Psychosocial factors in patients with lumbar disc herniation:
Enhancing postoperative outcome by the identification
of predictive factors and optimised physiotherapy

To Evald, Hanna and Fredrik

ÖREBRO UNIVERSITY

Ann-Christin Johansson

**Psychosocial factors in patients with lumbar disc herniation:
Enhancing postoperative outcome by the identification
of predictive factors and optimised physiotherapy**

ABSTRACT

Johansson, A-C (2008). Psychosocial factors have been advanced as an explanation for the development of chronic disability in 20 to 30% of patients treated by lumbar disc surgery.

Aims: The overall aim of this thesis was to study the role of psychosocial factors in patients undergoing first-time lumbar disc surgery in relation to the outcome of both surgery and subsequent physiotherapy.

Methods: Sixty-nine patients with lumbar disc herniation undergoing first-time disc surgery participated in the studies; in addition, Study I included 162 knee patients for comparison. Psychosocial factors were assessed preoperatively, as was the activation of the physiological stress response system. Pain, disability and quality of life were assessed before, and 3 and 12 months after surgery. Coping and kinesiophobia were analysed before and one year after surgery. The results of two different postoperative training programmes were compared.

Results: There were no differences between disc and knee patients regarding the presence of psychosocial stress factors preoperatively (Study I). Disc patients with low diurnal cortisol variability had lower physical function, perceived fewer possibilities to influence their pain and were more prone to catastrophise than patients with high diurnal cortisol variability (Study II). The results of clinic-based physiotherapy and home training did not differ regarding postoperative disability and pain 3 months after surgery. The home-based group had less pain and higher quality of life in comparison to the clinic-based group 12 months after surgery (Study III). Patients' expectations of returning to work could best predict pain, disability, quality of life and sick leave one year after surgery (Study IV). Psychosocial factors were only weakly associated to pain, disability, quality of life and sick leave preoperatively. However, these associations were stronger in patients with residual pain one year after surgery.

Conclusion: Psychosocial factors and, in particular, patients' expectations regarding outcome are associated with the results of lumbar disc surgery. Assessing psychosocial factors preoperatively and developing an active home training programme after surgery could create options leading to better results for these patients.

Keywords: Lumbar disc herniation, surgery, psychosocial factors, physiotherapy, expectations

PUBLICATIONS

I   Johansson AC, Cornefjord M, Bergkvist L, Öhrvik J, Linton SJ.
Psychosocial stress factors among patients with lumbar disc herniation, scheduled for disc surgery in comparison with patients scheduled for arthroscopic knee surgery.
Eur Spine J. 2007 Jul;16(7):961-70.

II   Johansson AC, Gunnarsson LG, Linton SJ, Bergkvist L, Stridsberg M, Nilsson O, Cornefjord M.
Pain, disability and coping reflected in the diurnal cortisol variability in patient scheduled for lumbar disc surgery.
Eur J Pain. 2008 Jul;12(5):633-40

III   Ann-Christin Johansson, Steven J Linton, Leif Bergkvist, Olle Nilsson, Michael Cornefjord
Clinic-based training in comparison to home-based training after first-time lumbar disc surgery: a randomized controlled trial.
In press

IV   Johansson AC, Linton SJ, Rosenblad A, Bergkvist L, Nilsson O
A prospective study of cognitive and behavioural factors as predictors of pain, disability and quality of life one year after lumbar disc surgery.
Submitted

ABBREVIATIONS

ACTH	Adrenocorticotrophic Hormone
ADL	Activities of Daily Living
AUC	Area under the response curve
CHAMP	The Centre for Health and Medical Psychology
CKF	Centre for Clinical Research
CRH	Corticotrophine-Releasing Hormone
CSQ	Coping Strategies Questionnaire
CT	Computer Tomography
EuroQol	European Quality of life questionnaire
EuroQol5D	The five dimensional scale of the EuroQol
EuroQolVAS	EuroQol visual analogue scale
HPA	Hypothalamic-Pituitary-Adrenal
LiSat-9	Life Satisfaction Scale 9
MRI	Magnetic Resonance Imaging
ODI	Oswestry Disability Index
OR	Odds Ratio
QWC	Quality-Work-Competence
RCT	Randomised Controlled Trial
SF-36	Medical Outcomes Study Short Form Health Survey 36
SPSS	Statistical Package for the Social Sciences
SRSS	Social Readjustment Scale
TSK	Tampa Scale for Kinesiophobia
VAS	Visual Analogue Scale

CONTENTS

PREFACE

Since ancient Greece, the term *sciatica* has been used to describe pain arising from around the hip and thigh. According to Hippocrates (460-370 BC), "ischiatic" pain mainly affected men between 40 to 60 years of age and lasted usually for 40 days in younger men. However, the term was not used for pain following the distribution of the sciatic nerve until modern times.

Since the beginning of the 20th century, recommending rest was traditionally the key orthopaedic treatment of low back pain. This also applied for sciatica, based on the idea that it, as well as low back pain, was due to a traumatic inflammation which needed to be allowed to heal in order to avoid the development of chronic back pain.

On July 30th 1932, in a corridor of the old Bullfinch Building of the Massachusetts General Hospital, the neurosurgeon William J Mixter and the orthopaedist Joseph S Barr met to discuss a surgical case from the previous day. From this interdisciplinary meeting the work started which identified the prolapsed intervertebral disc as a cause of sciatica. Six months later, the first patient with a preoperative diagnosis of a "ruptured intervertebral disc" entered the operating theatre of the Massachusetts General Hospital. The resulting original paper from 1936 described that disc herniation could cause neurological deficits, and surgical treatment was proposed.

Over the last few decades, diagnostic tools, surgical techniques and postoperative rehabilitation programmes have developed dramatically. The treatment principle of rest has gradually changed into a more active approach. Today it is widely accepted that the key to a well-functioning back is activity, and treatment principles involving early activation for back patients are well established.

Activity patterns are one aspect of behaviour and are therefore affected by beliefs and attitudes. This insight has opened up new perspectives for the postoperative care of back patients. Even though lumbar disc herniation is a precise and well-defined diagnosis, the resulting pain is a multidimensional phenomenon influenced by sensory, emotional and cognitive factors; therefore, understanding pain requires a broad perspective.

BACKGROUND

Some patients with lumbar disc herniation will have an excellent and others a poor outcome after the same type of surgical procedure, despite identical pre-operative clinical and magnetic resonance imaging (MRI) findings. The reasons for this are still largely unknown. Identifying and possibly eliminating or treating factors leading to a poor postoperative outcome is a challenge for all caregivers.

The intervertebral disc and disc herniation

The intervertebral disc connects the vertebrae to a functional unit. Its role is mechanical, acting as an absorber of load forces and as a joint allowing motion in all planes. The outer part, annulus fibrosus consists of lamellae rich in collagen which are structurally and functionally different from the inner part nucleus pulposus which is gelatinous in texture and rich in proteoglycan. The latter provides the disc with its osmotic properties and its ability to resist compressive loads [207].

A disc herniation was first described by Mixter and Barr [158] as a rupture of the annulus fibrosus with leakage of the nucleus pulposus into the intervertebral space. Today, herniation is categorised as a protrusion without perforation of the posterior longitudinal ligament (contained), an extrusion with perforation of the posterior longitudinal ligament (complete/non-contained) or an extrusion with free disc material within the spinal canal (sequestered/non-contained) [104]. This phenomenon usually occurs dorsally or dorsolaterally in the back, between the fourth and fifth lumbar vertebrae, or between the fifth vertebra and the sacrum. Herniation can cause compression and deformation of adjacent nerve structures and result in sciatic and/or back pain [223] (Figure 1).
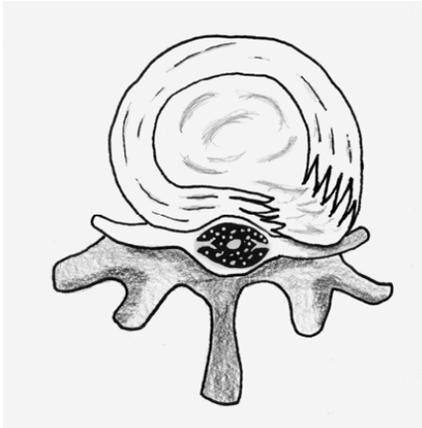
Figure 1. Lumbar disc hernia

Aetiology

Among several factors which can contribute to disc herniation, degenerative changes are most common [10, 63]. Disc degeneration is regarded as a weakening, complex multifactorial disease determined by the interplay between genes and the environment [28]. The morbidity curve for disc herniation, however, does not follow the corresponding curve for degeneration. While disc degeneration proceeds with time and is most pronounced in the aging spine, symptoms of lumbar disc herniation are most common in middle age [10, 120].

Genetic disposition, mechanical compression, e.g. heavy torque strain [9, 10, 110] and vigorous physical activity, low frequency vibrations, trauma, obesity and psychosocial stress are all factors which have been referred to as promoters of disc degeneration and subsequent herniation [96, 172].

Research from the last decade has resulted in a shift from heavy physical loading to genetic disposition being considered the main risk factor in the aetiology of disc degeneration [9, 183, 188]. Still, the degenerative progression may be influenced by environmental factors [10].

Pathogenesis

Symptoms of disc herniation may be induced by mechanical compression of the nerve root/s, but the pathogenesis also involves inflammatory and immunological components [67, 68]. Biochemical irritants from the nuclear tissues include an activation of the proinflammatory cytokines [67, 187]. The cytokines excite nociceptors either directly or indirectly via prostaglandin

synthesis [203]. In particular, the cytokine TNF-alpha [167] and interleukines [69] have been related to the onset of sciatic pain. Other clinical signs of this phenomenon are sensory deficits and/or muscle weakness [34, 168]. The different types of disc herniation have different inflammatory properties; inflammatory cells are more common in sequestered than in extruded discs without a sequester [215]. Moreover, the inflammatory response is influenced by genetic factors [69, 163].

Prevalence

The lifetime prevalence of disc herniation is 1-2% [64, 90, 213]. Men are more often affected than women (1.5-1.0) [220].

According to MRI analysis, the occurrence of disc herniation among symptom-free individuals is 20-30% (volunteers, aged 20-80 years) [13, 99]. In comparison, the corresponding proportion is 76% in symptomatic individuals matched for age, sex and work-related factors. The only highly significant difference between individuals with and without symptoms was shown to be the extent of nerve root compression [15].

Disc herniation is most common between 40 and 50 years of age [195] but can occur in all age groups [63, 195].

Symptoms

Radiating sciatic pain and back pain are the main symptoms of lumbar disc herniation [183, 223]. The distribution of leg pain usually follows the affected nerve root leaving the spinal canal one vertebral level caudal to the herniation [47]. Lumbar pain and neurological deficits with motor weakness and/or sensory and reflex disturbances specific for the nerve root distribution are other common symptoms [47, 183]. The pain is usually elicited by increased abdominal pressure like coughing and strain, and a pain-induced scoliosis can often be observed [96]. A herniation located centrally in the spinal canal may affect the nerve roots two levels below or nerve roots that exit several levels below. In the cauda equina syndrome, which is an emergency condition, the sacral roots are affected, usually with incontinence, and peroneal sensory loss in addition to bilateral sciatica [1, 41, 47].

Treatment

Since most disc herniations will regress with time [35, 101], a conservative treatment approach is usually the first choice. Physiotherapy and/or medical

treatment is frequently recommended to reduce the disabling symptoms. If no progress is observed within six to eight weeks surgery may be considered. The frequency for surgical treatment varies both in the western world and within Sweden [198]: according to Deyo, approximately 5-10% of patients with symptomatic lumbar disc herniation require surgery [46].

Surgery aims to reduce the nerve root irritation caused by compression, thereby relieving pain and improving function [197]. Recovery of adjacent non-compressed nerve roots after surgery may be due to less production of proinflammatory mediators when the disc material is removed [165].

Open discectomy, performed by macrotechnique with or without microscope, is the most common surgical procedure [96].

Indications for surgery are severe disabling leg pain radiating below the knee, a positive nerve tension test (positive Lasègue's sign at an elevation of less than 30^0) with or without neurological symptoms corresponding to the affected nerve root, no improvement despite six to eight weeks of conservative treatment and a positive MRI or computer tomography (CT) examination corresponding well to clinical findings [86]. Acute surgery may be required if a cauda equina syndrome with compromised bladder function develops [74].

It was reported from the Swedish national spine register that 1.7 to 2.1 per 10 000 inhabitants were treated by surgery between 1998 and 2003, 55% men and 45% women. The mean age of these patients was 43 years [197]. The number of surgically treated patients has been almost constant since the mid-1950's [96].

Systematic reviews on the outcome of disc surgery report a success rate of 65-90% for sciatic pain and disability [6, 73]. According to the Swedish national spine register, 76% of 2796 operations succeeded in reducing sciatic pain [197]. The rate of reherniation after discectomy is low (1%) within the first postoperative year [213]. A large Finnish long-term study found 12% repeated surgery, corresponding to a cumulative risk of 19% in the 9-year follow-up [111].

In the long run, differences between surgical and conservative treatment tend to level out [4, 52, 221]. The long-term results of surgery are difficult to evaluate, however, as the degenerative process is a lifelong progressive disease [176].

The most common residual symptom after disc surgery is low back pain [227].

Factors associated to the outcome of disc surgery

Several factors may influence the outcome of disc surgery. Mannion and Elfering emphasised that interactions between several risk factors make the identification of unequivocal predictive factors extremely difficult [144].

Individual patient characteristics are crucial, but assessing outcome is also a matter of defining success. In general, functions related to medical variables (e.g. pain duration, previous spine operations) are best predicted by pain and symptom-specific impairment, whereas disability, general well-being and return to work are better predicted by psychosocial variables [145].

Positively associated with a favourable outcome of disc surgery are factors such as sciatic pain duration of less than one year, a short period of preoperative sick leave [181], disc herniation not being caused by an occupational injury [144], high socioeconomic status and minimal psychosocial stress [105].

Conversely an extremely heavy work load is negatively associated to outcome [12, 137]. This also applies to factors such as smoking [143], low physical activity levels [56], short preoperative walking distance [97], overweight [144], joint-related comorbid conditions, systemic disease (e.g. inflammatory disease) [24, 224], a low educational level [224] and depression [23, 105, 109, 206] .

The severity of pathology based on preoperative MRI findings, e.g. characteristics of the herniated disc [24, 103] and the extent of nerve compression [189], have also been referred to as predictors of a poor outcome. Some authors have argued, however, that a preoperative neurological deficit is predictive of a good outcome after surgical treatment [105, 118]. Halldin came to the conclusion that morphologic characteristics of the herniation such as its position in the spinal canal, its direction and size, are of no importance for the postoperative clinical results [84].

Psychosocial factors associated to the outcome of lumbar disc surgery

Psychosocial factors can be described as individual characteristics, such as psychological, cognitive or behavioural aspects, but they can also be related to social circumstances in the individual's life, including work and family issues [210]. These factors are often interrelated, influencing and modulating pain perception and, thereby, perceived health.

Psychological key dimensions are distress, anxiety and depression, all of which have been reported to have a negative influence on the outcome of disc surgery [87, 105, 118, 206]. Cognitive components are represented by attitudes, beliefs and cognitions concerning pain, disability and perceived health. It is well known that these factors play an important role in the development of non-specific low back pain [37, 62, 153, 175, 202], but cognitive aspects also predict pain and disability after disc surgery [42, 43].

Expectations, which are one aspect of cognition, have also been studied in patients with lumbar disc herniation [42, 43, 139, 172]. Ostelo et al. found that a favourable prognosis after surgery was best predicted by high treatment expectancy [172]. In accordance with this den Boer et al. [43] as well as Lutz et al. [139] found that positive expectations before disc surgery could antici-pate a favourable treatment result. Moreover, Elfering concluded in his review that a low expectation of treatment success regarding early return to work is strongly linked to a poor work prognosis in patients with spinal disorders [55]. In patients with non-specific low back and neck pain, expectancy, pain-related fear and function are strongly interrelated [14, 77].

Behavioural activity patterns are also referred to as psychosocial factors. A passive attitude towards pain and avoidant and non-verbal pain behaviour can promote negative development of symptoms related to lumbar disc herniation [87].

Psychosocial aspects of work may also play an important role in the perpetuation of back pain in patients with disc herniation. In a case-control study by Seidler et al. it was concluded that psychological strain at work, and time pressure in particular, is more common in cases with symptomatic disc herniation than in healthy controls [191].

It has been suggested that pronounced family problems play a role in the modulation of pain, but the empirical support for this assumption is insuffi-cient [121]. Social support from the spouse in terms of overprotection [189], a search for social support (as a pain behaviour) [105] and family reinforcement of pain [12] have all been associated with a negative outcome after spine surgery.

The impact of demanding life events on the development and onset of low back pain is not yet fully understood. Originally, the instrument for its measurement was studied in cardiovascular diseases, but it has since been used in musculoskeletal research [107, 205]. Adverse life events also appear to be

associated with the development of chronic idiopathic low back pain [116, 121]. To the author's knowledge, the question of whether stressful life events are more common among patients with disc herniation and radicular pain than in others has not previously been studied.

A large number of studies have demonstrated an association between psychosocial factors and musculoskeletal disorders [5, 13, 65, 99, 121]. These factors may also contribute to an explanation for why discectomy is not universally successful even if the morphological problem is correctly addressed by surgery.

Coping

Applying cognitive and behavioural efforts to manage and adjust stress is defined as coping [123]. Pain causes stress for the individual, with pain coping being defined as an effort to manage or minimise the negative impact of pain.

Coping is the general plan, conscious or unconscious, that we have for dealing with pain. It is believed to be critical for understanding patient behaviour and may also serve as an important part of any treatment that is offered [134].

Problem-focused strategies aimed at altering person-environment relationships are called active coping, in comparison to passive/emotion-focused coping aimed at regulating emotional distress [60, 123]. With regards to pain, an active coping strategy means to try to control pain or continue activity in spite of it. Passive or maladaptive pain coping means negative thoughts, the assignment of the responsibility for pain to others and feelings of helplessness [21]. Catastrophising is defined as an exaggerated negative orientation towards pain [201], whereas kinesiophobia is the fear of physical movement and activity [119].

Passive pain coping and negative expectancies predict residual pain and disability after lumbar disc surgery independent of other biomedical factors such as the extent of disc degeneration and muscular instability [42]. Passive pain coping has also been suggested to contribute to the transition from acute to chronic pain [124, 132, 131]. Burton et al. observed that patients who were prone to catastrophise contributed to 47% of the variation predicting the development of chronic pain after an episode of acute low back pain [22].

Fear avoidance beliefs and the fear-avoidance model

Fear is a normal reaction to acute pain. However, if the pain is prolonged, fear and a belief that activity will cause injury and thereby exacerbate pain can result in avoidance of activity [219]. The fear-avoidance model was first introduced by Lethem [127] and later refined by Vlaeyen et al. [218]. It is a cognitive and behavioural framework explaining how pain-related fear can develop into persistent disability [219]. According to Vlaeyen and Linton, "confrontation and avoidance are postulated as the two extreme responses to this fear, of which the former leads to a reduction of fear over time" [219]. The model includes factors which contribute to deconditioning and in turn reinforce further pain experience, negative expectancies and avoidance. The concept is that fear of pain and (re)injury may be more disabling than the pain itself. Negative pain beliefs, fear and catastrophic misinterpretations, in particular, can lead to a vicious circle of exacerbated fear, avoidance of movements and activities, disuse, distress and disability [219]. According to the model, the anticipation of pain or the harm and (re)injury the pain might imply leads to avoidance of activity rather than the response to pain itself. On the other hand, confrontation strategies increase activity and thereby promote recovery [219].

Research supports the relationship between fear avoidance beliefs and disability both in acute, subacute and chronic phases of musculoskeletal pain [44, 79, 124]. Pain-related fear has been shown to be a salient predictor of pain in a chronic pain population, even more than biomedical status and pain intensity [218].

Studies on the consequences of fear of movement among patients treated by disc surgery are contradictory. Ostelo et al. found that fear of movement is not associated to recovery after disc surgery [172], whereas den Boer et al. concluded that it is predictive of pain and disability [42] as well as work capacity [43] six weeks and six months after disc surgery. There are still few studies available in which the consequences of fear and avoidant behaviour have been analysed in back patients after surgery.

The interplay between psychosocial factors, impairment and disability

In clinical practice, impairment, such as a disc herniation with nerve affection and disability are closely connected. Impairment is defined as a limitation of body functions and structures, causing disability. Both impairment and

disability can be associated with pain, but the direct relationship between pain and disability is weak [20, 135, 210].

There is a dynamic interaction between the two concepts in which disability incorporates cognitive, emotional and behavioural components [210]. Disability is lack of ability, which concerns physiological aspects but also how an individual cope with the impairment. Lack of ability is also a matter of psychological resources, reflected by the efforts an individual is capable of making. Consequently, disability is dependent on the interplay between impairment and psychosocial factors [20, 210]. This interplay differs both between the various stages of the pain process and between individuals. Mannion et al. have emphasized that for patients treated by disc surgery are disability, general well being and return to work after surgery best predicted by psychosocial variables [145].

The physiological stress response system

The physiological stress response system can be defined as a general, non-specific alarm system which alters the homeostatic balance, occurring whenever there is a discrepancy between what is expected or "normal" and what is actually happening. The alarm level depends on the expectancy of the outcome of the threat and the specific available coping responses [209].

The ability to respond to changes and challenges with a general alarm response are an essential element of the overall adaptive and self-regulating system of the organism [128]. The stress response is therefore a normal, healthy and necessary alarm system [208], through which psychological resources are mobilised to improve performance. However, a sustained response may increase the risk of illness or disease [209].

When exposed to stress, a first rapid wave of the stress hormones adrenaline and noradrenalin is released from the adrenal glands [151]. A second hormone wave is initiated if the stress becomes more prolonged and involves activation of the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis comprises a chain of hormonal reactions with increased production of corticotrophine-releasing hormone (CRH) from the hypothalamus, stimulating the pituitary gland to release adrenocorticotrophic hormone (ACTH), which in turn activates the adrenal gland to release cortisol [54].

A stimulus that triggers the stress response is known as a stressor; the most potent stimulus for triggering the HPA axis is psychological stress [148].

Stress hormone activity is dependent not only on the nature of the stressor, but also on an individual's assessment of available coping resources [113].

The release of cortisol normally follows a pulsatile circadian rhythm with levels peaking in the morning after awakening and than gradually decreasing throughout the day [113]. Cortisol is released and inhibited in an on-off fashion via a negative feed-back loop. This loop can be influenced by a stressor, which initially increases cortisol levels. Prolonged stress, however, results in exhaustion with a decreased morning peak as well as a flattened cortisol profile throughout the day [80, 178].

The way cortisol levels change during the day is a potentially important indicator of the function of the HPA axis [194]. In clinical populations, a flattening of the diurnal cortisol rhythm is seen among patients with depression [25], fibromyalgia [36], chronic fatigue syndrome [140] rheumatoid arthritis [162] and patients with residual pain after lumbar disc surgery [70].

Cortisol in human saliva, non-invasively measured in small samples, highly correlates with free cortisol concentrations in the blood [113]. The morning increase is approximately 50-160% of the awakening level, peaking about 30 minutes after awakening [31, 53, 85, 113, 180, 225]. The circadian rhythm in an individual is believed to be relatively stable over time [31, 53, 225]. When measured repeatedly and with reference to awakening, the morning response is considered to be a reliable biological measure of adrenocortical activity [180, 225].

The biochemical process associated with disc herniation involves an inflammatory reaction with activation of proinflammatory cytokines [17, 187]. These are potent stimulators of the HPA axis [8, 70], leading to an enhanced release of cortisol from the adrenal cortex [30, 161]. Cortisol plays a central role in the regulation of the inflammatory response to infection and injury inhibiting the release of cytokines [154]. The function of the HPA axis is one potential pathway through which stress could influence surgical outcome [69].

Furthermore, there are associations between behaviour and the function of the HPA axis. An active way of coping is associated with high cortisol levels, while a more passive one is linked to a low morning cortisol [16]. Low levels of salivary cortisol in the morning and high levels in the evening are also associated to the development of chronic widespread pain [16]. However, there remains a lack of knowledge regarding the causal directions of this possible link between body and mind.

Deconditioning after surgery

Deconditioning refers to a progressive process of worsening physical fitness as a result of reduced muscle activity [219]. Dependent on the duration and severity of symptoms, most patients already experience some degree of deconditioning when they present for disc surgery [91, 150].

Postoperatively, loss of back and abdominal muscle strength and endurance plays a significant role [40, 94]. Structural changes in the spine and spinal muscles are inevitable and are exacerbated by surgery [71, 149, 204]. Atrophy of both type 1 and type 2 fibres and alterations in the connective tissue of multifidus muscles have been observed [125, 174, 228, 230]. This might be the result of disuse, reflex inhibition [92] and/or nerve root impairment [93, 228]. The loss of strength and endurance has been shown to correlate well with activity limitations [40]. Furthermore, postural control, lumbar proprioception [126] and mobility [82, 149] are decreased after disc surgery.

According to Rantanen et al., who explored the structural changes in the multifidus muscles five years after disc surgery, these correlate well with the long-term outcome. There was less recovery of type 2 fibres among those with a negative outcome after surgery than in patients with a positive outcome. The authors suggested that these changes could be minimised by adequate surgical and physiotherapeutic treatment [182].

Rehabilitation after surgical treatment for lumbar disc herniation

Return to normal activity after surgery is dependent on the surgical success but also on the patients' physical recovery. Postoperative rehabilitation could be important for minimising complaints and deconditioning. Disc degeneration is a continuous process which can be accelerated by lack of physical activity [56], which might also be predictive of repeated spine surgery [108]. A Cochrane review confirmed that intensive postoperative exercises lead to an improved functional outcome [169].

There is a wide variety of post-disc surgery rehabilitation programmes in Sweden. An active treatment approach dominates, however, and most training programmes include exercises which aim to increase back stability, strength, endurance and mobility; recommendations of general future activity and ergonomic advice are also common. However, there is no official consensus and many patients still receive little or no formal rehabilitation after disc surgery.

Treatment models and graded activity

Two treatment models are commonly used in the management of patients with back pain: the medical and the biopsychosocial model.

The medical model implies that an interaction between the patient and a disease leads to an illness complex. It suggests recognising symptoms, identifying and treating the underlying disease and expecting the patient to recover [222]. In an orthopaedic setting this model needs to be in focus, but problems may occur when pain and perceived disability are influenced by psychosocial factors. Therefore, extended knowledge about these factors is needed [211].

According to the biopsychosocial model, pain is an interaction between biological, psychological and social phenomena. Consequently, it incorporates psychosocial variables into treatment programmes, e.g. kinesiophobia, passive pain coping, anxiety and lack of control [27, 45, 219]. This treatment model has favourably been applied to patients with non-specific low back pain [88, 129, 130, 134, 164, 173, 196] and has recently also attracted attention for the management of post-lumbar disc surgery patients.

Operant treatment, which is based on the biopsychosocial model, was first presented by Skinner [193] and introduced to the field of pain management by Fordyce [61]. Principles from learning theories have been employed, e.g. that behaviours are influenced by their consequences. Positive reinforcement of healthy behaviour, withdrawal of attention towards pain behaviour and the inclusion of a time instead of a pain contingent are important elements [61]. Cognitive and behavioural treatment approaches include intervention strategies such as self-instruction, relaxation, developing coping strategies, increasing assertiveness, minimising negative or self-defeating goals, changing mal-adaptive thoughts about pain and goal setting [133, 141].

Graded activity, which is one application of operant treatment, is a submaximal, gradually increasing exercise programme. Its essence is the development of individually graded exercises to teach the patient that it is safe to move while increasing the activity level. The therapist acts as a coach, and sets together with the patient exercise quotas to be performed at each treatment session. These quotas are systematically increased towards preset goals [171].

Previous research on rehabilitation after surgical treatment for lumbar disc herniation

A Cochrane review from 2002 [169] on rehabilitation after lumbar disc surgery concluded: "There is no evidence that patients need to have activity restrictions after first-time lumbar disc surgery. There is strong evidence that intensive exercise programmes starting four to six weeks post-surgery are more effective on functional status and faster return to work (short-term follow-up) as compared to mild exercise programmes. There is also strong evidence that at long-term follow-up there is no difference between intensive and mild exercise programmes with regard to overall improvement." Furthermore, it was concluded that it was unclear as to what the exact content of post-surgery rehabilitation should be.

Thirteen studies were included in this review of which six were of high quality. The studies were very heterogeneous regarding the type of exercise programmes; timing, duration of the intervention and long-term follow-up were to a large extent lacking. Two main future research topics were addressed in this review:

- Is a minimal care programme that incorporates a message about the importance of activity sufficient for patients with minimal complaints after surgery?
- Psychosocial factors should be taken into account in future research designs.

Since that review, ten randomised controlled studies [29, 50, 57, 59, 83, 114, 115, 170, 190, 226] and one prospective, controlled study [156] have been published on this topic. These add further support to early and active programmes which include trunk muscle strengthening and stabilising exercises. These exercises have above all been shown to be beneficial at short-term follow-up when compared with no postoperative training or a more conservative approach [57, 59, 115].

In long-term follow-ups (12 months or longer), the differences between various training programmes tend to level out [29, 50, 95, 114]. From this perspective, home training seems to be as effective as clinic-based training [29, 57, 59, 102].

In a prospective controlled (non-randomised) study by Millisdotter and Strömqvist, however, a specific stabilising programme which started two weeks after surgery and was employed twice weekly during four weeks

improved disability more than routine care which was less focused on stabilising training [156]. This difference persisted at the 12-month follow-up.

Neural mobilisation has been evaluated in one study in which patients with spinal fusions or laminectomy were also included, but the results indicated that this treatment did not provide any additional benefit in comparison to standard postoperative care for spine surgery patients [190].

Donceel et al. [51] compared a return to work-oriented rehabilitation with routine care which resulted in fewer patients being on sick leave one year after surgery (10% after work-oriented rehabilitation in comparison to 18% after routine care).

Behaviourally-oriented treatment principles have only been evaluated in one study of post-lumbar disc surgery patients where graded activity was applied [170]. It was concluded that these treatment principles did not offer any additional advantages to these patients. However, both Manniche et al. [142]. and Kjellby-Wendt et al. [115] suggested that the intensive and active training approach most benefited the active pain coping patterns the patients adopted, thus implying a positive behavioural effect.

Home training versus clinic-based training
According to earlier studies, home-based training can be a feasible treatment arrangement after arthroscopic orthopaedic surgery [39, 185], for patients with acute orthopaedic injuries [7] and with non-specific low back pain [160].

In a number of studies from the previous decade, home-based training was compared to clinic-based and supervised training after disc surgery [29, 38, 50, 57, 59, 83, 102, 142, 226]. Only one of these studies [226] found supervised training to be significantly more effective than home training, but the study sample was small (14 patients in each treatment group). All these studies except the one by Ostelo et al. [170] primarily aimed to evaluate physiotherapy which was entirely physical. Conventional physiotherapy with additional behavioural features has rarely been evaluated.
To conclude, early and active training is beneficial for patients after disc surgery, as well as training programmes including exercises which aim to regain back muscle activity and trunk stability. Furthermore, a passive attitude towards pain seems to be an obstacle for recovery. Previous studies add support to physiotherapist-led training in the short term, but the positive effects tend to equalise within the first postoperative year. Studies which have

evaluated behaviourally oriented physiotherapy are rare. In clinical practice it remains unclear whether minimal instructions regarding training and activity are sufficient, or if an additional comprehensive programme led by a physiotherapist is more appropriate.

Background summary

Symptoms related to disc herniation can be induced both by mechanical compression of nerve roots and by biochemical irritants from the disc tissues. It is still unknown if patients with symptomatic disc herniation already have more psychosocial stress than others when they present for surgery and which psychosocial factors most powerfully predict surgical outcome. Psychosocial stress is connected to the physiological stress response system, reflected in the function of the hypothalamic-pituitary-adrenal (HPA) axis. This in turn has an influence on the inflammatory reaction and is also associated to an individual's cognitive and behavioural stress response. The activation of the HPA axis in patients with disc herniation has only been estimated in a few studies. Therefore, it needs to be further explored to understand possible pathways between psychosocial stress, the physiological stress response, perceived pain and disability. Advantages of early and active training aiming to restore back muscle activity and trunk stability have previously been emphasised in rehabilitation studies. A passive attitude towards pain seems to be an obstacle for recovery. Previous studies add support for physiotherapist-led training in the short term, but the positive effects tend to equalise within the first postoperative year. Studies which have evaluated behaviourally oriented physiotherapy are rare. In clinical practice it remains unclear whether minimal instructions regarding training and activity are sufficient, or if an additional comprehensive programme led by a physiotherapist is more appropriate.

AIMS

The overall aim of this thesis is to study the role of psychosocial factors in patients undergoing first-time lumbar disc surgery in relation to the outcome of both surgery and subsequent physiotherapy. Furthermore, links between the physiological stress response system, psychosocial factors and subjective complaints are studied.

The specific aims of the individual studies are:

- To analyse preoperative psychosocial factors (e.g. work-related stress, life satisfaction and demanding life events) in patients with lumbar disc herniation in comparison with knee patients *(Study I)*.

- To explore the associations between pain, disability, quality of life and psychosocial factors in relation to the diurnal cortisol variability *(Study II)*.

- To compare clinic-based physiotherapy with a behavioural approach to a home-based training programme regarding disability, behavioural aspects, pain and global health measures *(Study III)*.

- To analyse the predictive value of cognitive behavioural factors in relation to pain, disability and quality of life one year after lumbar disc surgery *(Study IV)*.

- To analyse the associations between cognitive behavioural factors and pain, disability and quality of life preoperatively and 12 months after lumbar disc surgery *(Study IV)*.

METHODS

Study design

The study designs of studies I-IV are presented in Table 1.

Table 1. Studies and their design, number of patients, data collection and main outcome measures.

Study	Type of Study	Number of patients	Data collection	Main outcome measures
I	Cross-sectional	69 disc patients 162 knee patients	Questionnaire	Work-related stress Life satisfaction Life events Sick leave
II	Cross-sectional	42 disc patients	Questionnaire Salivary cortisol	Pain Disability Work-related stress Quality of life Coping Fear avoidance beliefs Diurnal cortisol variability
III	Randomised controlled trial	59 disc patients	Questionnaire Interview	Disability Pain Activity level Fear avoidance beliefs Coping Quality of life Patient satisfaction Compliance
IV	Prospective cohort study	59 disc patients	Questionnaire	Pain Disability Quality of life Sick leave Coping Fear avoidance beliefs Expectations

Study populations

The studies included in this thesis are based on a sample of 69 lumbar disc patients from the Departments of Orthopaedics at Uppsala University Hospital and at the Central Hospital in Västerås. Additionally, a sample of 162 knee patients from the same two orthopaedic clinics was included in Study I. All patients were scheduled for first-time lumbar disc surgery between March 2003 and May 2005.

The knee patients in Study I were planned for arthroscopic knee surgery for a suspected meniscus tear during the same time period.

For an overview of participating patients see Figures 2 and 3.

Inclusion and exclusion criteria

Inclusion criteria for all four studies were patient age between 18 and 60 years, no previous spine or knee (Study I) surgery and disc herniation as main indication for decompression surgery. Exclusion criteria were acute surgery, comorbidity influencing daily activities or working capacity and not being fluent in the Swedish language. Steroid treatment was an exclusion criterion in Study II.

Overall, 253 patients with lumbar disc herniation underwent surgery in the two participating orthopaedic clinics during the study period. Spine surgery was acute or repeated in 97 patients who could therefore not be included in the studies. Thus, a total of 156 disc patients were checked for eligibility of which 69 patients were allocated to Study I. Forty two of these patients were also included in Study II and 59 in Studies III and IV. For an overview of participating patients and reasons for exclusion see Figures 2 and 3.

Additionally, 232 knee patients were contacted, all agreeing to participate in Study I; 162 of these returned the completed questionnaire within the requested time limits.

```
┌─────────────────────────────────────────────────────────────────┐
│ Number of patients with lumbar disc herniation operated during    │
│ the study period, n=253                                           │
└─────────────────────────────────────────────────────────────────┘
                    │
                    │          ┌────────────────────────────────────┐
                    ├──────────│ Number of acute or reoperated      │
                    │          │ patients, n=97                     │
                    │          └────────────────────────────────────┘
                    │
                    │          ┌────────────────────────────────────────────┐
                    │          │ Number of patients excluded, n=87          │
                    │          │ 55 patients did not meet the inclusion     │
                    │          │     criteria;                              │
┌───────────────────────────┐  │     33 patients with age <18 or >60        │
│ Number of patients checked │  │     20 patients with comorbidity           │
│ for eligibility, n=156     │  │      2 patients not Swedish speaking        │
└───────────────────────────┘  │ 27 patients excluded for other reasons;    │
                    │          │     15 patients for geographical reasons   │
                    ├──────────│      4 patients planned for day surgery     │
                    │          │      8 patients could not be traced        │
                    │          │  5 patients refused to participate         │
                    │          └────────────────────────────────────────────┘
                    │
┌───────────────────────────┐
│ Informed consent           │
│ Baseline measurements,     │          ┌────────────────────────────────────┐
│ n=69 patients in Study I   │──────────│ Additional 10 patients excluded for │
└───────────────────────────┘          │ geographical reasons                │
                    │                   └────────────────────────────────────┘
      ┌─────────────┤
┌──────────────┐ ┌──────────────────┐
│ 42 patients  │ │ 59 patients par-  │
│ eligible for │ │ ticipating in Stud-│
│ participation│ │ ies III and IV,   │
│ in Study II  │ │ randomisation     │
└──────────────┘ └──────────────────┘
                    │
          ┌─────────┴─────────┐
┌───────────────────────┐ ┌───────────────────────┐
│ Allocated to the      │ │ Allocated to the      │
│ clinic-based training │ │ home-based training   │
│ group, n=29           │ │ group, n=30           │
│ (all received clinic- │ │ (all received home-   │
│ based training)       │ │ based training)       │
└───────────────────────┘ └───────────────────────┘
          │                   │
┌───────────────────────┐ ┌───────────────────────┐
│ Post-treatment        │ │ Post-treatment        │
│ measures at three     │ │ measures at three     │
│ months, n=29          │ │ months, n=30          │
└───────────────────────┘ └───────────────────────┘
          │                   │
┌───────────────────────┐ ┌───────────────────────┐
│ Post-treatment meas-  │ │ Post-treatment meas-  │
│ ures at 12 months, n=28│ │ ures at 12 months, n=29│
│ 1 patient did not return│ │ 1 patient did not return│
│ questionnaire         │ │ questionnaire         │
└───────────────────────┘ └───────────────────────┘
```
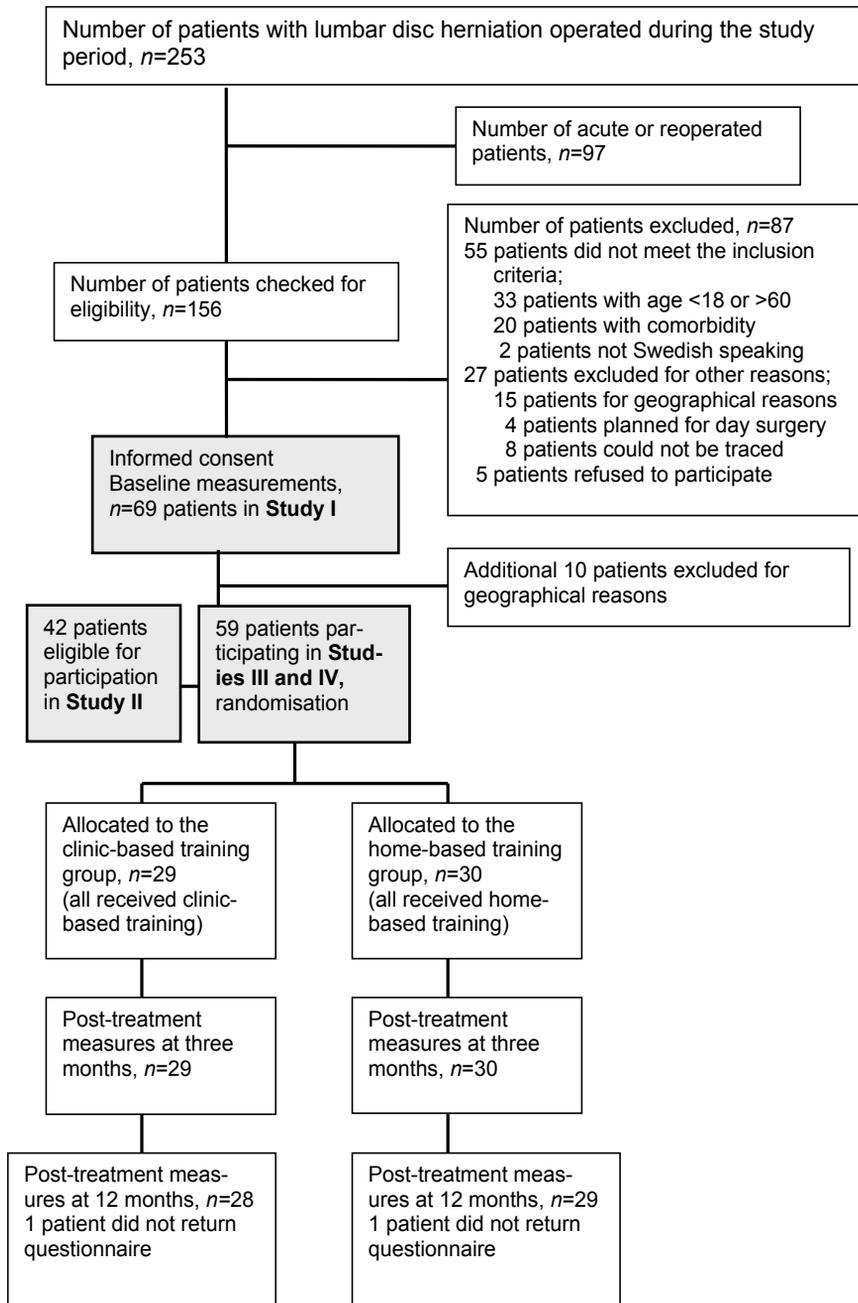
Figure 2. Flow chart of inclusion and exclusion, allocation to Studies I-IV and post-treatment measurements for patients operated for lumbar disc herniation.
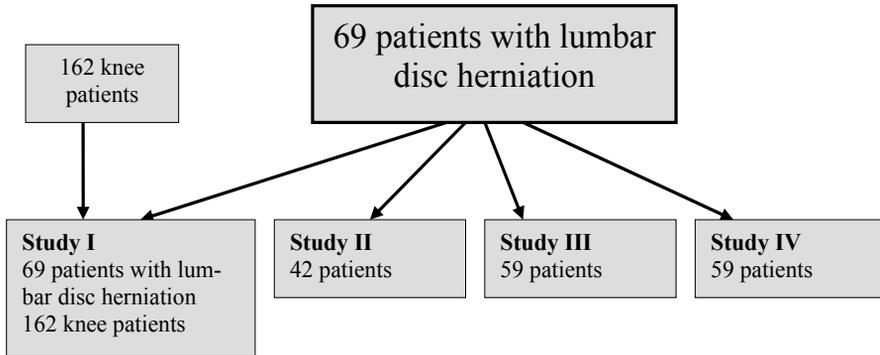
Figure 3. Numbers of patients participating in Studies I-IV

Measures

Assessment questionnaires

All lumbar disc herniation patients received a questionnaire at enrolment one to four weeks before surgery at their respective clinic. The completed questionnaire was returned the day before surgery.

Two follow-up questionnaires were sent by mail 3 and 12 months after surgery.

The knee patients in Study I were similarly sent a questionnaire which they returned by mail one to four weeks before planned arthroscopic knee surgery. For an overview of measurements see Table 1 and Figure 4.

The questionnaire to be answered preoperatively and 3 and 12 months after surgery included questions regarding:

Demographics (Studies I, II, III and IV)

Background variables, including age, sex, diagnosis, occupation, work load, sick leave (preoperatively and at 12-month follow-up), physical activity level, and preoperative duration of current back and leg pain.

Psychosocial stress at work (Studies I and II)

Work-related stress was measured by a short form of the Quality-Work-Competence (QWC) questionnaire. Its scales have been developed in a series of studies based on samples comprising approximately 100 000 employees overall. It has acceptable validity and reliability [3]. The questionnaire

34

contains three items on job satisfaction, concerning the current, previous and coming years. The subsequent indices cover areas such as mental energy, work climate, work tempo, performance management, participatory management, skills development, organisational efficacy and leadership. Each area consists of one to five items with standard Likert check-off scales. The scores on the enhancement indices range from 0 to 100.

Life satisfaction (Study I)

Life satisfaction was assessed using a modified Life Satisfaction Scale 9 (LiSat-9), a nine-item self-administered checklist, both regarding life as a whole (one item) and domain-specific (eight items) [152]. Its items have an acceptable test-retest reliability, specificity and sensitivity [19, 76]. We omitted one question on sex life and added one question on sleep satisfaction. The domains were vocation, personal finances, spare time, contact with friends, relationship with partner, family life, sleep and activities of daily living.

Levels of life satisfaction were reported on a six-grade scale ranging from very dissatisfied (1) to very satisfied (6).

Additionally, a dichotomy was used in the analysis with grades 5-6 classified as satisfied and grades 1-4 as not satisfied.

Life events (Study I)

A modification of the Social Readjustment Scale (SRSS) [121] was used to retrospectively assess stressful life events of the two years preceding surgery. This scale measures a number of events requiring life adjustment covering, for example, changes in family constellation, marriage, group and peer relations, occupation, economics, residence and health. It contains 18 questions with the response alternatives "Yes" or "No". A given number of points per item are multiplied with the factors 0 (no) or 1 (yes) and the total life events score is than obtained by addition of all points.

Disability (Studies II, III and IV)

Disability was assessed using the Oswestry Disability Index [58] with a possible score distribution from 0 (no disability) to 100 (maximal disability). The Swedish version of the ODI has a proven validity and a high degree of responsiveness [81].

Pain (Studies I-IV)

Back and leg pain intensity during activity in the previous week was assessed by visual analogue scales (VAS) [177].

In addition, the patients reported orally whether their leg pain was better, unchanged or worse three weeks after compared with before surgery.

Quality of life (Studies II, III and IV)

Generic health-related quality of life was measured by Medical Outcomes Study Short Form Health Survey 36 (SF- 36) [199, 212], which has an acceptable reliability, validity and responsiveness [229]. Quality of life was also measured by the five dimensional scale of the European Quality of life questionnaire (EuroQol 5D) (Study III and IV) and European Quality of life visual analogue scale (EuroQolVAS) (Study III) [18].

Coping (Studies II, III and IV)

The coping self-statement and catastrophising subscales of the Coping Strategies Questionnaire (CSQ) were used. Each of the two dimensions contains six questions and has a possible score ranging from 0 to 36. A higher score indicates higher coping self-statement and higher catastrophising, respectively [122, 186]. Reliability coefficients for each of the subscales range from 0.71 to 0.85 [186], with a value of 0.83 for the Swedish version [98].

Fear avoidance beliefs (Studies II, III and IV)

A modification of the Tampa Scale for Kinesiophobia (TSK) with a possible score distribution from 12 to 48 [155] was included. Low scores indicate no fear avoidance and high scores the opposite. Five questions of the TSK scale dealing with attitudes towards pain were omitted as they refer to pain not being caused by a serious condition. Most psychometric research has been done with the Dutch version which has a reliability of β=0.77 and an acceptable validity in acute and chronic low back pain populations [119, 155, 216]. The Swedish version has also been shown to have an acceptable reliability and validity in patients with chronic back pain [138].

Patient satisfaction (Study III)

Patient satisfaction regarding physiotherapy care was measured by two separate questions three months after surgery. The first question was "In your own view, did you receive enough help from the physiotherapist after your back operation?". Possible answers were "No, I received too little help" or "Yes, I

received enough help". The second question was "Would you recommend the physiotherapy you received to a friend who is going to be treated by disc surgery?" Possible answers were "Yes" or "No".

Therapies given by other caregivers (Study III)

Some separate questions were included at 3-month follow-up to ascertain whether patients had sought treatment by other caregivers during the study period. The first question was "Have you been treated by any caregiver/s other than those at the hospital since you had your back operation?" Possible answers were "Yes" or "No". For those patients who answered positively there was an attendant question regarding which caregiver they had visited and how many times.

Physical training habits (Study III)

Three separate questions assessed patients level of physical training and possible walking distance: whether the individual was regularly physically active ("Yes" or "No") and, if yes, in which way, how often they were regularly physically active (from occasionally to five times or more per week) [214] and how often they performed back exercises (from never to several times per day).

Expected outcome (Study IV)

A patient's own perception of his or her likeliness to recover was preoperatively measured with one item: "In your estimation, what are the chances that you will be back at work in three months?" This question was rated on a scale of 0 (no chance) to 10 (very high chance). This question is one item of the Örebro Screening Questionnaire [136].

Salivary cortisol measures (Study II)

Salivary cortisol levels were analysed in all patients in Study II. Four salivary samples were obtained from each patient three days before surgery using Salivates (Sarstedt, Nümbrecht, Germany). The patients collected the salivary samples at home, keeping the saliva test tubes in their refrigerator and bringing them, when presenting for surgery.

Salivary cortisol levels were analysed with a commercial radioimmunoassay (Spectria, Orion Diagnostica Oy, Espoo, Finland).

The salivary samples were collected at four time points:

- directly upon awakening

- 30 minutes after awakening
- before the evening meal
- at bedtime

Three different estimates on the reactivity of the diurnal cortisol levels were used:

- The diurnal cortisol variability, i.e. the difference between morning peak and last evening salivary cortisol value [192].
- The total area under the response curve including all four cortisol measures (AUC_G1) [179].
- The total area under the response curve including only the two morning values (AUC_G2).

Since the diurnal cortisol variability showed the highest association to pain and disability (calculations done using Spearman's rank correlation coefficient), this difference was used in the subsequent analysis in Study II. The patients were dichotomised into the low cortisol variability group (salivary differences of median 14.87 nmol/l or less than median) or the high cortisol variability group (difference between morning and evening salivary measures higher than median 14.87 nmol/l). These two groups were compared in the analysis in Study II.

Telephone interview (Study III)
Patients who were allocated to the home training group in Study III were followed up three months after surgery with a structured telephone interview regarding compliance with the training programme. The patients were asked if they had trained frequently ("Yes" or "No"), how frequently they had trained the first three months after surgery and if they thought the training instructions they had received were sufficient.

Treatment

For an overview of the measurement time points and the treatment patients received see Figure 4.
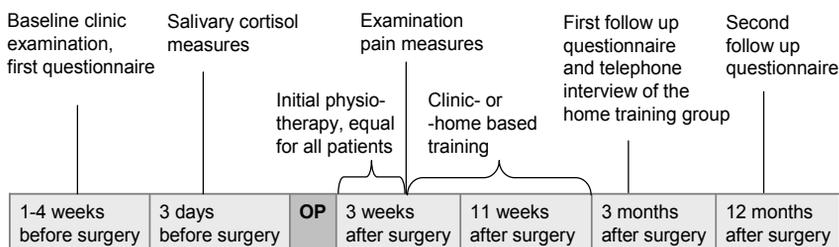
Figure 4. Timeline of measures and interventions for disc patients participating in Studies I-IV.

Surgery

All patients were operated with a standard lumbar discectomy using micro-surgical technique with magnifying glasses but without microscope.

Physiotherapy

Initial physiotherapy 0-3 weeks after surgery

All patients received oral and written information about postoperative training from a physiotherapist in the ward. Exercise started the first day after surgery and comprised stabilisation of the trunk by activation of the deep abdominal muscles [166], activation of the back, abdominal and buttock muscles, back and hip mobility and instructions about how to best get out of bed. Additionally, the patients received a written exercise programme which they were instructed to follow at least once a day. No sitting restrictions were given; daily walks and a gradual increase of daily activities were encouraged.

The same physiotherapist followed up all patients three weeks after surgery. For those patients in Study III who were allocated to the home-based training group this was the only physiotherapy visit they experienced. At this follow-up visit all patients were clinically examined and given a new training programme which they were recommended to follow daily. The importance of physical

activity for the healing process was emphasised. The new programme comprised back and hip mobility, trunk stability, strengthening of back, abdominal and leg muscles, and stretching of back, hamstring, quadriceps femoris and calf muscles. The patients were recommended to continue, and gradually extend, their daily walks and return to their work and normal daily routines as soon as possible. They were given no restrictions apart from heavy lifting during the first three months after surgery.

After this visit, the patients followed one of the two treatment groups (Study III), the clinic-based or the home-based training group.

The clinic-based training group

Patients who were randomised to the clinic-based training group visited the physiotherapy department once a week for eight weeks, starting at the first follow-up visit three weeks after surgery and continuing until ten weeks after surgery. They worked on their exercises under supervision by the same physiotherapist in addition to their daily home programme and were recommended to gradually resume normal daily activities. All patients were treated by the same physiotherapist (ACJ). The physiotherapy was influenced by a behavioural operant approach including graded activity with positive reinforcement of healthy behaviour, aiming to reduce fear and avoidant behaviour [61, 72, 129, 130, 170, 217]. The exercise programme comprised back and hip mobility, trunk stability, and strengthening of back, abdominal and leg muscles. Exercises with weight resistance were gradually added and increased. The programme also comprised general condition training by treadmill walking, stretching of back, hamstring, quadriceps femoris and calf muscles as well as a short relaxation. The patients also had the opportunity to discuss questions and thoughts about their condition at every visit. Active coping styles were encouraged; patients with residual pain were recommended to continue with their daily walks and home programme regardless. If a patient showed signs of passive pain coping, barriers to activity were identified and discussed and alternatives to painful exercises were given. The importance of future regular physical training was continuously emphasised and the patients were requested to establish goals for future regular weekly physical activity.

The home-based training group

Patients randomised to the home-based training group were informed and instructed at the above described occasion three weeks after surgery. No

additional instructions were given to this group. They were recommended to gradually increase the number of repetitions of the exercises and their daily walks as well as to resume normal daily activities. Future regular physical activity was encouraged. After this visit, the patients continued to train on their own. They had the possibility of contacting the physiotherapist if they had any questions concerning their training programme.

Statistical methods

Power analyses

<u>Study I</u>
It was determined that a total of 70 disc patients and 70 knee patients was needed to detect a mean score difference of 15 points on the QWC subscale of work-related stress with a 80% power at a 5% significance level. As we had access to 162 eligible knee patients, we included all these patients, to ensure high power.

<u>Study III</u>
According to the power analysis performed prior to the study, a total of 50 patients, 25 in each group, was needed to detect a clinically significant mean score difference of eight points in the ODI (SD=10) with 80% power and a significance level of 5%. To allow for possible drop-outs we decided to include 30 patients in each of the two groups.

No power analyses were made for Studies II and IV since they had an exploratory nature and were based on available patients.

Analysis methods
In this thesis most data were ordinal or not normally distributed and were therefore analysed mainly with nonparametric methods.

Median values were used as a measure of location and the interquartile range (q_1–q_3) as a measure of dispersion (Studies I-IV) means and standard deviation were correspondingly used for interval data (Studies II and IV).

Independent comparisons between groups were analysed using the Mann-Whitney rank sum test (Studies I-IV).

Changes within groups over time were studied using the Wilcoxon signed rank test (paired variable test) (Studies III and IV).

Differences in proportions were analysed by chi-square statistics and Fisher's exact test (Studies I-IV) and changes in proportions over time by McNemar's test (Study III).

The Spearman correlation coefficient (r_s) was applied when calculating correlations (Studies II and IV).

Analysis of interaction (Study I):

Since the variable representing job satisfaction in Study I was not normally distributed, a nonparametric test for interactions, based on aligned ranks (program written in FORTRAN) [231] was also applied. Briefly, the test is based on the joint ranking of all observations after removing the effect of the group affiliation (disc or knee patient). Suitably normalised, the weighted sum of squared differences between the two subcategories' mean rank (each combination of group affiliation and sick leave status) and the total mean rank will be approximately F-distributed. If the null hypothesis was rejected, a Kruskal-Wallis test was performed with each combination of group affiliation (disc herniation and controls) and sick leave status constituting a separate subcategory. A two-sided *p*-value of less than 0.05 was considered to be significant in all the analyses of main effects, while a significant *p*-value when testing for the presence of interactions had to be less than 0.1.

In Study IV, multiple backward stepwise logistic regression analysis was performed to study the contribution of the behavioural/cognitive factors (coping, fear avoidance beliefs and assessed chance to return to work within three months) to pain, disability and quality of life 12 months after surgery. To check the possible multicollinearity of predictor variables (i.e. insufficient unique variance of different predictors due to high intercorrelation) we calculated correlation coefficients for all studied variables with each other. Only those variables with a correlation coefficient *r*<0.40 were included in the regression model (e.g. the coping variables were omitted since their correlation to the variable "chance to return to work within three months" was too high). A regression model including independent variables which fulfilled the multicollinearity restrictions and had a *p*-value <0.10 was used. The variables were divided into high or low scores based on median values. The variables age, sex, work load, duration of leg pain preoperatively, and the behavioural variables coping catastrophising, fear avoidance beliefs and expectations of chance to return to work within three months after surgery were included in the final regression model. Furthermore, the two rehabilitation groups were

controlled for in the regression analysis. To check for possible influence of the type of rehabilitation received we investigated this variable's effect on the relationship between the independent and the dependent variables. No significant effects were found. The influence of the independent variables on dependent variables was presented by odds ratios and 95% confidence intervals. The explanation value of the regression model was calculated using Nagelkerke R^2.

Intention to treat principle (Study III):
According to the intention-to-treat principle, the two patients who underwent repeated surgery during the first postoperative period were included in the data analysis. We performed a separate analysis without these two patients and found only minor differences concerning group median values; moreover, these differences did not influence any of the outcome variables.

The chosen level of significance was $p<0.05$, two-tailed.

Ethics
All studies were approved by the Research Ethics Committee of Uppsala University (No 02-115 and 02-116) and performed in accordance with the principles of the Helsinki Declaration (World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. Adopted by the 18th WMA General Assembly, Helsinki June 1964. Revised in Tokyo, 2004).

RESULTS

Presence of psychosocial factors preoperatively (Study I)
Sick leave was considerably more common in the disc patients: 62% had been on sick leave for a mean of almost eight months, while only 14% of the knee patients had been on sick leave for a mean of four months.

There were no significant differences between the two groups regarding work-related stress measured by the Quality-Work-Competence (QWC) questionnaire which includes aspects of work such as work-related exhaustion, work climate, work tempo, performance management, participatory management, skills development, organisational efficacy and leadership.

The overall satisfaction of disc patients with their present work situation (one item of the QWC questionnaire) was lower (median score 50) than in knee patients (median score 70). Being on sick leave had significantly negative impact on job satisfaction in disc patients (median score 35 *versus* 70). This pattern was not seen in knee patients. Consequently, there was an interaction between the variables of group affiliation (disc or knee patient), sick leave and current job satisfaction.

Both disc patients on sick leave and knee patients on sick leave expected significantly higher job satisfaction the following year than they currently experienced. The expected improvement was significantly larger in disc patients than in knee patients (45 *versus* 10).

Less work satisfaction in the disc patient group in comparison to the knee patient group was also reflected in the results of the LiSat-9 questionnaire. There was also a significant difference between the two groups regarding leisure time, activities of daily living and sleep. Satisfaction with life overall, with personal finances, contacts with partner or friends, and family life, was similar between the two groups (Figure 5).
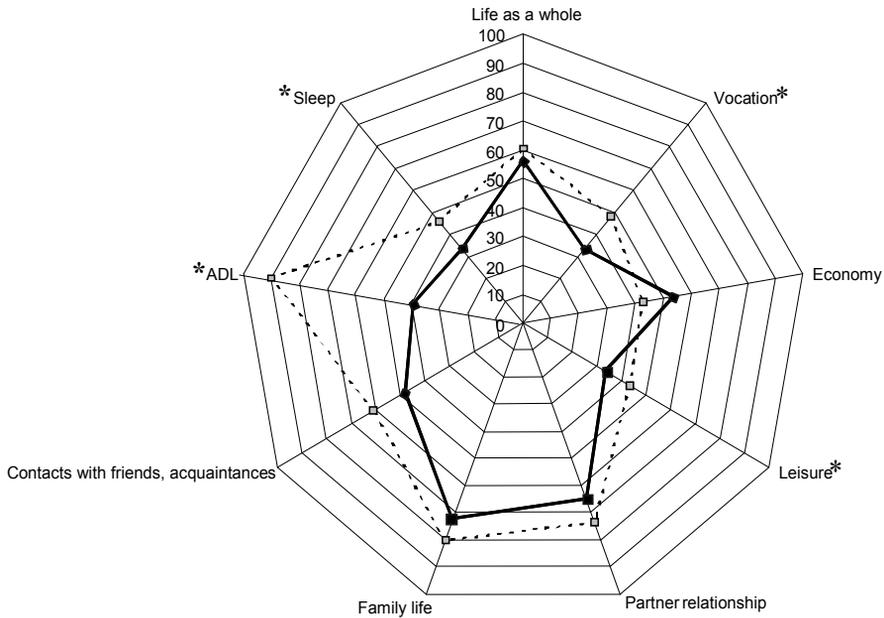
Figure 5. Life satisfaction. Proportions (%) of disc and knee patients, respectively who were satisfied or very satisfied (grade 5 or 6) according to LiSat-9 questionnaire.

*Denotes $p < 0.05$.

⎯◆⎯ Disc patients

··⎯□⎯·· Knee patients

Self-reported occurrence of demanding life events during the two years before planned disc surgery was also similar in both groups (mean 3.0 for disc and 2.9 for knee patients).

The diurnal cortisol variability in relation to pain disability, quality of life and coping (Study II)

No significant differences in background variables between the high and the low cortisol group were found.

Scores for pain, disability, coping fear avoidance beliefs and quality of life are presented in Table 2. Leg and back pain intensity varied markedly but did not differ between the two groups. The low cortisol group was more disabled according to the Oswestry Disability Index than the high cortisol group.

Health-related quality of life, estimated with the SF-36 dimension physical function, was poorer in the low cortisol group than in the high cortisol group. Fear avoidance beliefs were comparable in both groups.

Patients in the low cortisol group had lower coping self-statement scores than the high cortisol group but higher pain catastrophising scores.

There were only small and negligible differences between the two groups regarding work-related stress.

Table 2. Median score (interquartile range) for pain, disability and coping in the low and high cortisol group, respectively. *P*-values for the comparison between both groups.

	Low cortisol group median (interquartile range)	High cortisol group median (interquartile range)	Difference between groups *p*-value
Leg pain intensity, VAS range 0-100	79 (52-92)	68 (39-77)	0.10
Back pain intensity, VAS range 0-100	70 (42-80)	68 (61-78)	0.83
Oswestry Disability Index range 0-100	40 (34-51)	30 (26-45)	0.03
Coping self-statement range 0-36	18 (15-21)	23 (18-28)	0.01
Coping catastrophising range 0-36	15 (12-18)	10 (4-17)	0.04
Fear avoidance beliefs (TSK) range12-48	33 (27-36)	31 (27-38)	0.74
SF-36: (range 0-100) physical function	45 (28-53)	60 (45-68)	0.02
role physical	0	0	0.53
bodily pain	31 (17-41)	31 (22-41)	0.56
general health	67 (56-87)	77 (51-87)	0.43
vitality	33 (25-48)	40 (28-50)	0.42
social function	63 (38-88)	75 (44-81)	0.94
role emotional	66 (0-100)	33 (0-100)	0.94
mental health	68 (46-76)	68 (50-78)	0.68

Clinic-based training in comparison to home-based training after first-time lumbar disc surgery (Study III)

Three months after surgery there were no significant differences between the two groups regarding ODI, level of physical training, maximum walking distance, kinesiophobia, coping, pain or quality of life. Compliance to prescribed training was high in both groups.

The home-based training group had the opportunity to contact the physiotherapist during the eight weeks of home training. Six patients (20%) used this opportunity; a total of 13 telephone calls. They all had questions and concerns about residual leg or back pain.

Comparisons of differences between the two groups at baseline and the different time points are presented in Table 3.

Most patients in the home-based training group (86%) thought they had got on well with their exercises at home, while four patients were dissatisfied. Three patients had not undertaken the home programme at all.

Three months after surgery, significantly more patients in the clinic-based training group than in the home-based training group (28 *versus* 20) reported that they had received sufficient help from the physiotherapist. In line with this finding, significantly more patients in the clinic-based than in the home-based training group was willing to recommend their treatment to other patients (27 *versus* 21).

At 12-month follow-up there were no significant differences between the two treatment groups regarding disability, kinesiophobia or coping (Table 3). Back pain was, however, significantly more reduced in the home-based than the clinic-based training group. Reduction of leg pain showed the same pattern, but this difference was not statistically significant (Table 3).

Quality of life as measured by EuroQol VAS increased significantly more in the home-based training group than in the clinic-based training group at 12-month follow-up (Table 3). This difference was also reflected in the dimensions physical function, bodily pain and vitality of the SF-36 questionnaire.

All patients in the clinic-based training group but only 23 patients (79%) in the home-based training group reported that they trained regularly.

Table 3.
Median preoperative values for the two treatment groups. Medians of outcome scores and medians and interquartile range for differences between the two treatment groups at the different time points. P-values for comparisons of differences between the two treatment groups 3 and 12 months after disc surgery.

	Preoperative value		3 months post intervention			12 months post intervention		
	Clinic-based training group	Home-based training group	Clinic-based training group	Home-based training group	p-value	Clinic-based training group	Home-based training group	p-value
ODI[1] (0-100) median	38	39	16	14	0.49	15	6	0.09
median for difference			-20	-20		-23	-32	
(interquartile range)			(-5, -36)	(-13, -36)		(-9, -38)	(-17, -42)	
Back pain VAS[2] (0-100) median	70	70	23	14	0.33	34	9	0.04
median for difference			-31	-42		-19	-45	
(interquartile range)			(-11, -69)	(-25, -61)		(-10, -43)	(-13, -73)	
Leg pain VAS[2] (0-100) median	75	70	18	7	0.34	23	5	0.06
median for difference			-32	-53		-23	-58	
(interquartile range)			(-14, -71)	(-23, -77)		(-11, -67)	(-32, -80)	
TSK[3] (12-48) median	31	33	20	22	0.34	20	24	0.96
median for difference			-10	-9		-7	-10	
(interquartile range)			(-5, -16)	(-4, -11)		(-2, -15)	(-3, -14)	
CSQ[4] Self-statement (0-36) median	19	21	21	24	0.29	19	19	0.34
median for difference			2	4		1	1	
(interquartile range)			(-4, 6)	(-2, -8)		(-3, 5)	(-4, 3)	
CSQ[4] Catastrophising (0-36) median	15	13	7	3	0.37	8	10	0.39
median for difference			-6	-9		-7	-5	
(interquartile range)			(-1, -12)	(-2, -14)		(0, -10)	(5, -15)	
EuroQol[5] 5D (-0.594 -1) median	0.19	0.33	0.76	0.76	0.91	0.70	0.80	0.35
median for difference			0.24	0.27		0.36	0.48	
(interquartile range)			(0.06, 0.76)	(0.11, 0.64)		(0.04, 0.63)	(0.11, 0.74)	
EuroQol[5] VAS (0-100) median	50	49	80	80	0.58	70	70	0.03
median for difference			23	32		13	30	
(interquartile range)			(10, 43)	(12, 49)		(0.8, 33)	(15, 55)	

ODI[1]= Oswestry Disability Index, **VAS[2]**= Visual Analogue Scale, **TSK[3]**= Tampa Scale for Kinesiophobia, **CSQ[4]** = Coping Strategy Questionnaire, **EuroQol[5]** = Quality of Life

Cognitive and behaviour variables as predictors of pain, disability and quality of life one year after surgery (Study IV)

A low score on the item "In your estimation, what are the chances that you will be working in three months?" was significantly predictive of all outcome variables, with the highest odds ratio for being on sick leave 12 months after surgery (OR=19.5).

Of the 13 patients who preoperatively had assessed their chance of returning to work within three months as low, six patients were still on sick leave 12 months after surgery.

The strongest predictor for low quality of life 12 months after surgery was a high score of fear avoidance beliefs (OR=6.6). Being a woman was also predictive of low quality of life 12 months after surgery (OR=6.0).

The regression model explained 26-40% of the variation in the outcome variables pain (leg pain 26%, back pain 24%), disability (26%), quality of life (35%) and sick leave (40%), as measured by Nagelkerke R^2. Almost 40% of the variation in sick leave 12 months after surgery could be explained by low preoperative scores on the item "In your estimation, what are the chances that you will be working in three months?"

Associations between cognitive behavioural factors and pain disability and quality of life (Study IV)

Preoperatively

Associations between behavioural variables and pain, disability and quality of life were generally weak before surgery. High coping self-statement was positively associated to high quality of life, (r_s=0.4), whereas there was an inverse association between coping catastrophising and quality of life, (r_s=-0.4). A high score on the item "In your estimation, what are the chances that you will be working in three months?" was associated with low scores on back pain (r_s=0.3).

One year after surgery

Generally, the associations between behavioural variables and pain, disability, quality of life and being on sick leave were stronger among patients with residual pain after 12 months (*n*=35) compared to corresponding associations before surgery based on all patients (*n*=59).

Coping catastrophising was highly related to residual leg pain (r_s=0.6), back pain (r_s=0.7) and disability (r_s=0.8) 12 months after surgery.

Fear avoidance beliefs were also highly significantly associated to residual leg pain (r_s=0.5), back pain (r_s=0.6) and disability (r_s=0.5)*.

GENERAL DISCUSSION

The overall aim of this thesis was to study the role of psychosocial factors in the outcome of surgical and physiotherapeutic treatment for patients undergoing first-time lumbar disc surgery.

Psychosocial factors were explored preoperatively, their predictive value for outcome was assessed and links between the biological stress response system, psychosocial factors and subjective complaints were analysed. Furthermore, two different rehabilitation programmes were compared, both of which aimed at increasing activity and decreasing disability and pain after surgery.

Briefly, our results suggest that psychosocial factors such as work-related stress, life satisfaction and life events were not more common preoperatively in patients with disc herniation than in knee patients. The patients' own expectancy of their postoperative return to work was the strongest predictor of pain, disability and quality of life one year after surgery. Furthermore, patients with low diurnal cortisol variability preoperatively had worse physical function, perceived less ability to influence their pain and were more prone to catastrophising than patients with high diurnal cortisol variability. When active pain coping was encouraged together with careful training instructions, home-based training was a feasible treatment arrangement after surgery.

Study population

It is important to note that, even though lumbar disc herniation is a clearly defined diagnosis, the patient group undergoing surgery is very heterogeneous regarding the intensity of pain and dysfunction both pre- and postoperatively [106]. The results of this thesis derive from a selected group of Swedish speaking patients between 18 and 60 years of age and without comorbidity who underwent planned first-time spine surgery. It must be emphasised that the results can only be valid for this patient group, which constituted approximately 44% of all patients who underwent disc surgery at the two Swedish hospitals between 2003 and 2005. The most frequent reasons for exclusion were age over 60 years and comorbidity. It is possible that psychosocial factors in general would have been more pronounced if patients with comorbidity had been included since it influences most aspects of life [75]. The age limitations might also have affected the results as the clinical presentation in older patients is somewhat different [106]. Walking capacity, for example, can be expected to be more limited and the accomplishment of

the prescribed training more difficult. Additionally, comorbidity should be more common among older patients. One year after surgery, our study group had somewhat lower pain scores compared with corresponding values of the Swedish National Spine Register [197]. This may further emphasise that our results are based on a strictly selected study group.

Psychosocial factors preoperatively and one year after surgery

Psychosocial factors in patients with lumbar discs herniation in comparison to knee patients
In Study I our aim was to investigate if the presence of psychosocial stress in general was common already preoperatively among patients with disc herniation. The psychosocial factors we explored were limited to work-related stress and life satisfaction which covered areas such as family life, contacts with acquaintances, relationship with a partner, personal finances and stressful life events that had occurred during the previous two years. When disc patients were compared with knee patients, these factors did not differ. One could have expected work-related stress to be more common in disc patients since Boos et al. had described higher occupational and mental stress and less job satisfaction in symptomatic disc patients compared with asymptomatic controls [15]. This discrepancy could either be due to differences in those patients chosen as controls or different methods of measuring work stress.

As expected, sick leave was more common among patients with disc herniation. The patients with disc herniation on sick leave had higher expectations regarding future work satisfaction than knee patients on sick leave. This probably reflects the fact that patients with disc herniation are more compromised regarding their work than knee patients. Furthermore, disc patients expected that the planned surgical treatment would increase their reduced work capacity. They also expected higher work satisfaction for the coming year than that they had experienced during the previous year; this could partly be explained by their longer preoperative sick leave (mean duration eight months). The shorter preoperative sick leave of knee patients (mean duration four months) might imply that most of them had been able to accomplish their work the previous year, leading to better work satisfaction. Expectations of better postoperative work satisfaction in patients with disc herniation were irrespective of sick leave. This might indicate that their symptoms affected work capacity even if they were not on sick leave preoperatively.

Coping

In Study IV, associations between coping (self-statement and catastrophising) and pain, disability and quality of life preoperatively were assessed. These associations were generally weak. The strongest link was between high scores on the coping dimension self-statement and a high quality of life (r_s= 0.4), indicating that strategies for pain control will have a positive impact on quality of life, even if pain is severe. An inverse association was seen between coping catastrophising and quality of life.

One year after surgery, coping was analysed in 35 patients with residual pain (Study IV). Here, the association between the coping dimension catastrophising and pain was much stronger than in the overall study group before surgery. Patients are often able to muster resources to cope with pain reasonably successfully if the duration of pain is short [141]. Prolonged pain, however, requires a much wider range of coping skills, and residual pain despite surgery might be a source of anxiety and fear of future persistent pain. This in turn can set the stage for behavioural changes towards a more pronounced passive pain coping. According to Main et al. [141], pain patients are concerned about the cause of their pain, its likelihood to respond to treatment, and what they can expect in the future. High levels of residual pain despite surgery might for some patients trigger an anxiety of persistent and treatment-resistant pain. This can intensify pain perception and initiate a self-perpetuating vicious cycle of anxiety, increased pain, catastrophising and possibly also avoidant behaviour.

Fear avoidance beliefs

Associations between fear avoidance beliefs and pain, disability and quality of life preoperatively followed the same pattern as coping and were generally weak (Study IV). Corresponding associations 12 months after surgery were stronger in patients with residual pain.

Pain despite surgery might give raise to fear and avoidant behaviour since these patients must have experienced that their attempts to increase activity had worsened pain. A belief that treatment-resistant pain and disability are best handled by avoiding activity might be linked to this experience.

In unspecific low back pain, evidence suggests that fear avoidance beliefs [62, 117] and passive pain coping [26, 78, 153] are present at a very early stage and can be significantly predictive of future disability. Studies on the consequences

of fear of movement in patients treated by disc surgery are, however, sparse. Ostelo et al. found that fear of movement is not associated to recovery after disc surgery [172], while den Boer et al. came to the conclusion that it predicts pain, disability and work capacity six weeks and six months postoperatively [43]. In Study IV, high preoperative scores of fear avoidance beliefs were predictive of a reduced quality of life one year after surgery (OR=6.6), but not of pain or disability.

Expectations

The patients' own preoperative perception of early return to work (as measured by a screening questionnaire) was significantly predictive of the outcome variables pain, disability, quality of life and sick leave (Study IV). Scoring low on this item had an odds ratio of 19.5 for still being on sick leave 12 months after surgery. This finding is in accordance with several other studies [33, 42, 43, 89, 147, 159] in which positive recovery expectations have been pointed out as an important predictor of outcome.

Different mechanisms can explain how expectations, which are one aspect of cognition, can affect outcome; examples are the triggering of physiological responses which help motivate patients to achieve better results and psychologically condition them to perceive certain symptoms and ignore others. The expectation itself can thus be directly self-confirming [112]. Feelings and perceptions may also influence biological processes in diseases through behavioural and non-behavioural mechanisms [32]. It has been suggested that expectations, beliefs and affect should be seen as interrelated components of pain-related anxiety [14], which in turn may be driven by pain experience and, for surgical patients, by unexpected residual pain after surgery. It is possible that this process also interacts with more individual vulnerability factors in general [157].

Expectations of future work disability might additionally reflect aspects which were not directly explored in this study, such as how firmly patients are established at work, their beliefs about how their work might influence their future prognosis, or their psychological well-being. Expectations are also linked to an individual's view of what is possible and what he or she can manage regarding work demands [11]. Assessing patients' beliefs about future work capacity might help in identifying those who are at risk for unfavourable outcome after surgery.

Preoperative expectations seem to have a strong influence on outcome after surgery. It would be interesting to evaluate expectations in relation to outcome in future studies on treatment effects.

Taken together, the results of the present studies indicate that the presence of psychosocial stress is not more common in patients scheduled for lumbar disc surgery than in knee patients. For the prediction of residual disability and pain one year after surgery, the patients' own perception of future return to work is the most important variable. Fear avoidance beliefs are the most significant predictor of quality of life one year after surgery. The associations between behavioural and cognitive variables and pain, disability and quality of life preoperatively are generally weak. They are, however, stronger in patients with residual pain and disability one year after surgery.

The physiological stress response in relation to pain, disability and cognitive and behavioural variables

The release of hypothalamic-pituitary-adrenal axis hormones as a physiological response to psychosocial stress is a well-established phenomenon [48]. This and the subsequent release of gloucocorticoids from the adrenal cortex are important components of psychobiological processes to maintain or regain the homeostatic equilibrium under stress [66].

The diurnal salivary cortisol variability as an estimate for the preoperative function of the stress response system was analysed in Study II. The patients with low diurnal cortisol variability had more disability and catastrophising, but lower coping self-statement scores than patients with high diurnal cortisol variability. These findings are in line with the studies of Geiss et al. who found that patients with residual pain despite lumbar disc surgery had an attenuated cortisol increase after awakening. These patients were also more depressed, had more work-related strains and were more prone to maladaptive coping strategies than patients with less residual pain [70]. Further Geiss et al. reported that reduced preoperative cortisol levels could predict the failure of disc surgery. A decreased cortisol secretion might promote the postoperative production of proinflammatory cytokines; this was suggested to serve as an explanation for the higher risk of a poor surgical outcome in chronically stressed patients [69].

Reduced cortisol levels are associated to a passive coping style [16] and could have two possible effects on disc patients: an altered immune function with synthesis of proinflammatory cytokines resulting in increased pain and a reduced ability to cope with it. Our results show that neither pain duration nor work-related stress differed between the groups with high and low cortisol levels, respectively, whereas the ability to cope with pain did. The causal direction is still unclear and is comparable to the "chicken or egg" dilemma. One possible explanation is that patients who tend to catastrophise pain develop an altered HPA axis function due to the stress involved in this cognitive and behavioural pattern. On the other hand, the severe pain these patients experience could be a potent stressor which might affect the function of the HPA axis, resulting in less effective coping skills. Both models are plausible and interrelated, and might be true in either direction [2].

The results of Study II, however, indicate that the stress response in patients with lumbar disc herniation might be a link between the physiological stress response system and psychosocial stress factors.

Physiotherapy after surgery

The results of Study III suggest that instructions for subsequent home training are a feasible arrangement after lumbar disc surgery given the possibility for patients to contact the physiotherapist, if they need further advice. Back pain reduction and quality of life were significantly higher in the home-based training group one year after surgery than in the clinic-based training group. The compliance to prescribed training was high in both treatment groups, indicating that patients were motivated to manage their training on their own.

All patients received the same information regarding the importance of general activity and were encouraged to gradually resume their normal daily activities. The similarity of the treatment approaches might explain why the outcome of the groups was equal. According to den Boer et al. [42, 43], passive pain coping is the most important obstacle for recovery after disc sur-gery. In both groups of Study III, active pain coping was encouraged; most patients seem to have followed this advice as training compliance was high. This encouragement might have been the most important treatment aspect and was similar in both training programmes. Furthermore, patients in the home-based training group had the possibility to call the physiotherapist if questions arouse during rehabilitation. Six patients did so (20%) and obtained further

advice on how to cope with residual pain. This support was probably an important option for patients in this group and might have attenuated fear and anxiety, further reducing the differences between the two groups.

Manniche et al. suggested one important effect of an intensive training programme to be the confrontation with fears and insecurities and the reduction of pain-related anxiety [142]. Similarly, Kjellby-Wendt et al. emphasised that the benefit of their active treatment approach derived from the active pain coping patterns the patients adopted [115]. Doland et al. presumed that the physiotherapist was probably able to increase the patients' confidence in their ability to exercise and to become more active in daily life after disc surgery, thereby reducing anxiety and fear [49]. Moreover, active 3-month therapies have previously shown positive effects on psychological variables (i.e. fear avoidance beliefs and psychological distress) in chronic low back pain patients, even though none of them involved psychological or cognitive-behavioural interventions [146]. These studies imply that active treatment approaches have a positive behavioural effect, which might be the most important essence in of physiotherapy after disc surgery. The additional behavioural support of the clinic-based training group did not further improve outcome one year after surgery, which is in line with results reported by Ostelo et al. [170].

In earlier studies that evaluated treatments aiming to minimise psychosocial barriers to the rehabilitation progress, it was concluded that the behavioural intervention was most effective in patients who had pronounced kinesiophobia and passive pain coping strategies [72, 200]. Thus, programmes with behaviour-oriented principles might be of advantage for selected patients with pronounced kinesiophobia and passive pain coping after surgery, but not necessarily for all patients. Identifying patients at risk and developing effective treatment programmes for these patients are challenging future research tasks.

Three months after surgery there were no significant differences between the two treatment groups regarding pain and disability. The home-based training group had, however, significantly higher back pain reduction and quality of life than the clinic-based training group at 1-year follow-up. This difference actually developed after the physiotherapy intervention was finished. It is unlikely that the intervention itself is responsible for the differences seen after 12 months. This result might possibly indicate that a confounder was unevenly distributed in the two treatment groups.

The clinic-based training group was significantly more regularly physically active at 1-year follow-up than the home-based training group. Should this difference persist, in the long term it might positively affect outcome for the clinic-based training group, since lack of physical activity is an independent predictor of repeated surgery [108]. To answer this question, however, lies beyond the scope of this thesis.

Methodological considerations

The knee patients used as a comparison group in Study I represented a sample within which psychosocial factors were not expected to be more pronounced than in the general population. To the author's knowledge, there are no studies that have examined psychosocial factors in a comparable group, which does not necessarily imply that such factors are absent in these patients. A different study approach would have been to choose controls from the general population, but this might on the other hand have increased the risk of a higher number of drop-outs. The reason for choosing knee patients as a control group was that they also experience pain and disability, which for most individuals are stress factors.

The use of the Tampa Scale for Kinesiophobia (TSK) and the Coping Strategies Questionnaire (CSQ) in Studies II, III and IV also deserves consideration. Both the TSK and the CSQ were developed for patients with chronic non-specific musculoskeletal pain and its relationship to behavioural performance. However, all patients in the present studies had the exact diagnosis of a MRI-verified lumbar disc herniation, and the validity of the questionnaires for this patient group is therefore uncertain. The five questions which were excluded from the TSK all referred to pain not being caused by a serious disease. This might have impaired the validity of the TSK scale and makes it difficult to compare the scores of the included patients with those of other populations. Another question is whether the fears and beliefs the TSK scale captures reflect the patients' general fear of pain or the fear and beliefs concerning the individual diagnosis. At present, there are no scales available for the evaluation of comparable variables in surgically treated back patients; a further adaptation of the TSK to this specific patient group is therefore needed. To keep the number of items in the questionnaires within reasonable limits, we only used two of the six subscales of the CSQ, coping self-statement and coping catastrophising. The subscales of the CSQ are, however, always

reported separately, as it was suggested that the scores of the CSQ's individual scales may be more useful than composite scores for the identification of different coping strategies [100].

In general, the sample sizes in the present studies were small, which must be considered in the interpretation of the results. The patients included in Study II needed careful instructions on how to obtain and store their salivary samples. It was important that the samples were taken at the right time. All these were complicating circumstances for inclusion. The relatively small sample size in Study III increased the risk for uncontrolled confounders; a larger sample size would have reduced this risk. The small sample size in Study IV resulted in wide confidence intervals for prediction, indicating that the precision of the odds ratio estimates is uncertain.

Emotions, such as depression, are additional psychosocial factors which can have had an impact on the variables measured in the present studies. It might have been of value if depression had been measured, however, the number of items of the questionnaires needed to be limited to make their use reasonable.

CONCLUSIONS

- Psychosocial factors such as work-related stress and demanding life events were not more common preoperatively in patients with lumbar disc herniation than in knee patients. Patients with disc herniation were, however, less satisfied with their work situation preoperatively and had higher expectations of improved work satisfaction after surgery, in comparison with knee patients.

- Patients with disc herniation and a low diurnal cortisol variability had more disability, perceived fewer possibilities of influencing their pain and were more prone to catastrophising than patients with a high diurnal cortisol variability.

- Clinic-based physiotherapy with a behavioural approach did not differ from home-based physiotherapy regarding pain, disability and quality of life three months after surgery. Twelve months after surgery, back pain and quality of life were significantly more improved in the home-based than in the clinic-based training group.

- Patients who completed the regular clinic-based physiotherapy programme were more satisfied with physiotherapy care three months after surgery and were more motivated to continue regular physical activity twelve months after surgery.

- Patients' expectations of returning to work within three months after surgery could predict pain, disability, quality of life and sick leave one year after surgery. Fear avoidance beliefs and being a woman were predictive of a low quality of life one year after surgery.

- Cognitive and behavioural factors were only weakly associated to pain, disability, quality of life and sick leave preoperatively, however, corresponding associations were stronger in patients with residual pain 12 months after surgery.

- Eliciting patients' expectations about returning to work after surgery might be a helpful tool in the early identification of those individuals who run the risk of developing long-term disability and sick leave after first-time lumbar disc surgery.

ACKNOWLEDGEMENTS

Anders Westman, for friendship, engagement, inspiring discussions and your generosity during these years.

Tuula Wallsten and Eva Thors Adolfsson for your inspiration, friendship and many laughs.

Bertil Vinnars, for your positive attitude to research and life, inspiring discussions and for being continuously supportive.

All PhD and doctoral students at the Centre for Clinical Research in Västerås for all inspiring discussions at the seminars and all joy we had together in Västerås and in Camargue.

All physiotherapists and co-workers at the Physiotherapy ward at the Orthopaedic Department Västerås even if I have been absent for quit a time I have felt your support during the years with this work, which meant a lot to me.

The CHAMP group in Örebro, for many fruitful seminars and discussions and generous support during these years.

Rosanne Forberg, Head of Department of Clinical Chemistry Västerås for your kind help and collaboration regarding specimens and serum analysis.

Therese Wandebäck, Head of the Department of Physiotherapy Akademiska Sjukhuset, for welcoming me to your department and showing interest and having a positive attitude to my work.

Sune Larsson, Akademiska Sjukhuset, for introducing me to Michael Cornefjord. I am not sure that you are aware of the consequences of that action but from my heart, thank you.

The staff at the Central Hospital Library for being so helpful and supportive.

Hanna and Fredrik, for everything you are, my pride and happiness in life.

Evald, my beloved husband for your generous and endless love and for invaluable support with the most various things from keeping things running and going at home to improving my manuscripts.

Lastly I would like to express my very special thanks to *all participating patients*, without you there had been no studies.

REFERENCES

1   Ahn UM, Ahn NU, Buchowski JM, Garrett ES, Sieber AN, Kostuik JP (2000) Cauda equina syndrome secondary to lumbar disc herniation: a meta-analysis of surgical outcomes. Spine 25:1515-22

2   Anderberg UM (1999) Stress can induce neuroendocrine disorders and pain. Lakartidningen 96:5497-9

3   Arnetz JE, Arnetz BB (1996) The development and application of a patient satisfaction measurement system for hospital-wide quality improvement. Int J Qual Health Care 8:555-66

4   Atlas SJ, Chang Y, Kammann E, Keller RB, Deyo RA, Singer DE (2000) Long-term disability and return to work among patients who have a herniated lumbar disc: the effect of disability compensation. J Bone Joint Surg Am 82:4-15

5   Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE (2005) Long-term outcomes of surgical and nonsurgical management of lumbar spinal stenosis: 8 to 10 year results from the Maine lumbar spine study. Spine 30:936-43

6   Barrios C, Ahmed M, Arrotegui JI, Bjornsson A (1990) Clinical factors predicting outcome after surgery for herniated lumbar discs: an epedemiological multivariate analysis. J Spinal Disorders 3:205-209

7   Bassett SF, Prapavessis H (2007) Home-based physical therapy intervention with adherence-enhancing strategies versus clinic-based management for patients with ankle sprains. Phys Ther 87:1132-43

8   Bateman A, Singh A, Kral T, Solomon S (1989) The immune-hypothalamic-pituitary-adrenal axis. Endocr Rev 10:92-112

9   Battie MC, Videman T, Parent E (2004) Lumbar disc degeneration: epidemiology and genetic influences. Spine 29:2679-90

10   Beattie PF (2008) Current understanding of lumbar intervertebral disc degeneration: a review with emphasis upon etiology, pathophysiology, and lumbar magnetic resonance imaging findings. J Orthop Sports Phys Ther 38:329-40

11   Berglind H, Gerner U (2002) Motivation and return to work among the long-term sicklisted: an action theory perspective. Disabil Rehabil 24:719-26

12   Block AR, Ohnmeiss DD, Guyer RD, Rashbaum RF, Hochschuler SH (2001) The use of presurgical psychological screening to predict the outcome of spine surgery. Spine J 1:274-82

13   Boden SD, Davis DO, Dina TS, Patronas NJ, Wiesel SW (1990) Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am 72:403-8

14   Boersma K, Linton SJ (2006) Expectancy, fear and pain in the prediction of chronic pain and disability: a prospective analysis. Eur J Pain 10:551-7

15   Boos N, Rieder R, Schade V, Spratt KF, Semmer N, Aebi M (1995) 1995 Volvo Award in clinical sciences. The diagnostic accuracy of magnetic resonance imaging, work perception, and psychosocial factors in identifying symptomatic disc herniations. Spine 20:2613-25

16   Brandtstadter J, Baltes-Gotz B, Kirschbaum C, Hellhammer D (1991) Developmental and personality correlates of adrenocortical activity as indexed by salivary cortisol: observations in the age range of 35 to 65 years. J Psychosom Res 35:173-85

17   Brisby H (2000) Nerve injury markers, inflammatory mechanism and immunologic factors in lumbar disc herniation. Doctoral Thesis, Göteborg University, Göteborg

18   Brooks R (1996) EuroQol: the current state of play. Health Policy 37:53-72

19   Brännholm I-B, Lundmark P, Fugl-Mayer K, Fugl-Mayer A (1991) On work and life satisfaction. Journal of Rehabilitation Science 4:29-34

20   Buer N, Linton SJ (2002) Fear-avoidance beliefs and catastrophizing: occurrence and risk factor in back pain and ADL in the general population. Pain 99:485-91

21   Buitenhuis J, Spanjer J, Fidler V (2003) Recovery from acute whiplash: the role of coping styles. Spine 28:896-901

22   Burton AK, Tillotson KM, Main CJ, Hollis S (1995) Psychosocial predictors of outcome in acute and subchronic low back trouble. Spine 20:722-8

23   Carragee EJ (2001) Psychological screening in the surgical treatment of lumbar disc herniation. Clin J Pain 17:215-9

24   Carragee EJ, Kim DH (1997) A prospective analysis of magnetic resonance imaging findings in patients with sciatica and lumbar disc herniation. Correlation of outcomes with disc fragment and canal morphology. Spine 22:1650-60

25   Carrol BJ, Curtis GC, Mendels J (1976) Neuroendocrine regulation in depression. I:limbic system adrenocortical dysfunction. Archievs of General Psychiatry 33:1039-1044

26   Carroll L, Mercado AC, Cassidy JD, Cjte P (2002) A population-based study of factors associated with combinations of active and passive coping with neck and low back pain. J Rehabil Med 34:67-72

27   Cedraschi C, Allaz AF (2005) How to identify patients with a poor prognosis in daily clinical practice. Best Pract Res Clin Rheumatol 19:577-91

28   Chan D, Song Y, Sham P, Cheung KM (2006) Genetics of disc degeneration. Eur Spine J 15 Suppl 3:S317-25

29   Choi G, Pai-Raiturker P, Kim MJ, Dai Jin C, Chae YS, Lee YS (2005) The effect of early isolated lumbar extension exercise program for patients with herniated disc undergoing lumbar discectomy. Neurosurgery 57:764-772

30   Chrousos GP, Gold PW (1992) The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. Jama 267:1244-52

31   Clow A, Thorn L, Evans P, Huckelbridge E (2004) The awakening cortisol response: methodical issues and significance. Stress 7:29-37

32   Cohen S, Herbert TB (1996) Health psychology: psychological factors and physical disease from the perspective of human psychoneuroimmunology. Annu Rev Psychol 47:113-42

33   Cole DC, Mondloch MV, Hogg-Johnson S (2002) Listening to injured workers: how recovery expectations predict outcomes-a prospective study. Cmaj 166:749-54

34   Cornefjord M, Olmarker K, Rydevik R, Nordborg C (1996) Mechanical and biochemical injury of spinal nerve roots: a morphological and neurophysi-ological study. Eur Spine J 5:187-92

35   Cribb GL, Jaffray DC, Cassar-Pullicino VN (2007) Observations on the natural history of massive lumbar disc herniation. J Bone Joint Surg Br 89:782-4

36   Crofford LJ, Pillemer SR, Kalogeras KT, Cash JM, Michelson D, Kling MA, Sternberg EM, Gold PW, Chrousos GP, Wilder RL (1994) Hypotha-lamic-pituitary-adrenal axis perturbations in patients with fibromyalgia. Arthritis Rheum 37:1583-92

37   Crombez G, Vlaeyen JW, Heuts PH, Lysens R (1999) Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability. Pain 80:329-39

38   Danielsen J, Johnsen R, Kibsgaard S (2000) Early, aggresive exercise for postoperative rehabilitation after discectomy. Spine 25:1015-1020

39   De Carlo MS, Sell KE (1997) The effects of the number and frequency of physical therapy treatments on selected outcomes of treatment in patients with anterior cruciate ligament reconstruction. J Orthop Sports Phys Ther 26:332-9

40   Dedering A, Harms-Ringdahl K, Nemeth G (2006) Back extensor muscle fatigue in patients with lumbar disc herniation. Pre-operative and post-operative analysis of electromyography, endurance time and subjective factors. Eur Spine J 15:559-69

41   Delamarter RB, Sherman JE, Carr JB (1991) 1991 Volvo Award in experi-mental studies. Cauda equina syndrome: neurologic recovery following immediate, early, or late decompression. Spine 16:1022-9

42 den Boer J, Oosendorp R, Beems T, Munneke M, AW. E (2006) Continued disability and pain after lumbar disc surgery: The role of cognitive-behavioural factors. Pain 123:45-52

43 den Boer JJ, Oostendorp RA, Beems T, Munneke M, Evers AW (2006) Reduced work capacity after lumbar disc surgery: the role of cognitive-behavioral and work-related risk factors. Pain 126:72-8

44 Denison E, Asenlof P, Lindberg P (2004) Self-efficacy, fear avoidance, and pain intensity as predictors of disability in subacute and chronic musculo-skeletal pain patients in primary health care. Pain 111:245-52

45 Deyo RA, Battie M, Beurskens AJ, Bombardier C, Croft P, Koes B, Malmivaara A, Roland M, Von Korff M, Waddell G (1998) Outcome measures for low back pain research. A proposal for standardized use. Spine 23:2003-13

46 Deyo RA, Loeser JD, Bigos SJ (1990) Herniated lumbar intervertebral disk. Ann Intern Med 112:598-603

47 Deyo RA, Rainville J, Kent DL (1992) What can the history and physical examination tell us about back pain. JAMA 268:760-5

48 Dickerson SS, Kemeny ME (2004) Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol Bull 130:355-91

49 Doland P, Greenfield K, Nelson RJ, Nelson IW (2000) Can exercise therapy improve the outcome of microdiscectomy? Spine 25:1523-1532

50 Donaldson BL, Shipton EA, Inglis G, Rivett D, Frampton C (2006) Comparison of usual surgical advice versus a nonaggravating six-month gym-based exercise rehabilitation program post-lumbar discectomy: results at one-year follow-up. Spine J 6:357-63

51 Donceel P, Du Bois M, Lahaye D (1999) Return to work after surgery for lumbar disc herniation. A rehabilitation-oriented approach in insurance medicine. Spine 24:872-6

52 Dvorak J, Valach L, Fuhrimann P, Heim E (1988) The outcome of surgery for lumbar disc herniation. II. A 4-17 years' follow-up with emphasis on psychosocial aspects. Spine 13:1423-7

53 Edwards S, Clow A, Evans P, Hucklebridge F (2001) Exploration of the awakening cortisol response in relation to diurnal cortisol secretory activity. Life Sci 68:2093-103

54 Ehlert U, Gaab J, Heinrichs M (2001) Psychoneuroendocrinological contributions to the etiology of depression, posttraumatic stress disorder, and stress-related bodily disorders: the role of the hypothalamus-pituitary-adrenal axis. Biol Psychol 57:141-52

55 Elfering A (2006) Work-related outcome assessment instruments. Eur Spine J 15 Suppl 1:S32-43

56 Elfering A, Semmer N, Birkhofer D, Zanetti M, Hodler J, Boos N (2002) Risk factors for lumbar disc degeneration: a 5-year prospective MRI study in asymptomatic individuals. Spine 27:125-34

57 Erdogmus CB, Resch KL, Sabitzer R, Muller H, Nuhr M, Schoggl A, Posch M, Osterode W, Ungersbock K, Ebenbichler GR (2007) Physiotherapy-based rehabilitation following disc herniation operation: results of a randomized clinical trial. Spine 32:2041-9

58 Fairbank JC, Couper J, Davies JB, O'Brien JP (1980) The Oswestry low back pain disability questionnaire. Physiotherapy 66:271-3

59 Filiz M, Cakmak A, Ozcan E (2005) The effectiveness of exercise programmes after lumbar disc surgery: a randomized controlled study. Clin Rehabil 19:4-11

60 Folkman S, Lazarus RS, Gruen RJ, DeLongis A (1986) Appraisal, coping, health status, and psychological symptoms. J Pers Soc Psychol 50:571-9

61 Fordyce WE (1976) Behavioral methods for chronic pain and illness. Mosby, St Louis, MS

62 Fritz JM, George SZ, Delitto A (2001) The role of fear-avoidance beliefs in acute low back pain: relationships with current and future disability and work status. Pain 94:7-15

63 Frymoyer JW (1988) Back pain and sciatica. N Engl J Med 318:291-300

64 Frymoyer JW, Pope MH, Clements JH, Wilder DG, MacPherson B, Ashikaga T (1983) Risk factors in low-back pain. An epidemiological survey. J Bone Joint Surg Am 65:213-8

65 Fugl-Meyer K, S (1997) Health, sexual ability and life satisfaction. In: B Lewin (editor) 219-233

66 Gaab J, Sonderegger L, Scherrer S, Ehlert U (2006) Psychoneuroendocrine effects of cognitive-behavioral stress management in a naturalistic setting-a randomized controlled trial. Psychoneuroendocrinology 31:428-38

67 Garfin SR, Rydevik B, Lind B, Massie J (1995) Spinal nerve root compression. Spine 20:1810-20

68 Geiss A, Larsson K, Junevik K, Rydevik B, Olmarker K (2008) Autologous nucleus pulposus primes T cells to develop into interleukin-4-producing effector cells: An experimental study on the autoimmune properties of nucleus pulposus. J Orthop Res

69 Geiss A, Rohleder N, Kirschbaum C, Steinbach K, Bauer HW, Anton F (2005) Predicting the failure of disc surgery by a hypofunctional HPA axis: evidence from a prospective study on patients undergoing disc surgery. Pain 114:104-17

70 Geiss A, Varadi E, Steinbach K, Bauer HW, Anton F (1997) Psychoneuro-immunological correlates of persisting sciatic pain in patients who underwent discectomy. Neurosci Lett 237:65-8

71   Gejo R, Matsui H, Kawaguchi Y, Ishihara H, Tsuji H (1999) Serial changes in trunk muscle performance after posterior lumbar surgery. Spine 24:1023-8

72   George SZ, Fritz JM, Bialosky JE, Donald DA (2003) The effect of a fear-avoidance-based physical therapy intervention for patients with acute low back pain: results of a randomized clinical trial. Spine 28:2551-60

73   Gibson JN (2007) Surgery for disc disease. Bmj 335:949

74   Gibson JN, Waddell G (2007) Surgical interventions for lumbar disc prolapse: updated Cochrane Review. Spine 32:1735-47

75   Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GA (2001) Causes and consequences of comorbidity: a review. J Clin Epidemiol 54:661-74

76   Gil A, Martinez E, Oyaguez I, Palacios G, Rejas J (2001) Erectile dysfunction in a primary care setting: results of an observational, no-control-group, prospective study with sildenafil under routine conditions of use. Int J Impot Res 13:338-47

77   Goossens ME, Vlaeyen JW, Hidding A, Kole-Snijders A, Evers SM (2005) Treatment expectancy affects the outcome of cognitive-behavioral interventions in chronic pain. Clin J Pain 21:18-26; discussion 69-72

78   Grossi G, Soares JJ, Angesleva J, Perski A (1999) Psychosocial correlates of long-term sick-leave among patients with musculoskeletal pain. Pain 80:607-19

79   Grotle M, Vollestad NK, Veierod MB, Brox JI (2004) Fear-avoidance beliefs and distress in relation to disability in acute and chronic low back pain. Pain 112:343-52

80   Gunnarsson LG, Bäck H, Jones H, Olsson T (2004) Stress recovery during an ocean boat race. Stress and Health 20:165-171

81   Hagg O, Fritzell P, Oden A, Nordwall A (2002) Simplifying outcome measurement: evaluation of instruments for measuring outcome after fusion surgery for chronic low back pain. Spine 27:1213-22

82   Hakkinen A, Ylinen J, Kautiainen H, Airaksinen O, Herno A, Tarvainen U, Kiviranta I (2003) Pain, trunk muscle strength, spine mobility and disability following lumbar disc surgery. J Rehabil Med 35:236-40

83   Hakkinen A, Ylinen J, Kautiainen H, Tarvainen U, Kiviranta I (2005) Effects of home strength training and stretching versus stretching alone after lumbar disk surgery: a randomized study with a 1-year follow-up. Arch Phys Med Rehabil 86:865-70

84   Halldin K (2005) Lumbar disc herniation. Clinical outcome and segmental stability using a new radiological classification and radiostereometry. Doctoral Thesis, Institute of Surgical Sciences Sahlgrenska Academy Göteborg University, Göteborg

85   Hansen AM, Garde AH, Christensen JM, Eller NH, Netterstrom B (2003) Evaluation of a radioimmunoassay and establishment of a reference interval for salivary cortisol in healthy subjects in Denmark. Scand J Clin Lab Invest 63:303-10

86   Hansson T, Jansson KA (2007) Surgical or non-surgical treatment of lumbar disc herniation? SPORT can't give an answer-unpredictability of the natural course was a too difficult match. Lakartidningen 104:1678-9

87   Hasenbring M, Marienfeld G, Kuhlendahl D, Soyka D (1994) Risk factors of chronicity in lumbar disc patients. A prospective investigation of bio-logic, psychologic, and social predictors of therapy outcome. Spine 19:2759-65

88   Hayden JA, van Tulder MW, Malmivaara AV, Koes BW (2005) Meta-analysis: exercise therapy for nonspecific low back pain. Ann Intern Med 142:765-75

89   Heijbel B, Josephson M, Jensen I, Stark S, Vingard E (2006) Return to work expectation predicts work in chronic musculoskeletal and behavioral health disorders: prospective study with clinical implications. J Occup Rehabil 16:173-84

90   Heliovaara M, Impivaara O, Sievers K, Melkas T, Knekt P, Korpi J, Aromaa A (1987) Lumbar disc syndrome in Finland. J Epidemiol Community Health 41:251-8

91   Hides JA, Richardson CA, Jull GA (1996) Multifidus muscle recovery is not automatic after resolution of acute, first-episode low back pain. Spine 21:2763-9

92   Hides JA, Stokes MJ, Saide M, Jull GA, Cooper DH (1994) Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. Spine 19:165-72

93   Hyun JK, Lee JY, Lee SJ, Jeon JY (2007) Asymmetric atrophy of multi-fidus muscle in patients with unilateral lumbosacral radiculopathy. Spine 32:E598-602

94   Häkkinen A, Kuukkanen T, Tarvainen U, Ylinen J (2003) Trunk muscle strength in flexion, extension, and axial rotation in patients managed with lumbar disc herniation surgery and healthy control subjects. Spine 28:1068-1073

95   Häkkinen A, Ylinen J, Kautianen H, Tarvainen U, Kiviranta I (2005) Effects of home strength training versus stretching alone after lumbar disc surgery: A randomized study with a 1-year follow up. Arch Phys Med Rehabil 86:865-870

96   Jansson K-Å (2005) On lumbar spinal stenosis and disc herniation surgery. Doctoral Thesis, Department of surgical sciences, Karolinska Institutet, Stockholm

97   Jansson KA, Nemeth G, Granath F, Jonsson B, Blomqvist P (2005) Health-related quality of life in patients before and after surgery for a herniated lumbar disc. J Bone Joint Surg Br 87:959-64

98   Jensen IB, Linton SJ (1993) Coping strategy questionnaire: reliability of the Swedish version of the CSQ. Scandinavian Journal of Behavior Therapy 22:139-145

99   Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS (1994) Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 331:69-73

100   Jensen MP, Turner JA, Romano JM (1992) Chronic pain coping measures: individual vs. composite scores. Pain 51:273-80

101   Jensen TS, Albert HB, Soerensen JS, Manniche C, Leboeuf-Yde C (2006) Natural course of disc morphology in patients with sciatica: an MRI study using a standardized qualitative classification system. Spine 31:1605-12; discussion 1613

102   Johannsen F, Remvig L, Kryger P, Beck P, Lybeck K, Larsen LH, Warming S, Dreyer V (1994) Supervised endurance exercise training compared to home training after first lumbar diskectomy: a clinical trial. Clin Exp Rheumatol 12:609-14

103   Jonsson B, Stromqvist B (1996) Clinical appearance of contained and non-contained lumbar disc herniation. J Spinal Disord 9:32-8

104   Jonsson B, Stromqvist B (1996) Clinical characteristics of recurrent sciatica after lumbar discectomy. Spine 21:500-5

105   Junge A, Dvorak J, Ahrens S (1995) Predictors of bad and good outcomes of lumbar disc surgery. A prospective clinical study with recommendations for screening to avoid bad outcomes. Spine 20:460-8

106   Jönsson B, Strömqvist B (1995) Influence of age on symptoms and signs in lumbar disc herniation. Eur Spine J 4:202-205

107   Kaila-Kangas L, Kivimaki M, Riihimaki H, Luukkonen R, Kirjonen J, Leino-Arjas P (2004) Psychosocial factors at work as predictors of hospitalization for back disorders: a 28-year follow-up of industrial employees. Spine 29:1823-30

108   Kara B, Tulum Z, Acar U (2005) Functional results and the risk factors of reoperations after lumbar disc surgery. Eur Spine J 14:43-8

109   Katz JN, Stucki G, Lipson SJ, Fossel AH, Grobler LJ, Weinstein JN (1999) Predictors of surgical outcome in degenerative lumbar spinal stenosis. Spine 24:2229-33

110   Kelsey JL, Githens PB, White AA, 3rd, Holford TR, Walter SD, O'Connor T, Ostfeld AM, Weil U, Southwick WO, Calogero JA (1984) An epidemiologic study of lifting and twisting on the job and risk for acute prolapsed lumbar intervertebral disc. J Orthop Res 2:61-6

111 Keskimaki I, Seitsalo S, Osterman H, Rissanen P (2000) Reoperations after lumbar disc surgery: a population-based study of regional and interspecialty variations. Spine 25:1500-8

112 Kirsch I (1997) Response expectancy theory and application: a decennial review. Appl Prev Psychol 6:69-79

113 Kirschbaum C, Hellhammer DH (1989) Salivary cortisol in psycho-biological research: an overview. Neuropsychobiology 22:150-69

114 Kjellby-Wendt G, Carlsson SG, Styf J (2002) Results of early active rehabilitation 5-7 years after surgical treatment for lumbar disc herniation. J Spinal Disord Tech 15:404-9

115 Kjellby-Wendt G, Styf J, Carlsson SG (2001) Early active rehabilitation after surgery for lumbar disc herniation: a prospective, randomized study of psychometric assessment in 50 patients. Acta Orthop Scand 72:518-24

116 Klapow JC, Slater MA, Patterson TL, Atkinson JH, Weickgenant AL, Grant I, Garfin SR (1995) Psychosocial factors discriminate multidimensional clinical groups of chronic low back pain patients. Pain 62:349-55

117 Klenerman L, Slade PD, Stanley IM, Pennie B, Reilly JP, Atchison LE, Troup JD, Rose MJ (1995) The prediction of chronicity in patients with an acute attack of low back pain in a general practice setting. Spine 20:478-84

118 Kohlboeck G, Greimel KV, Piotrowski WP, Leibetseder M, Krombholz-Reindl M, Neuhofer R, Schmid A, Klinger R (2004) Prognosis of multi-factorial outcome in lumbar discectomy: a prospective longitudinal study investigating patients with disc prolapse. Clin J Pain 20:455-61

119 Kori SH, Miller RP, Todd DD (1990) Kinisophobia a new view of chronic pain behaviour. Pain Management Jan/F:35-43

120 Kraemer J (1995) Natural course and prognosis of intervertebral disc dis-eases. International Society for the Study of the Lumbar Spine Seattle, Washington, June 1994. Spine 20:635-9

121 Lampe A, Sollner W, Krismer M, Rumpold G, Kantner-Rumplmair W, Ogon M, Rathner G (1998) The impact of stressful life events on exacerbation of chronic low-back pain. J Psychosom Res 44:555-63

122 Lawson K, Reesor KA, Keefe FJ, Turner JA (1990) Dimensions of pain-related cognitive coping: cross-validation of the factor structure of the Cop-ing Strategy Questionnaire. Pain 43:195-204

123 Lazarus RS (1993) Coping theory and research: past, present, and future. Psychosom Med 55:234-47

124 Leeuw M, Goossens ME, Linton SJ, Crombez G, Boersma K, Vlaeyen JW (2007) The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. J Behav Med 30:77-94

125   Lehto M, Hurme M, Alaranta H, Einola S, Falck B, Jarvinen M, Kalimo H, Mattila M, Paljarvi L (1989) Connective tissue changes of the multifidus muscle in patients with lumbar disc herniation. An immunohistologic study of collagen types I and III and fibronectin. Spine 14:302-9

126   Leinonen V, Kankaanpaa M, Luukkonen M, Kansanen M, Hanninen O, Airaksinen O, Taimela S (2003) Lumbar paraspinal muscle function, perception of lumbar position, and postural control in disc herniation-related back pain. Spine 28:842-8

127   Lethem J, Slade PD, Troup JD, Bentley G (1983) Outline of a Fear-Avoidance Model of exaggerated pain perception. Behav Res Ther 21:401-8

128   Levine S, Ursin H (1991) What is stress? in Stress: Neurobiology and Neuroendocrinology. Marcel Deccer Inc New York, 3-21 pp

129   Lindstrom I, Ohlund C, Nachemson A (1995) Physical performance, pain, pain behavior and subjective disability in patients with subacute low back pain. Scand J Rehabil Med 27:153-60

130   Lindstrom I, Öhlund C, Eek C, Wallin L, Peterson LE, Fordyce WE, Nachemson AL (1992) The effect of graded activity on patients with subacute low back pain. Phys Ther 72:279-293

131   Linton SJ (2002) Early identification and intervention in the prevention of musculoskeletal pain. Am J Ind Med 41:433-42

132   Linton SJ (2000) A review of psychological risk factors in back and neck pain. Spine 25:1148-56

133   Linton SJ, Andersson T (2000) Can chronic disability be prevented? A randomized trial of a cognitive-behavior intervention and two forms of information for patients with spinal pain. Spine 25:2825-31

134   Linton SJ, Boersma K, Jansson M, Svard L, Botvalde M (2005) The effects of cognitive-behavioral and physical therapy preventive interventions on pain-related sick leave: a randomized controlled trial. Clin J Pain 21:109-19

135   Linton SJ, Buer N (1995) Working despite pain: factors associated with work attendance versus dysfunction. Int J Behav Med 2:252-62

136   Linton SJ, Hallden K (1997) Risk factors and the natural course of acute and recurrent musculoskeletal pain: developing a screening instrument. IASP Press, 527-36 pp

137   Loupasis GA, Stamos K, Katonis PG, Sapkas G, Korres DS, Hartofilakidis G (1999) Seven- to 20-year outcome of lumbar discectomy. Spine 24:2313-7

138   Lundberg MKE, Styf J, Carlsson SG (2004) A psychometric evaluation of the Tampa Scale for Kinesiophobia - from a physiotherapeutic perspective. Physiotherpy Theory and Pratice 20:121-133

139   Lutz GK, Butzlaff ME, Atlas SJ, Keller RB, Singer DE, Deyo RA (1999) The relation between expectations and outcomes in surgery for sciatica. J Gen Intern Med 14:740-4

140 MacHale SM, Cavanagh JT, Bennie J, Carroll S, Goodwin GM, Lawrie SM (1998) Diurnal variation of adrenocortical activity in chronic fatigue syndrome. Neuropsychobiology 38:213-7

141 Main CJ, Sullivan MJ, Watson PJ (2008) Pain management. Practical applications of the biopsychosocial perspective in clinical and occupational settings. Elsevier London, 29-55 pp

142 Manniche C, Asmussen K, Lauritsen B, Vinterberg H, Karbo H, Abildstrup SK, Ischer-Nielsen K, Krebs R, Ibsen K (1993) Intensive dynamic back exercises with or without hyperextension in chronic back pain after surgery for lumbar disc protrusion. Spine 18:560-567

143 Manniche C, Asmussen KH, Vinterberg H, Rose Hansen EB, Kramhoft J, Jordan A (1994) Analysis of preoperative prognostic factors in first-time surgery for lumbar disc herniation, including Finneson´s and modified Sprengler´s score systems. Dan Med Bull 41:110-115

144 Mannion AF, Elfering A (2006) Predictors of surgical outcome and their assessment. Eur Spine J 15 Suppl 1:S93-108

145 Mannion AF, Elfering A, Staerkle R, Junge A, Grob D, Dvorak J, Jacobshagen N, Semmer NK, Boos N (2007) Predictors of multidimensional outcome after spinal surgery. Eur Spine J 16:777-86

146 Mannion AF, Taimela S, Muntener M, Dvorak J (2001) Active therapy for chronic low back pain part 1. Effects on back muscle activation, fatigability, and strength. Spine 26:897-908

147 Marhold C, Linton SJ, Melin L (2002) Identification of obstacles for chronic pain patients to return to work: evaluation of a questionnaire. J Occup Rehabil 12:65-75

148 Mason JW (1968) A review of psychoendocrine research on the sympathetic-adrenal medullary system. Psychosom Med 30:Suppl:631-53

149 Mayer TG, Mooney V, Gatchel RJ, Barnes D, Terry A, Smith S, Mayer H (1989) Quantifying postoperative deficits of physical function following spinal surgery. Clin Orthop Relat Res 147-57

150 Mayer TG, Vanharanta H, Gatchel RJ, Mooney V, Barnes D, Judge L, Smith S, Terry A (1989) Comparison of CT scan muscle measurements and isokinetic trunk strength in postoperative patients. Spine 14:33-6

151 McEwen BS, Sapolsky RM (1995) Stress and cognitive function. Current Opinion in Neurobiology 5:205-216

152 Melin R, Fugl-Meyer AR (2003) On prediction of vocational rehabilitation outcome at a Swedish employability institute. J Rehabil Med 35:284-9

153 Mercado AC, Carroll LJ, Cassidy JD, Cote P (2005) Passive coping is a risk factor for disabling neck or low back pain. Pain 117:51-7

154 Miller GE, Cohen S, Ritchey AK (2002) Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoid-resistance model. Health Psychol 21:531-41

155 Miller RP, Kori SH, Todd DD (1991) The Tampa Scale. Unpublished Report, Tampa, FL

156 Millisdotter M, Stromqvist B (2007) Early neuromuscular customized training after surgery for lumbar disc herniation: a prospective controlled study. Eur Spine J 16:19-26

157 Mineka S, Zinbarg R (2006) A contemporary learning theory perspective on the etiology of anxiety disorders: it's not what you thought it was. Am Psychol 61:10-26

158 Mixter W, Barr J (1936) Rupture of the intervertebral disc with involvment of the spinal canal. N Engl J Med 211:210-215

159 Mondloch MV, Cole DC, Frank JW (2001) Does how you do depend on how you think you'll do? A systematic review of the evidence for a relation between patients' recovery expectations and health outcomes. CMAJ 165:174-9

160 Moore JE, Von Korff M, Cherkin D, Saunders K, Lorig K (2000) A randomized trial of a cognitive-behavioral program for enhancing back pain self care in a primary care setting. Pain 88:145-53

161 Munck A, Guyre PM, Holbrook NJ (1984) Physiological functions of glucocorticoids in stress and their relation to pharmacological actions. Endocr Rev 5:25-44

162 Neeck G, Federlin K, Graef V, Rusch D, Schmidt KL (1990) Adrenal secretion of cortisol in patients with rheumatoid arthritis. J Rheumatol 17:24-9

163 Noponen-Hietala N, Virtanen I, Karttunen R, Schwenke S, Jakkula E, Li H, Merikivi R, Barral S, Ott J, Karppinen J, Ala-Kokko L (2005) Genetic variations in IL6 associate with intervertebral disc disease characterized by sciatica. Pain 114:186-94

164 Nordin M, Balague F, Cedraschi C (2006) Nonspecific lower-back pain: surgical versus nonsurgical treatment. Clin Orthop Relat Res 443:156-67

165 Nygaard OP, Kloster R, Solberg T, Mellgren SI (2000) Recovery of function in adjacent nerve roots after surgery for lumbar disc herniation: use of quantitative sensory testing in the exploration of different populations of nerve fibers. J Spinal Disord 13:427-31

166 O´Sullivan PB, Twomey LT, Allison GT (1997) Evaluation of specific stabilizing exercise in the treatment of chronic low back pain with radiologic diagnosis of spondylosis or spondylolisthesis. Spine 22:2959-2967

167 Olmarker K, Larsson K (1998) Tumor necrosis factor alpha and nucleus-pulposus-induced nerve root injury. Spine 23:2538-44

168 Omarker K, Myers RR (1998) Pathogenesis of sciatic pain: role of herniated nucleus pulposus and deformation of spinal nerve root and dorsal root ganglion. Pain 78:99-105

169 Ostelo RJ, de Vet HCW, Wadell G, Kerckhoffs MR, Leffers P, van Tulder MW (2002) Rehabilitation after lumbar disc surgery. Cochrane Database of Systematic Reviews

170 Ostelo RW, de Vet HC, Vlaeyen JW, Kerckhoffs MR, Berfelo WM, Wolters PM, van den Brandt PA (2003) Behavioral graded activity following first-time lumbar disc surgery: 1-year results of a randomized clinical trial. Spine 28:1757-65

171 Ostelo RW, Koke AJ, Beurskens AJ, de Vet HC, Kerckhoffs MR, Vlaeyen JW, Wolters PM, Berfelo MW, van den Brandt PA (2000) Behavioral-graded activity compared with usual care after first-time disk surgery: considerations of the design of a randomized clinical trial. J Manipulative Physiol Ther 23:312-9

172 Ostelo RW, Vlaeyen JW, van den Brandt PA, de Vet HC (2005) Residual complaints following lumbar disc surgery: prognostic indicators of outcome. Pain 114:177-85

173 Ostelo RWJG, van Tulder MW, Vlaeyen JWS, Linton SJ, Morley SJ, Assendelft WJJ (2005) Behavioural treatment for chronic low-back-pain. Cochrane Database of Systematic Reviews

174 Parkkola R, Rytokoski U, Kormano M (1993) Magnetic resonance imaging of the discs and trunk muscles in patients with chronic low back pain and healthy control subjects. Spine 18:830-6

175 Peters LM, Vlaeyen JW, Weer WEJ (2005) The joint contribution of physical pathology, pain related fear and catastrophizing to chronic back pain disability. Pain 113:45-50

176 Postacchini F (2001) Lumbar disc herniation: a new equilibrium is needed between nonoperative and operative treatment. Spine 26:601

177 Price DD, McGrath PA, Rafii A, Buckingham B (1983) The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 17:45-56

178 Pruessner JC, Hellhammer DH, Kirschbaum C (1999) Burnout, perceived stress, and cortisol responses to awakening. Psychosom Med 61:197-204

179 Pruessner JC, Kirschbaum C, Meinlschmid G, Hellhammer DH (2003) Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28:916-31

180 Pruessner JC, Wolf OT, Hellhammer DH, Buske-Kirschbaum A, von Auer K, Jobst S, Kaspers F, Kirschbaum C (1997) Free cortisol levels after awakening: a reliable biological marker for the assessment of adrenocortical activity. Life Sci 61:2539-49

181 Puolakka K, Ylinen J, Neva MH, Kautiainen H, Hakkinen A (2008) Risk factors for back pain-related loss of working time after surgery for lumbar disc herniation: a 5-year follow-up study. Eur Spine J 17:386-92

182 Rantanen J, Hurme M, Falck B, Alaranta H, Nykvist F, Lehto M, Einola S, Kalimo H (1993) The lumbar mulitfidus muscle five years after surgery for a lumbar intervertebral disc herniation. Spine 18:568-574

183 Rhee JM, Schaufele M, Abdu WA (2006) Radiculopathy and the herniated lumbar disc. Controversies regarding pathophysiology and management. J Bone Joint Surg Am 88:2070-80

184 Robinson ME, Riley JL, Myers CD, Sadler IJ, Kvaal SA, Geisser ME, Keefe FJ (1997) The Coping Strategies Questionnaire: a large sample, item level factor analysis. Clin J Pain 13:43-9

185 Roddey TS, Olson SL, Gartsman GM, Hanten WP, Cook KF (2002) A randomized controlled trial comparing 2 instructional approaches to home exercise instruction following arthroscopic full-thickness rotator cuff repair surgery. J Orthop Sports Phys Ther 32:548-59

186 Rosenstiel AK, Keefe FJ (1983) The use of coping strategies in chronic low back pain patients: Relationship to patient characteristics and current adjustment. Pain 17:33-44

187 Rydevik B, Brown MD, Lundborg G (1984) Pathoanatomy and pathophysiology of nerve root compression. Spine 9:7-15

188 Sambrook PN, MacGregor AJ, Spector TD (1999) Genetic influences on cervical and lumbar disc degeneration: a magnetic resonance imaging study in twins. Arthritis Rheum 42:366-72

189 Schade V, Semmer N, Main CJ, Hora J, Boos N (1999) The impact of clinical, morphological, psychosocial and work-related factors on the outcome of lumbar discectomy. Pain 80:239-49

190 Scrimshaw SV, Maher CG (2001) Randomized controlled trial of neural mobilization after spinal surgery. Spine 26:2647-52

191 Seidler A, Bolm-Audorff U, Siol T, Henkel N, Fuchs C, Schug H, Leheta F, Marquardt G, Schmitt E, Ulrich PT, Beck W, Missalla A, Elsner G (2003) Occupational risk factors for symptomatic lumbar disc herniation; a case-control study. Occup Environ Med 60:821-30

192 Sjögren E, Leanderson P, Kristenson M (2006) Diurnal saliva cortisol levels and relations to psychosocial factors in a population sample of middel-aged Swedish men and women. Int J Behav Med 13:193-200

193 Skinner BH (1953) Science and human behaviour. McMillan, New York

194 Smyth JM, Ockenfels MC, Gorin AA, Catley D, Porter LS, Kirschbaum C, Hellhammer DH, Stone AA (1997) Individual differences in the diurnal cycle of cortisol. Psychoneuroendocrinology 22:89-105

195 Spangfort EV (1972) The lumbar disc herniation. A computor-aided analysis of 2504 operations. Acta Orthop Scand Suppl 95:1421-1495

196 Staal JB, Hlobil H, Twisk JW, Smid T, Koke AJ, van Mechelen W (2004) Graded activity for low back pain in occupational health care: a randomized, controlled trial. Ann Intern Med 140:77-84

197 Stromqvist B, Fritzell P, Hagg O, Jonsson B (2005) One-year report from the Swedish National Spine Register. Swedish Society of Spinal Surgeons. Acta Orthop Suppl 76:1-24

198 Strömqvist B, Hedlund R, Jönsson B, Tullberg T (2007) Ländryggens sjukdomar. Läkartidningen 104:1498-1502

199 Sullivan M, Karlsson J, Ware JE (1994) Hälsoenkät SF-36. Svensk manual och tolkningsguide (SF-36 Health survey, Swedish Manual and Interpretation Guide), Sahlgrenska University Hospital, Göteborg.

200 Sullivan MJ, Adams H, Rhodenizer T, Stanish WD (2006) A psychosocial risk factor-targeted intervention for the prevention of chronic pain and disability following whiplash injury. Phys Ther 86:8-18

201 Sullivan MJ, Stanish W, Waite H, Sullivan M, Tripp DA (1998) Catastrophizing, pain, and disability in patients with soft-tissue injuries. Pain 77:253-60

202 Swinkels-Meewisse IE, Roelofs J, Verbeek AL, Oostendorp RA, Vlaeyen JW (2003) Fear of movement/(re)injury, disability and participation in acute low back pain. Pain 105:371-9

203 Takahashi H, Suguro T, Okazima Y, Motegi M, Okada Y, Kakiuchi T (1996) Inflammatory cytokines in the herniated disc of the lumbar spine. Spine 21:218-24

204 Taylor ME (1989) Return to work following back surgery: a review. Am J Ind Med 16:79-88

205 Theorell T (1996) Possible mechanisms behind relationship between the demand-control-support model and disorders of the locomotor system. Taylor & Frances, London 65-73 pp

206 Trief PM, Grant W, Fredrickson B (2000) A prospective study of psychological predictors of lumbar surgery outcome. Spine 25:2616-21

207 Urban JP (2000) Present perspectives on cartilage and chondrocyte mechanobiology. Biorheology 37:185-90

208 Ursin H, Eriksen H (2007) Cognitive activation theory of stress, sensitization, and common health complaints. Ann N Y Acad Sci 1113:304-10

209 Ursin H, Eriksen HR (2004) The cognitive activation theory of stress. Psychoneuroendocrinology 29:567-92

210 Wadell G (1998) The back pain revolution. Churchill Livingstone, Edinburgh

211 Wadell G (1996) Low back pain: A twentieth century health care enigma. Spine 21:2820-2825

212 Ware JEJ, Sherbourne CD (1992) The MOS 36-item Short-Form health survey (SF-36). 1. Conceptual framework and item selection. Med Care 30:473-483

213 Wera GD, Dean CL, Ahn UM, Marcus RE, Cassinelli EH, Bohlman HH, Ahn NU (2008) Reherniation and failure after lumbar discectomy: a comparison of fragment excision alone versus subtotal discectomy. J Spinal Disord Tech 21:316-9

214 Vingård E (2000) Hållbar arbetshälsa i kommuner och landsting inför 2000-talet. Sektionen för personskadeprevention, Karolinska Institutet, Stockholm

215 Virri J, Gronblad M, Seitsalo S, Habtemariam A, Kaapa E, Karaharju E (2001) Comparison of the prevalence of inflammatory cells in subtypes of disc herniations and associations with straight leg raising. Spine 26:2311-5

216 Vlaeyen J, W, S., Kole-Snijders AMJ, Rotteveel AM, Ruesink R, Heuts PHTG (1995) The role of fear of Movement/(re)injury in pain disability. J Occup Rehabil 5:235-252

217 Vlaeyen JW, Haazen IW, Schuerman JA, Kole-Snijders AM, van Eek H (1995) Behavioural rehabilitation of chronic low back pain: comparison of an operant treatment, an operant-cognitive treatment and an operant-respondent treatment. Br J Clin Psychol 34:95-118

218 Vlaeyen JW, Kole-Snijders AM, Boeren RG, van Eek H (1995) Fear of movement/(re) injury in chronic low back pain and its relation to behavioural performance. Pain 62:363-72

219 Vlaeyen JW, Linton SJ (2000) Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain 85:317-32

220 Woertgen C, Rothoerl RD, Breme K, Altmeppen J, Holzschuh M, Brawanski A (1999) Variability of outcome after lumbar disc surgery. Spine 24:807-11

221 Woertgen C, Rothoerl RD, Holzschuh M, Breme K, Brawanski A (1998) Are prognostic factors still what they are expected to be after long-term follow-up? J Spinal Disord 11:395-9

222 Wood PH (1986) The basis of rheumatological practice, including nomenclature and classification. Churchill and Livingstone, 19-58 pp

223 Vroomen PC, de Krom MC, Knottnerus JA (1999) Diagnostic value of history and physical examination in patients suspected of sciatica due to disc herniation: a systematic review. J Neurol 246:899-906

224 Vucetic N, Astrand P, Guntner P, Svensson O (1999) Diagnosis and prognosis in lumbar disc herniation. Clin Orthop Relat Res 116-22

225 Wüst S, Hellhammer DH, Federenko I, Schommer N, Kirschbaum C (2000) The cortisol awakening response - normal values and confounders. Noise Health 2:79-88

226 Yilmaz F, Yilmaz A, Merdol F, Parlar D, Sahin F, Kuran B (2003) Efficacy of dynamic lumbar stabilization exercise in lumbar microdiscectomy. J Rehabil Med 35:163-7

227 Yorimitsu E, Chiba K, Toyama Y, Hirabayashi K (2001) Long-term outcomes of standard discectomy for lumbar disc herniation: a follow-up study of more than 10 years. Spine 26:652-7

228 Yoshihara K, Shirai Y, Nakayama Y, Uesaka S (2001) Histochemical changes in the multifidus muscle in patients with lumbar intervertebral disc herniation. Spine 26:622-6

229 Zanoli G (2005) Outcome assessment in lumbar spine surgery. Acta Orthop Suppl 76:5-47

230 Zhu XZ, Parnianpour M, Nordin M, Kahanovitz N (1989) Histochemistry and morphology of erector spinae muscle in lumbar disc herniation. Spine 14:391-7

231 Öhrvik J (2002) Nonparametric methods in the two-way layout. Chiang Mai J Sci 29:103-115