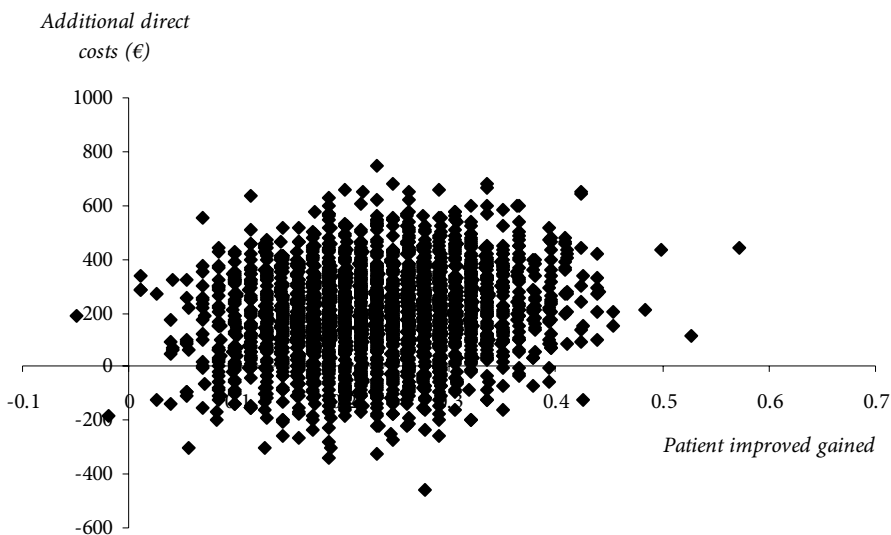
With the outcomes of the bootstrap procedure, a so-called cost effectiveness acceptability curve was constructed (Figure 4).

Figure 4: Acceptability curve presenting, for each possible threshold on the ICER, the probability that the ICER is acceptable.
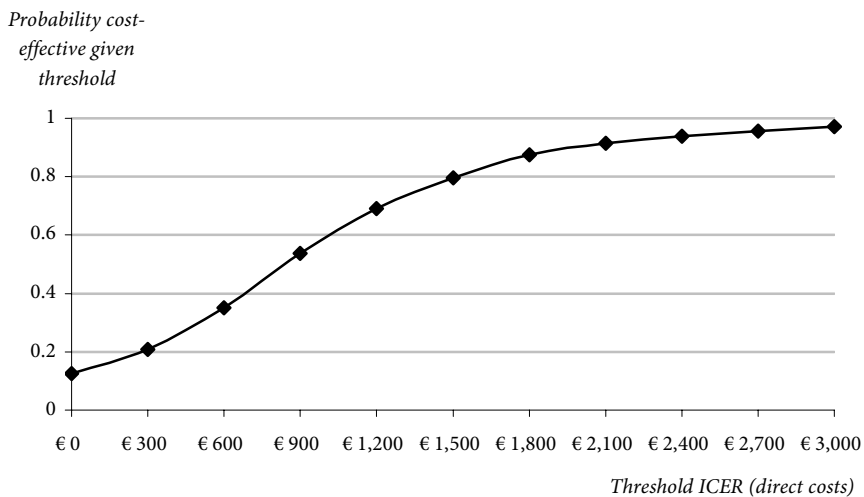
This curve shows for every threshold value society may define for the ICER, the probability that the ICER is below that limit. When we assume a threshold of € 600 direct costs per patient improved gained as acceptable, the ICER is acceptable with 35% certainty.
When we assume a threshold of € 1200 per patient improved gained as acceptable, the ICER is acceptable with 69% certainty.

In case total costs are used, we have to assume a threshold of € 4000 and € 12000 respectively per patient improved gained as acceptable, to consider the ICER acceptable with 37% and 68% certainty (C/E-acceptability curve using total costs not shown).
We refrained from cost utility analysis because there was no effect on quality of life between the two groups together with higher costs for the intervention group.

Discussion

An economic evaluation was performed alongside a randomised clinical trial identifying the most efficient intervention for patients with LRS in primary care. Physical therapy added to general practitioners' care resulted in more perceived recovery than the general practitioners' care alone. However, the direct and indirect costs for the intervention group were higher than in the control group. If decision makers value additional perceived recovery at much less than € 6244, general practitioners care alone is probably the best strategy. If their valuation lies between € 6244 and € 12000, physical therapy added to general practitioners care is likely to be the best treatment for patients with LRS. Overall, this study showed that physical therapy provided no cost effective addition to care in general practice, for patients with LRS

The total costs were dominated by productivity losses; the direct costs by the costs of physical therapy. This means that treating patients with physical therapy, as expected, resulted in more utilisation of physical therapy. But, could also mean that physical therapy as treatment affected absence from work and therefore productivity costs. In spite of this, an active treatment approach by physical therapists resulted in more perceived recovery in patients with LRS than general practitioners' care alone.[118]

In terms of QALYs gained the additional physical therapy showed no health effect. To calculate QALYs patients were asked to complete EQ-5D at baseline and 6, 12 and 52 weeks follow-up. EQ-5D is a generic preference-based measure of health. The results of our study suggest that this instrument is not sensitive enough to capture the health effects of the additional physical therapy. Therefore, the cost effectiveness of additional physical therapy was assessed using GPE as the health outcome measure.

Waiting times are expected to influence costs, health effects and cost-effectiveness of health care.[125] In our study the waiting time for health care utilisation was unknown. The economic evaluation performed, ignored waiting time for health care utilisation and this might have biased the cost-effectiveness results. Moreover, it is very reasonable that this waiting time affected absence from work and therefore productivity costs. In future studies there should be paid more attention to analysing the impact of waiting time on absence from work and costs effects.

The measurements of the direct and indirect costs were cumulative at the follow-up moments. Therefore, recall bias in patients could have occurred because we asked for the direct and indirect costs from baseline to the follow-up moment. It is more precise and uniform to measure costs according methods described in the handbook for cost studies from Oostenbrink et al.[121]
Nevertheless, the patients were randomised in two groups, therefore, we suggest that the between group conclusion about cost effectiveness was not affected very much.

As far as known, no full economic evaluation alongside a randomised clinical trial that involved patients with LRS treated by physical therapy has yet been published. Our economic evaluation showed ICERs of € 837 (direct costs) and € 6224 (total costs) per improved patient gained. Therefore, in the treatment of patients with LRS, physical therapy added to general practitioners' care is not more cost-effective than general practitioners' care alone, but significant more patients reported perceived recovery.

General discussion

Providers of health care are constantly aiming to provide their patients with the best possible treatment. Currently, the most efficient tools available for healthcare givers are clinical guidelines. These guidelines generally recommend diagnosis and treatment options that are, as much as possible, based on the available scientific (published) evidence within a certain time frame. When patients are treated according to such guidelines, this is called evidence-based practice.

The research described in this thesis focused on the conservative treatment of patients with the lumbrosacral radicular syndrome (LRS). As reported in the General Introduction many (para)medical professions are involved in the conservative treatment of LRS, for which there are currently two guidelines available in the Netherlands. One guideline for LRS (issued in 1995 by the Dutch Institute of Quality Health Care) contains consensus recommendations established by 12 (para)medical specialties (Chapter 3). Only one healthcare profession, the general practitioners (GPs), has its 'own' guideline for LRS (issued in 1996 and updated in 2005).

As reported in Chapter 1, GPs followed their clinical guideline for patients with LRS to a great extent with regard to history taking, physical examination, diagnosing and treatment(s). When they did deviate from the recommendations of the guideline, this was because of evidence-based knowledge that had recently become available. It is indeed possible that new evidence becomes available during the time period in which guidelines are updated. Currently, with ever-faster computers and Internet connections, access to the scientific literature has increased enormously. Therefore, caregivers can rapidly implement the latest evidence into their daily practice, which at that time may outdate the guideline. For example, in the GP guideline of LRS issued in 1996, bed rest is a treatment option. In 1999 to 2000 data were published showing a lack of efficacy regarding bed rest in the treatment of patients with LRS.[17,46] As reported in Chapter 1, GPs already implemented this knowledge (i.e. no prescription of bed rest) in their daily practice before the guideline was updated.

The GP guideline of 1996[11] also stated that physical therapy was not a treatment option because the efficacy had not been demonstrated. In spite of this, GPs referred 49% of their patients with LRS to physical therapy (Chapter 1). In the updated GP guideline (2005)[5] physical therapy is recommended for those patients with LRS who need a more active approach than a GP can offer. Therefore, it is very important to frequently update the LRS guidelines, especially if new evidence may lead to changes in the recommendations.[21]

Neurosurgeons in the Netherlands do not have their 'own' guideline for LRS. In the Netherlands we estimate - that since 1988 - about 10,000 patients undergo surgery each year due to LRS.[23] In this respect, it should be noted that the surgical rate in the Netherlands is relatively high compared to other western countries.[24] Six times as many lumbar discectomies are performed compared to Scotland, 4 times the number in England, and 2 times the number performed in Sweden. Only in the USA were more operations performed for LRS than in the Netherlands.

The findings in this thesis (Chapters 2 and 3) show that neurosurgeons subscribed to and followed the recommendations as stated in the multidisciplinary LRS guideline (1996).[2] Despite this, there are no indications that the surgical rate has changed over the years since 1996. This could mean that the (high) surgical rate reflected and still reflects good clinical practice.[126]

In Chapter 4 we reported the 19-month follow-up data of patients with LRS who had undergone surgery. It appeared that 63% of these patients still reported LRS complaints after a 19-month period. The (cost) effectiveness of surgery in patients with LRS has not yet been established. There is one prospective low-quality study included in the systematic review (Chapter 5) that evaluated surgery compared with a conservative treatment.[25] From the systematic review (Chapter 5) we concluded that there is only limited evidence that surgery is more effective for patients with LRS regarding improvement compared to physical therapy at 1-year follow-up.[25] At 4 and 10-years follow-up no difference regarding overall improvement between surgery and physical therapy has been found.[25]

In Chapter 4 we report that the median time between the first visit to the neurosurgeon and surgery was 6 weeks (IQR 9). Although there is consensus that surgery should be offered in case of persistent pain, the timing of surgery seems to depend on local production capacity and on the preferences of the patients and neurosurgeons rather than on evidence-based practice. This lack of evidence for the timing of surgery after the 6 to 8 weeks conservative treatment period could explain the large variations in daily practice. The results of an ongoing high-quality study of Peul et al.[126] evaluating the (cost) effectiveness and timing of surgery in patients with LRS will contribute data to counteract this lack of evidence.

To gain insight into the available evidence on the effectiveness of conservative treatment regarding LRS, we performed a systematic review of the literature (Chapter 5). We used the methods as recommended by the Cochrane Collaboration Back Review Group[47] for transparency and comparability with other systematic reviews in this field. Only randomised clinical trials were included, because these provide the best evidence on the effectiveness of interventions. The 30 publications included in the review were, however, very heterogeneous, especially with respect to the duration of the LRS, (control) treatment(s), length of follow-up, and outcome measures. Therefore, a qualitative analysis was performed, using the five levels of evidence rather than a quantitative meta-analysis.[47]

Strikingly, almost all of the studies in this review reported no differences in outcomes between the intervention and control group. So, as a consequence, we do not recommend clinicians to use corticosteroid injections or traction therapy in the treatment of patients with LRS, as in several trials no clear evidence of a positive effect could be found. Whether clinicians should prescribe physical therapy, bed rest, manipulation or medication could not be concluded from this review. In the updated GP guideline of LRS[5] (2005) the recommendations regarding conservative treatment are in concordance with the results of our systematic review.

Whilst conducting the review the question arose as to how many trials are required or, in other words, how strong does the evidence need to be, to allow the conclusion that a treatment is not effective or should not be recommended as a treatment option. For example, regarding injection therapy, 14 trials were included of which 4 trials (1 high and 3 low-quality studies) reported significant differences between groups whereas 10 trials (6 high and 4 low-quality studies) did not.

Based on these findings we decided not to recommend injection therapy as a treatment option for patients with LRS. However, there is no consensus, in general, on how to weigh this evidence.

Recently, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) working group developed a new system for rating evidence; this system is simple to use and applicable to a wide variety of recommendations spanning the full spectrum of medical specialties and clinical care.[127]

Applying the GRADE classification to the injection therapy in LRS, we should conclude that there is a high degree of evidence that further research is most unlikely to change the estimated effect. Therefore, our conclusions regarding injection therapy are in line with the rating system of the GRADE working group.

A pragmatic randomised clinical trial in primary care was performed to assess the effectiveness of physical therapy in addition to GP care, in patients with acute LRS (Chapter 7). It was concluded that physical therapy is more effective in the treatment of patients with acute LRS than GP care alone.

In this trial the sample size of 135 randomised patients was somewhat lower than the 182 patients that were aimed for. In spite of this, the results show a clinically relevant difference of 23% in primary outcome between groups in favour of the physical therapy group at 12 months follow-up. The dropout rate and loss to follow-up at follow-up measurements were generally acceptable. In the literature no clear prognostic factors have been reported that influence the response to physical therapy or GPs' care. Thus, no arguments were found to exclude particular subtypes of LRS, to pre-stratify on particular baseline characteristics, or to make the study population more homogeneous.

In this pragmatic trial, it was impossible to perform blinding on patient and on caregiver level. This may have produced some bias, because knowledge of the type of treatment received may influence the response to that treatment. It was assumed hat GPs followed their clinical LRS guideline[11], and that physical therapists gave exercise therapy as well as information and advice about LRS.

The intention-to-treat analysis showed that at 12-months follow-up there was a significant health effect in the primary outcome (i.e. patients' global perceived effect) in favour of the physical therapy group. However, at 3, 6 and 12 weeks follow-up there were no significant differences between the groups either in primary outcome or in secondary outcomes. We can only hypothesize why a significant health effect was only found after 12-months follow-up. One reason could be that patients with LRS, who do not have a favourable natural course in the first 3 to 6 months, benefit significantly on the long term from the physical therapy received in a relatively early stage. This could be due to better coping strategies with the LRS complaints learned through physical therapy. Another reason could be that we did not have enough 'power' in the trial to reach statistically significant differences, because we aimed to enrol 182 patients (Chapter 6) but finally randomised only 135 patients. On the other hand, the subgroup analysis in patients with severe disability at baseline indicated a significant difference in perceived recovery at 3 and 12 months follow-up in favour of the physical therapy group.

The economic evaluation in Chapter 8 showed that the physical therapy provided may not be a cost-effective addition to care in general practice, for patients with LRS. The higher costs in the physical therapy group were mainly due to the direct costs of the physical therapy sessions.

It appeared that more absenteeism from work was an adverse event of the intervention group, although this difference was not significant compared with the control group. The policymakers should decide how to value the additional perceived recovery achieved with physical therapy. If they value the additional perceived recovery at much less than € 6,244, then the GPs' care alone is probably the best strategy. If their valuation lies between € 6,244 and € 12,000, then the physical therapy in addition to the GPs' care is likely to be the best treatment for patients with LRS.

Overall it can be concluded that, regarding the GP guideline for LRS[5], our research results contribute to the scientific evidence for the underlying recommendation that patients with LRS could be referred to physical therapy with an active treatment program, particularly for those patients suffering severe disability at presentation. This could be included in the next update of the GP guideline. The perceived extra recovery has its price, as we calculated in the cost-effectiveness analyses. Policymakers need to decide whether or not these extra costs are acceptable. Furthermore, it is advised that more professions dealing with LRS patients should develop their own clinical guidelines, especially the physical therapists and neurosurgeons, in order to perform transparent, evidence-based practice.

Suggestions for future research regarding LRS

Guidelines
The research conducted in this thesis mainly concerned the GPs' and neurosurgeons' management of patients with LRS. To obtain a full picture of adherence to LRS guidelines, future studies should also involve physical therapists, neurologists, orthopedic surgeons and rehabilitation physicians.

Physical therapy
It would be interesting to conduct a follow-up lasting two years or more of the patients randomised in the trial described in Chapter 7, to establish whether the delayed effect in perceived recovery in the physical therapy group persists over time.

Neurosurgeons
Chapter 4 describes the mid-long-term outcomes after surgery in patients with LRS. A substantial part of the patients reported LRS-related complaints at 19 months after surgery. More research about the (cost) effectiveness of surgery due to LRS and the timing of surgery is required.

Additional research
There is conflicting evidence as to whether corticosteroid injection could play a role in short-term pain relief. Also the (long-term) effects of traction, bed rest, manipulation and medication are largely unknown. For these topics we recommend high-quality randomised clinical trials of sufficient sample size with long-term follow-up (up to two years or more). The outcome measures should include overall improvement, patients' satisfaction, severity of pain in the leg, functional health status, quality of life status, return to work, and adverse reactions.

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Summary

The lumbosacral radicular syndrome causes pain in the leg and disability, often resulting in utilisation of healthcare resources and absenteeism from work. In general practice this syndrome is the most frequently seen specific low-back disorder. The aim of the research described in this thesis was to establish general practitioners' and neurosurgeons' current management of patients with a lumbosacral radicular syndrome compared with their guidelines, and to assess the (cost) effectiveness of physical therapy in addition to the general practitioners' care, in patients with an acute lumbosacral radicular syndrome.

Chapter 1 reports a survey that investigated the current treatment policy of general practitioners in patients with a lumbosacral radicular syndrome compared with their clinical guideline. Sixty-three general practitioners completed questionnaires about their treatment policy in individual patients with a lumbosacral radicular syndrome at baseline and at 6-months follow-up. Simultaneously, 136 patients of these general practitioners were interviewed at baseline, and at 3 and 6-months follow-up. Of the 12 recommendations in the guideline related to history taking, four were not adhered to by the general practitioners in about 25% of the patients. Of the 10 recommended physical examinations, three were not frequently carried out by the general practitioners. Almost 40% of the patients were referred to physiotherapy and 27% received muscle relaxants. It was concluded that the majority of the general practitioners support the content of the lumbosacral radicular syndrome guideline. Overall, there was a good adherence with the guideline for history taking and physical examination, and a moderate adherence for treatment policy.

Chapter 2 presents a survey of the opinion of neurosurgeons on the multidisciplinary clinical guideline 'lumbosacral radicular syndrome'. The aim was to describe to what extent neurosurgeons in the Netherlands endorse the content of this guideline. The guideline was issued in 1996 by the Netherlands Institute of Quality Health Care and this is the first attempt to evaluate the implementation of this guideline. All active neurosurgeons in the Netherlands (n=92) were invited to complete a questionnaire investigating to what extent they agree with the 26 recommendations in the guideline 'lumbosacral radicular syndrome'. Overall, 75% of the neurosurgeons responded and, of these, 94% agreed (at least partially) with the content of the guideline. Of the 26 recommendations in the guideline, seven were not fully endorsed by the neurosurgeons. This survey showed that almost all neurosurgeons subscribed (at least partially) to the multidisciplinary lumbosacral radicular syndrome guideline. Therefore, one important aspect of the implementation process has been fulfilled, i.e. acceptance of the content of the guideline.

In **Chapter 3** we present a survey that established to what extent neurosurgeons subscribe to the lumbosacral radicular syndrome guideline, and also evaluated their current management of patients with a lumbosacral radicular syndrome against this guideline. All active neurosurgeons in the Netherlands (n=92) were mailed a questionnaire about the guideline and data from 66 responders were analysed. Patients were recruited via seven of the participating neurosurgeons and were interviewed once by telephone. The medical records of the participating patients (n=163) were also examined.
Of the 26 propositions in the lumbosacral radicular syndrome guideline, seven are not fully endorsed by the neurosurgeons.

Three of these seven propositions may need updating based on 'new evidence'. The time between the onset of the lumbosacral radicular syndrome episode and the actual moment of surgery was considerably longer than that recommended in the guideline. It was concluded that, based on their current management of patients with a lumbosacral radicular syndrome, the neurosurgeons largely adhere with the guideline.

In **Chapter 4** we determined the mid-long-term outcomes after surgery in patients with a lumbosacral radicular syndrome and identified prognostic factors for persisting lumbosacral radicular syndrome symptoms. A total of 250 consecutive patients operated on by seven neurosurgeons in four hospitals between May and December 2001 were selected from medical records. They were asked to take part in a telephone questionnaire at 6 and 19 months after operation. All patients had undergone discectomy for lumbosacral radicular syndrome at L4-L4 or L5-S1 and were aged from 18 to 65 years. Of the 250 patients, 163 participated in the study: 63% reported they still had lumbosacral radicular syndrome related complaints 19 months after surgery. However, severe leg pain had decreased in 83% of the patients. In general the patients were satisfied with their treatment. Female gender and an age of 51-65 years were prognostic factors for persistent LRS symptoms. It was concluded that more than half of the patients reported lumbosacral radicular syndrome related complaints 19 months after surgery.

Chapter 5 presents a systematic review that assessed the effectiveness of conservative treatments of the lumbosacral radicular syndrome. A search was made in relevant electronic databases and in the reference lists of articles up to May 2004. Included were randomised clinical trials of all types of conservative treatments for patients with the lumbosacral radicular syndrome selected by two reviewers. Two other reviewers independently assessed the methodological quality and the clinical relevance. Because the trials were considered heterogeneous we decided not to perform a meta-analysis but to summarise the results using the rating system of levels of evidence. Thirty trials were included that evaluated injections, traction, physical therapy, bed rest, manipulation, medication, and acupuncture as a treatment for the lumbosacral radicular syndrome. It was concluded not to recommend corticosteroid injections and traction as a treatment option because several trials indicated no evidence of an effect. Whether clinicians should prescribe physical therapy, bed rest, manipulation or medication could not be concluded from this review. At present there is no evidence that one type of treatment is clearly superior to others (including no treatment) for patients with a lumbosacral radicular syndrome.

Chapter 6 presents the design of a randomised clinical trial that investigated the effectiveness of physical therapy in addition to the general practitioners' care, compared to the general practitioners' care alone in patients with an acute lumbosacral radicular syndrome. Patients in general practice diagnosed with an acute (less than 6 weeks) lumbosacral radicular syndrome and an age above 18 years are eligible for participation. The general practitioners' treatment follows their clinical guideline. The physical therapy treatment consists of patient education and exercise therapy. The primary outcome measure is the patient's self-reported global perceived effect. Secondary outcome measures are severity of complaints, functional status, health status, fear of movement, medical consumption, sickness absence, costs and treatment preference. The follow-up is 52 weeks. Treatment by general practitioners and physical therapists in this study will be transparent and not a complete "black box".

The results of this trial will contribute to the decision of the general practitioner regarding referral to physical therapy in patients with an acute lumbosacral radicular syndrome.

Chapter 7 describes the results of the randomised clinical trial that aimed to assess the effectiveness of physical therapy in addition to the general practitioners' care compared to the general practitioners' care alone, in patients with an acute lumbosacral radicular syndrome. A total of 135 patients with an acute lumbosacral radicular syndrome (recruited from May 2003 to November 2004) were randomised in two groups: 1) the intervention group received physical therapy added to the general practitioners' care, and 2) the control group with general practitioners' care only. The outcomes were measured at 3, 6, 12 and 52 weeks after randomisation. At 3-months follow-up, 70% of the intervention group and 62% of the control group reported improvement (RR 1.1; 95% CI 0.9; 1.5). At 12-months follow-up, 79% of the intervention group and 56% of the control group reported improvement (RR 1.4; 95% CI 1.1; 1.8). No significant differences in secondary outcomes were found at short-term or long-term follow-up. In conclusion, at 12-months follow-up, evidence was found that physical therapy in addition to the general practitioners' care is more effective in the treatment of patients with acute lumbosacral radicular syndrome than the general practitioners' care alone. There are indications that physical therapy is particularly effective in patients reporting severe disability at presentation.

In **Chapter 8** we performed an economic evaluation alongside the randomised clinical trial, described in Chapter 7, and evaluated the cost-effectiveness of physical therapy and general practitioners' care for patients with an acute lumbosacral radicular syndrome. The direct and indirect costs were measured by means of questionnaires in a 1-year follow-up period. The Incremental Cost Effectiveness Ratio (ICER) between both study arms was constructed. Confidence intervals for the ICER were calculated using Fieller's method and using bootstrapping. There was a significant difference on perceived recovery at 1-year follow-up in favour of the physical therapy group. The additional physical therapy did not have an incremental effect on quality of life. At 1-year follow-up, the ICER for the total costs was € 6224 (95% CI: -10419; 27551) per improved patient gained. For direct costs only, the ICER was € 837 (95% CI: -731; 3186). It is concluded that physical therapy did result in a higher level of perceived recovery, but provided no cost effective addition to care in general practice for patients with a lumbosacral radicular syndrome.

Samenvatting

Het lumbosacraal radiculair syndroom kenmerkt zich door pijn in het been en belemmeringen in het functioneren, hetgeen vaak resulteert in een hulpvraag binnen de gezondheidszorg en ziekteverzuim op het werk. Binnen de huisartspraktijk is dit syndroom de meest voorkomende oorzaak van specifieke lage rugpijn. Het doel van het onderzoek beschreven in dit proefschrift was het vaststellen in welke mate huisartsen en neurochirurgen de patiënten met een lumbosacraal radiculair syndroom behandelen in vergelijking met hun richtlijnen, en het vaststellen van de (kosten)effectiviteit van fysiotherapie toegevoegd aan de huisartsbehandeling bij patiënten met een acuut lumbosacraal radiculair syndroom.

Het onderzoek beschreven in **hoofdstuk 1** beschrijft in welke mate huisartsen de patiënten met een lumbosacraal radiculair syndroom behandelden in vergelijking met hun richtlijn. Op baseline en na 6 maanden follow-up vulden 63 huisartsen vragenlijsten in over de ingestelde behandeling bij in totaal 136 individuele patiënten met een lumbosacraal radiculair syndroom. Tegelijkertijd werden deze 136 patiënten telefonisch geïnterviewd op baseline, en op 3 en 6 maanden follow-up. Van de 12 aanbevelingen in de richtlijn betreffende de anamnese, werden er vier niet opgevolgd door de huisartsen bij 25% van hun patiënten. Van de 10 aanbevelingen betreffende het lichamelijk onderzoek, werden er drie niet frequent uitgevoerd door de huisartsen. Bijna 40% van de patiënten werd naar de fysiotherapie verwezen en aan 27% werd spierverslappende medicatie voorgeschreven. De conclusie was dat huisartsen de richtlijn goed opvolgen ten aanzien van het afnemen van de anamnese en het uitvoeren van het lichamelijk onderzoek, en dat ze deze redelijk opvolgen wat betreft de ingestelde behandeling.

In **hoofdstuk 2** wordt beschreven in welke mate de neurochirurgen in Nederland de inhoud van de multidisciplinaire richtlijn 'lumbosacraal radiculair syndroom' onderschrijven. Deze richtlijn was samengesteld en gepubliceerd in 1996 door het Kwaliteitsinstituut voor de Gezondheidszorg CBO (Centraal BegeleidingsOrgaan). Alle in Nederland actieve neurochirurgen (n=92) werden uitgenodigd mee te werken aan dit onderzoek en een vragenlijst in te vullen over de 26 aanbevelingen uit deze multidisciplinaire richtlijn. 75% van de neurochirurgen reageerde en hiervan was 94% het (geheel of gedeeltelijk) eens met de inhoud van de richtlijn. Zeven van de 26 aanbevelingen uit de richtlijn werden niet (geheel) onderschreven door de neurochirurgen. Het onderzoek toonde aan dat bijna alle neurochirurgen de inhoud van de richtlijn (bijna geheel) onderschrijven. Dit betekent dat er voor de implementatie van die richtlijn aan een belangrijk aspect was voldaan namelijk het accepteren van de inhoud van de richtlijn 'lumbosacraal radiculair syndroom'.

In het onderzoek beschreven in **hoofdstuk 3** werd onderzocht in welke mate neurochirurgen volgens de richtlijn 'lumbosacraal radiculair syndroom' handelen bij patiënten met een lumbosacraal radiculair syndroom. Bij 7 neurochirurgen werden de medische dossiers van 163 patiënten die waren geopereerd vanwege een lumbosacraal radiculair syndroom nader onderzocht. Met name de tijd tussen het ontstaan van de klachten en het moment van opereren was aanzienlijk groter dan voorgesteld in de richtlijn.

Dit onderzoek toonde aan dat op basis van het handelen bij patiënten met een lumbosacraal radiculair syndroom de neurochirurgen de aanbevelingen in de richtlijn grotendeels opvolgen.

Het doel van het onderzoek beschreven in **hoofdstuk 4** was te inventariseren wat de (middel)lange termijn uitkomsten zijn bij patiënten met een lumbosacraal radiculair syndroom op basis van een discus hernia op niveau L4-L5 of L5-S1 na operatie. Tevens werd nagegaan welke prognostische factoren samenhangen met aanhoudende klachten na een operatie op de (middel)lange termijn. In dit beschrijvend onderzoek werden bij 163 geopereerde patiënten gemiddeld 6 en 19 maanden na operatie telefonische vragenlijsten afgenomen. 63% van de patiënten rapporteerde op (middel)lange termijn nog in meer of mindere mate klachten te hebben gerelateerd aan het lumbosacraal radiculair syndroom. De ernstige beenpijn nam met 83% af en de patiënten waren tevreden over de ontvangen behandeling. Het geslacht (vrouw) en een leeftijd van 51-65 jaar bleken prognostische factoren voor aanhoudende LRS klachten op de (middel)lange termijn. Geconcludeerd werd dat veel patiënten op de (middel)lange termijn nog lumbosacraal radiculair syndroom gerelateerde klachten rapporteerden.

In **hoofdstuk 5** wordt een systematische review beschreven waarin de effectiviteit van conservatieve behandelingen bij het lumbosacraal radiculair syndroom werd onderzocht. Relevante studies werden gezocht in electronische databases en de referenties van publicaties tot mei 2004. Door twee reviewers werden gerandomiseerde klinische trials geïncludeerd met allerlei conservatieve behandelingen bij patiënten met een lumbosacraal radiculair syndroom. Twee reviewers beoordeelde, onafhankelijk van elkaar, de methodologische kwaliteit en de klinische relevantie van deze studies. Er was besloten geen meta-analyse uit te voeren omdat de studies te heterogeen waren. De resultaten van de studies zijn samenvattend weergegeven waarbij gebruik is gemaakt van de 'levels of evidence'. Er werden 30 trials geïncludeerd die injecties, tractie therapie, fysiotherapie, bedrust, manipulatie, medicatie, en acupunctuur onderzochten. Uit de resultaten van de review werd geconcludeerd dat corticosteroïd injecties en/of tractie niet zijn aan te bevelen vanwege het gebrek aan bewijs voor een effect. Of artsen fysiotherapie, bedrust, manipulatie, of medicatie moeten voorschrijven kon niet worden bepaald uit deze review. Op dit moment is er geen bewijs dat één type behandeling superieur is boven de anderen, inclusief géén behandeling, voor patiënten met een lumbosacraal radiculair syndroom.

In **hoofdstuk 6** wordt het 'design' van een gerandomiseerde klinische trial (RCT) beschreven die de effectiviteit onderzoekt van fysiotherapie toegevoegd aan de huisartsbehandeling vergeleken bij de huisartsbehandeling alleen, bij patiënten met een lumbosacraal radiculair syndroom. Patiënten uit de huisartsenpraktijk die zijn gediagnostiseerd met een acuut (minder dan 6 weken) lumbosacraal radiculair syndroom en met een leeftijd van 18 jaar of ouder zijn geschikt voor deelname. De huisartsen dienen voor de behandeling van deze patiënten hun richtlijn aan te houden. De fysiotherapie zal bestaan uit voorlichting over het syndroom en actieve oefentherapie. De primaire uitkomstmaat is het door de patiënt 'ervaren herstel'. Secundaire uitkomstmaten zijn ernst van de (pijn)klachten, functionele belemmeringen, algemene gezondheidstoestand, angst voor bewegen, medische consumptie, kosten en voorkeur voor behandeling. De follow-up is 52 weken.

De behandeling van de huisarts als die van de fysiotherapeut(e) zijn transparant en niet een gehele 'black box'. Het is de bedoeling dat de resultaten van dit onderzoek de huisarts ondersteunen in zijn of haar beslissing om een patiënt met een lumbosacraal radiculair syndroom al dan niet te verwijzen naar fysiotherapie.

Hoofdstuk 7 beschrijft de resultaten van de gerandomiseerde klinische trial die de effectiviteit onderzocht van fysiotherapie toegevoegd aan de huisartsbehandeling vergeleken met de huisartsbehandeling alleen, bij patiënten met een lumbosacraal radiculair syndroom. De 135 gerekruteerde (van mei 2003 tot november 2004) patiënten werden gerandomiseerd in twee groepen: 1) de interventiegroep; die fysiotherapie ontving toegevoegd aan de huisartsbehandeling, en 2) de controle groep; die alleen de huisartsbehandeling ontving. De uitkomstmaten werden gemeten op baseline en op 3, 6, 12, en 52 weken follow-up. Op 12 weken follow-up, rapporteerden 70% van de patiënten in de interventiegroep en 62% van de patiënten in de controle groep herstel (RR 1.1; 95% CI 0.9; 1.5). Op 52 weken follow-up, rapporteerden 79% van de patiënten in de interventiegroep en 56% van de patiënten in de controle groep herstel (RR 1.4; 95% CI 1.1; 1.8). In de secundaire uitkomstmaten werden geen statistisch significante verschillen gemeten op de korte en lange termijn follow-up. De conclusie uit de resultaten was dat op 52 weken follow-up, fysiotherapie toegevoegd aan de huisartsbehandeling effectiever is dan de huisartsbehandeling alleen, bij patiënten met een lumbosacraal radiculair syndroom. Er zijn indicaties dat fysiotherapie vooral effectiever is bij patiënten die ernstige functionele belemmeringen rapporteren bij de presentatie van hun klachten.

Het onderzoek in **hoofdstuk 8** evalueerde de kosteneffectiviteit van fysiotherapie en huisartsbehandeling bij patiënten met een lumbosacral radiculair syndroom. Een economische evaluatie was uitgevoerd tegelijk met de gerandomiseerde trial beschreven in hoofdstuk 7. De directe en indirecte kosten waren gemeten met vragenlijsten gedurende de 52 weken follow-up. De Incremental Cost Effectiveness Ratio (ICER) tussen beide groepen werd geconstrueerd. De betrouwbaarheidsintervallen (CI) voor de ICER waren berekend met de methode van Fieller en middels 'bootstrapping' technieken. Er was een significant verschil op ervaren herstel na 1 jaar follow-up in het voordeel voor de groep die fysiotherapie ontving. De toegevoegde fysiotherapie had geen effect op de 'kwaliteit van leven'. Na 1 jaar follow-up was de ICER voor de totale kosten € 6224 (95% CI: -10419; 27551) per herstelde patiënt. De ICER voor alleen de directe kosten was € 837 (95% CI: -731; 3186). Concluderend, blijkt dat de toevoeging van fysiotherapie aan de huisartsbehandeling meer patiënten die herstel ervaren, maar niet kosteneffectief is, voor patiënten met een lumbosacraal radiculair syndroom.

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Wat mij betreft: laten we ons leven, (gewoon) zoals nu, verder leven.

Over de auteur

Pim Luijsterburg werd geboren op 24 augustus 1971 te Halsteren. Hij behaalde in 1993 z'n diploma Fysiotherapie aan de Hogeschool te Breda. In 1996 het diploma Gezondheidswetenschappen, richting Bewegingswetenschappen aan de Universiteit Maastricht. In 1997 werd hij geregistreerd Epidemioloog A.

Vanaf 1993 is hij regelmatig als fysiotherapeut werkzaam in de fysiotherapiepraktijk van zijn vader. Van 1997-2000 deed hij onderzoek naar arbeidsomstandigheden van metselaars en oppermannen in opdracht van TNO Arbeid te Hoofddorp. Van 2001-2006 verrichtte hij een promotieonderzoek naar het lumbosacraal radiculair syndroom bij de afdeling Huisartsgeneeskunde van het Erasmus Medisch Centrum te Rotterdam.

Pim is getrouwd met Birgitta Gorree, en hebben samen twee kinderen, Diana en Max.