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Cognitive-behavioural therapy for lumbar spinal fusion patients

A clinical and economic evaluation

PhD dissertation

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Preface

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People are not disturbed by things,
but by the view they take on them.
(Epictetus)

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Abbreviations

CBT	Cognitive-behavioural therapy
CEA	Cost-effectiveness analysis
CI	Confidence Interval
CLBP	Chronic low back pain
CSQ	Coping Strategies Questionnaire
CUA	Cost-utility analysis
DREAM	The Danish Register for Evaluation of Marginalization
DRG	The Diagnosis-Related-Grouping
FABQ	Fear-avoidance Beliefs Questionnaire
ICER	Incremental cost effectiveness ratio
IQR	Interquartile range (25th and 75th percentiles)
LSF	Lumbar spinal fusion
LBPRS	Low back pain rating scale
NHSR	The National Health Service Register
NPR	The National Patient Registry
ODI	Oswestry Disability Scale
PLF	Posterior lateral fusion
RCT	Randomized clinical trial
TLIF	Transforaminal interbody fusion
QALY	Quality-adjusted life years
SD	Standard deviation

1. English summary

Background: In the last decades the Western World has seen a significant increase in lumbar spinal fusion (LSF) rates due to degenerative spinal disorders. Although surgical outcomes have improved, equivalent improvements in functional recovery and return to work seems to lag behind. Few published studies have looked at the potential of rehabilitation to improve the surgical outcome, but rehabilitation programmes using cognitive-behavioural therapy (CBT) are recommended. Further, initiating interventions preoperatively seems beneficial in terms of reducing bed days and hospital costs. Only limited data exists in the field of LSF regarding the use of interventions using a CBT approach, initiated already prior to surgery.

Objective: The aim of the thesis was to develop and evaluate a preoperative CBT intervention on outcomes of LSF in terms of 1) in-hospital pain, analgesic use, mobilisation and discharge, 2) disability, pain coping, pain and return to work and 3) the cost-effectiveness from a societal perspective.

Materials and methods: The study was a randomised clinical trial with 1 year follow-up. A total of 90 patients undergoing LSF due to disc degeneration, stenosis or spondylolisthesis were included. The patients were allocated to either usual care (control group) or usual care extended with a preoperative CBT intervention (CBT group). Questionnaires regarding disability, pain, quality of life, psychological variables and costs were completed at baseline, 3 months, 6 months and 1 year after surgery. Additional data was gathered from national registers and medical records. A health economic evaluation was conducted alongside the trial.

Results: 1) During the first three postoperative days significantly more patients in the CBT group achieved independent mobility, and their analgesic use was slightly lower. There was no difference between the two groups in terms of back and leg pain or length of stay.

2) Three months after surgery the CBT group reported a significantly larger reduction in disability compared to the control group. At the 1-year follow-up this difference was no longer significant due to improvements in the control

group. Back and leg pain, pain coping and return to work was comparable between groups.
3) Preoperative CBT was more effective and at the same time cost neutral when considering the overall health care sector and labour market perspective. Our results remained largely unaffected by the sensitivity analyses performed, confirming the robustness of our findings.
Conclusion: Our findings support the use of a preoperative CBT intervention for patients undergoing LSF, as we found patients to achieve faster recovery of function and increased quality of life at limited extra costs. With a few adjustments we recommend that the intervention be implemented into the course of treatment for patients undergoing LSF.

2. Danish summary

Baggrund: Vesten har i de sidste årtier set en kraftig stigning i antallet af stivgørende rygoperationer (LSF) som følge af degenerative lidelser. Selvom udfaldet af operationen kirurgisk set er god, kan de tilsvarende forbedringer på funktionelle mål og arbejdstilbagevendelse stadig optimeres. Kun få studier har undersøgt hvordan rehabilitering kan bidrage til at forbedre udfaldet efter operationen. Dog anbefales det at anvende kognitiv adfærdsterapi i rehabiliteringen (CBT). Yderligere ser det ud til, at indlæggelsestid og hospitalsomkostninger kan reduceres, hvis indsatserne påbegyndes allerede før operationen. Effekten af en præoperativ rehabiliteringsindsats med brug af CBT er endnu ikke undersøgt til denne patientgruppe.

Formål: At udvikle og evaluere en præoperativ CBT intervention til patienter der gennemgår LSF i forhold til 1) smerte, forbrug af smertestillende, mobilitet samt indlæggelsestid 2) funktionsevne, smerte, smerte coping og arbejdstilbagevendelse samt 3) omkostningseffektivitet i et samfundsøkonomisk perspektiv.

Materiale og metode: Studiet er en klinisk randomiseret undersøgelse med 1 års opfølgning. Der blev inkluderet 90 patienter, som gennemgik LSF på grund af discus degeneration, stenose eller spondylolistese. Patienterne blev tilfældigt udtrukket til enten vanlig behandling (kontrol gruppe) eller vanlig behandling *plus* en præoperativ CBT intervention (CBT gruppe). Patienterne udfyldte spørgeskemaer om funktionsevne, smerte, livskvalitet, og psykologiske faktorer ved baseline, 3 mdr., 6 mdr. og 1 år efter operationen. Yderligere blev der indhentet data via nationale registre og patient journaler. Der blev foretaget en sundhedsøkonomisk evaluering sideløbende med det randomiserede studie.

Resultater: 1) Signifikant flere patienter i CBT gruppen opnåede selvstændig mobilitet i løbet af de første 3 dage efter operationen, og deres forbrug af smertestillende medicin var lavere. Der var ingen forskel mellem grupperne i forhold til smerter og indlæggelsestid.

2) 3 mdr. efter operationen rapporterede CBT gruppen en signifikant bedre funktionsevne end kontrol gruppen. Ved 1 års opfølgningen var forskellen udlignet, grundet en forbedring i kontrolgruppens funktionsniveau. Smerte, smerte håndtering og arbejdstilbagevendelse var ens i de to grupper.
3) Præoperativ CBT var både mere effektivt og uden ekstra omkostninger i forhold til både sundhedsvæsenet og arbejdsmarkedet. Resultaternes robusthed blev bekræftet med sensitivitetsanalyser.
Konklusion: Overordnet set støtter vores fund anvendelsen af en præoperative CBT indsats til patienter der gennemgår LSF, da vi fandt at patienterne hurtigere genvandt deres funktionsevne og fik forbedret livskvalitet, uden ekstra omkostninger. Vi anbefaler at interventionen implementeres i behandlingsforløbet for patienter der gennemgår LSF med nogle enkelte små justeringer.

3. Introduction

3.1 The role of cognitive-behavioural therapy in surgical treatment of chronic pain

Since the introduction of cognitive-behavioural therapy (CBT) for management of depression in the late 1970s[1], CBT has become an increasingly popular treatment modality for a wide range of psychological and musculoskeletal disorders [2-4]. The positive effects of CBT in chronic low back pain (CLBP) management are by now well-established[3-5]. The traditional therapeutic approach to CLBP is a purely biomedical one where pain is ascribed to physical pathology and symptoms are thought to be directly proportional to the physical pathology[6, 7]. This biomedical model has been criticized for its failure to address the roles of psychosocial variables and the dynamic interaction of these variables with physiological factors, as described in the biopsychosocial model of chronic pain [6-8]. In CBT pain is acknowledged as a complex, subjective phenomenon and the use of CBT in the management of CLBP thus fits well into the biopsychosocial perspective[2, 9, 10].

The use of CBT in a surgical treatment course for chronic pain is, however, a poorly explored area, despite the fact that continued pain, disability and reduced quality of life are well-known consequences following surgery for chronic pain conditions [11, 12]. Surgery rates for CLBP, one of the most common and costly chronic pain conditions in the Western World[13] , have risen significantly during the past two decades, with lumbar spinal fusion surgery (LSF) being the most common procedure performed for degenerative disc disease and spondylolisthesis [14-19]. Many of the patients seeking surgical treatment due to intractable CLBP have developed negative expectations about the consequences of their pain and about their ability to cope with the pain and they have eventually become affected both physically, socially and emotionally [8, 20]. Such negative pain beliefs and maladaptive coping strategies have been found to play a significant role in predicting poorer surgical outcomes [21-25]. This supports the use of a biopsychosocial approach to support rehabilitation for patients undergoing spine surgery for CLBP. The use of CBT has shown

promising results both in studies comparing LSF with a structured exercise intervention using CBT[26-28], and in studies investigating the use of CBT in postoperative rehabilitation following spine surgery[29, 30]. Moreover, studies have found beneficial effects of initiating rehabilitation already prior to surgery [31-33]. With the preoperative CBT intervention developed for the present study we aimed to design an intervention built on the best existing knowledge and evidence. It is important to remember that this is not a matter of replacing medical therapy with psychological therapy, but about bringing the insights of different professions to productive, integrated use to treat this difficult group of patients in the best possible way.

4. Background

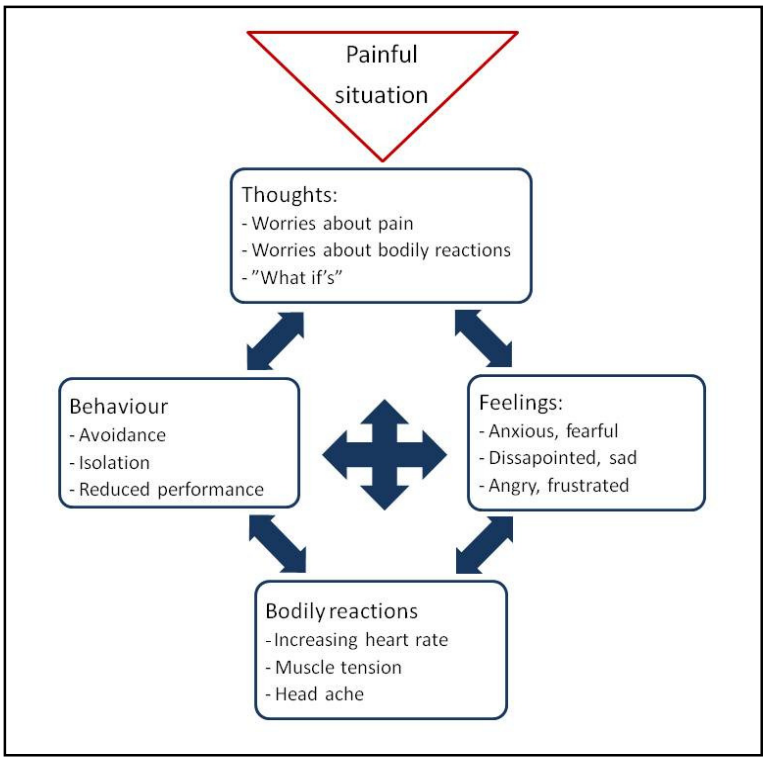
4.1 Cognitive-behavioural therapy

Many different variations of CBT exist and elements of CBT are frequently used alone or in combination with other treatment modalities. CBT can be provided as individual therapy or in group sessions, in sessions of different duration and as short-term or long-term therapy. Studies using CBT principles for pain-management have found no difference in treatment outcome between group treatment and individual treatment and between programmes lasting 15, 30 or 60 hours [4, 34]. In the following section a brief introduction to the cognitive-behavioural model and its underlying assumptions is given.

The cognitive-behavioural model

According to this model, an individual's cognitions are rooted in fundamental self-images, shaped by previous experiences and learning. The different perceptions and assumptions we possess are important for the way we process information as we selectively extract information that confirms our fundamental self-images. Thus, two individuals may interpret the same situation quite differently due to their unique cognitions, and in consequence thereof their behaviour in response to the same situation will also differ. The CB model further hypothesises that when exposed to a stressful situation or condition, such as a prolonged period of ongoing pain, our self-image and perception of the world tend to become negatively biased. This induces a negative pattern of thinking which may increase emotional distress and unhealthy behavioural patterns related to the painful experience, reinforcing the experience of pain. This link between thoughts, feelings, bodily reactions and behaviour is illustrated in Figure 1. Knowledge about the individual's beliefs, appraisals and coping repertoires is therefore critical for optimal treatment planning and evaluation of treatment outcome [2, 10].

Figure I. The cognitive diamond illustrating the link between thoughts, feelings, bodily reactions and behaviour



A wide range of cognitive and behavioural techniques are used in CBT [2, 10]. *Cognitive techniques* target the negative cognitive factors (thoughts, beliefs, appraisals and expectations) that contribute to negative emotions such as fear, anxiety, depression, guilt and anger, reinforcing the pain experience. The two main goals of cognitive techniques are 1) to build awareness of how negative thoughts affect mood, behaviour and pain; 2) to challenge or modify these thoughts in order to promote improved pain coping. *Behavioural techniques* are based on the learning principles derived from Fordyce's operant conditioning theory, where social reinforcement and learning processes play a central role[35]. The goals of behavioural techniques are 1) to increase the frequency of well behaviours and involvement in pleasurable activities; 2) to decrease maladaptive pain behaviours (e.g. excessive bed rest or exaggerated verbal pain behaviour).

The overall aim of CBT is to help the patients reconceptualise their situation and their own role in improving their physical and mental health. Furthermore, CBT aims to help the patients reach a positive adaptation to the limitations that their physical impairments inflict.

4.2. A biopsychosocial perspective on chronic low back pain

The first attempt to develop a more integrative model of pain was the gate control theory[36], which differentiated between three systems related to the processing of nociceptive stimulation. These systems were the sensory-discriminative, the motivational-affective, and the cognitive-evaluative systems, which were all thought to contribute to the subjective experience of pain. A new era was initiated a decade later with Fordyce's theory of the role of operant factors in chronic pain [35]. Here, behavioural manifestations of pain rather than pain per se were considered central. Although operant factors undoubtedly play a role in the maintenance of pain and disability, the behavioural model was criticised for not considering the emotional and cognitive aspects of pain. In response Vlayen and Linton presented the fear-avoidance model, a hypothetical model for framing chronic pain[37]. This model focuses on the importance of the individual's attitudes and beliefs based on prior experiences and learning history. This means that a negative interpretation of pain (e.g. as a sign of serious pathology) often leads to an excessive fear of pain and injury, thereby increasing disability and hampering participation in everyday life. CBT fits well into the biopsychosocial model of pain as it recognises the important role of contextual factors and the principles of learning theory, and because it incorporates these elements within an integrated perspective on pain management [2, 8, 10].

In a societal perspective, low back pain is considered one of the leading causes of disability, reduced quality of life and work absence, imposing a high economic burden on individuals, communities and health care

systems [13, 38]. In Denmark, the National Institute of Public Health has estimated the societal costs of low back pain to be in the region of €1,6 billion per year[39].

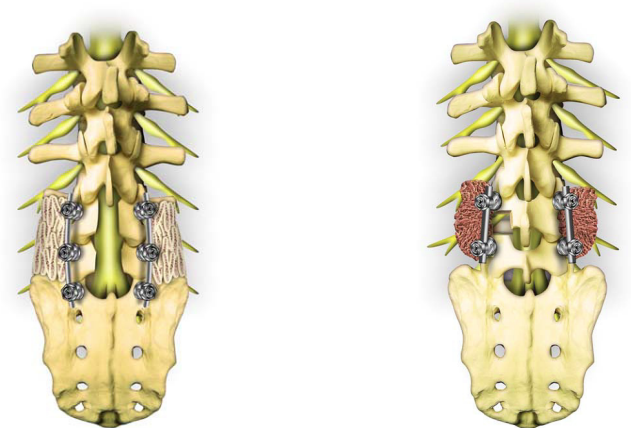
4.3. Lumbar spinal fusion for chronic low back pain

When conservative treatment has failed, LSF is a commonly offered treatment for selected groups of patients suffering CLBP. The past decades have seen a significant increase in LSF rates due to CLBP caused by degenerative spinal disorders. The largest increase has been seen in the US where the annual rates of LSF procedures performed rose by 170% in the period 1998-2008, corresponding to a frequency of 61 operations per 100,000 in the year 2008 [15, 40]. Similar increases have been reported in Australia and Europe, although surgery rates here are somewhat lower than in the US. Thus, in the period 1997 to 2006, the LSF rates rose by 374% in Australia (to 23.4 operations per 100,000 in 2006)[17]. In Denmark, 30 operations per 100,000 were performed in 2010[41]. A variety of factors may have contributed to this increase, such as an improved biomechanical understanding of the spine, improved diagnostic imaging techniques, increased availability of fixation devices, and the overall increase in the population's life expectancy.

Since the earliest descriptions of spinal fusion by Russel Hibbs in 1911[42], fusion surgery has become one of the most commonly deployed procedures for treating various conditions of the spine including deformity, trauma, degenerative disc disease, stenosis and spondylolisthesis[15][42]. The term *spinal fusion* covers surgical procedures aimed at limiting movement between painful joints of the spine by fusing one or more adjacent vertebrae with a view to relieving persistent pain of the back and/or legs. There are three main components to the surgical procedure: decompression of trapped nerve tissue, stabilisation of the spine, and restoration of the natural curves of the spine. Although the underlying principles of spinal fusion have remained the same for several years, the techniques have evolved dramatically to include a number of different implant devices, e.g. cages, pedicle screws and rods. Today, LSF can be handled through minimal invasive surgery, which reduces the surgical trauma and potentially improves rehabilitation[43].

In the present study, the two LSF techniques applied were *posterolateral fusion* (PLF) and *transforaminal interbody fusion* (TLIF) (Figure 2). The PLF involves fusion of the posterior elements by placing bone graft alongside the transverse and spinous processes, eventually causing the two vertebrae to fuse together. The TLIF involves fusing of the anterior elements of the spine (the vertebral bodies) by removing the intervertebral disc and replacing it with interbody spacers (not shown).

Figure 2. PLF (left) and TLIF (right) procedures[44]



The optimisation of LSF techniques has improved surgical outcomes (i.e. low complication rates and high fusion rates)[43], but an equivalent improvement in patient-perceived complications, functional recovery and return to work seems to lag behind [19, 45-47]. Several reviews have been published, some investigating the effect of LSF in various subpopulations, others comparing different surgical techniques [43, 48-51], or comparing LSF with non-surgical initiatives [45, 47, 52, 53]. Overall there seems to be a superior effect of LSF in certain patient subpopulations, but the suitability of LSF is questionable in patients with intractable CLBP with an unclear diagnosis. This may be explained by the complex nature of CLBP, described in Chapter 4.2., which possibly commands a more multi-faceted approach than what can be achieved with surgery and/or exercise therapy alone.

4.4. Lumbar spinal fusion and rehabilitation

The past 12 years have seen the publication of a number of rehabilitation studies in the field of LSF, with the aim to improve postoperative outcomes through the application of different rehabilitation strategies. A literature search was performed to identify studies investigating rehabilitation for patients undergoing LSF. The following databases were used: PubMed, Cochrane Database of Systematic Reviews, PEDro, PsycInfo and EMBASE. We identified five studies examining the clinical outcomes of using different rehabilitation strategies in LSF populations. Three of these studies examined interventions using cognitive-behavioural elements[29, 30, 54], whereas the other two studies focused on the effect of the timing of rehabilitation[31, 55]. Three of these studies additionally provided health economic evaluations or a cost-analysis [56-58] In the following two sections a description of these studies will be given. An overview of the studies is presented in Table 1 (clinical outcomes) and Table 2 (health economic outcomes).

4.4.1. Clinical studies in LSF rehabilitation

In 2003, Christensen *et al* published a study evaluating the effect of a "Back Café" in postoperative rehabilitation[54]. Patients were allocated to either: A) A video group (n=29) receiving a video instruction of the exercises to be performed at home for 8 weeks; B) A "back-café" group (n=26) receiving exercises similar to those given to the video group and, additionally, three "back-café" meetings with a physiotherapist and peer patients for social and psychological support; C) an exercise group (n=26) receiving supervised exercises biweekly for 8 weeks. The back-café group was superior to both the video group and the exercise group in terms of daily function and return to work, and reported less pain than the exercise intervention.

In 2010, Nielsen *et al* investigated a prehabilitation intervention consisting of a home-based exercise programme to be performed 6-8 weeks prior to surgery[31]. The intervention also involved optimised nutrition, patient-controlled epidural analgesia and intensified postoperative mobilisation. The

control group received no preoperative intervention and standard postoperative care. Their findings were in favour of prehabilitation with patients reaching recovery milestones faster and having shorter hospital stay. After 6 months, however, there were no differences between groups in terms of functional mobility and quality of life.

In another study published in 2010, Abbott and colleagues documented the superiority of a psychomotor therapy intervention consisting of three outpatient sessions targeting maladaptive pain-coping strategies using CBT techniques in combination with a home-based exercise programme focused on motor control[29]. The control intervention was a home programme designed to strengthen the back-, abdominal- and leg muscles and to improve cardiovascular fitness. Psychomotor therapy resulted in significantly better outcomes at 2-3 years follow-up both in terms of disability, pain, psychological variables and return to work.

In 2012, the effect of initiating postoperative rehabilitation 6 weeks as opposed to 12 weeks after LSF was examined by Oestergaard et al. The rehabilitation intervention was a group-based, supervised exercise programme consisting of four 2-hour sessions. The group initiating rehabilitation after 6 weeks reported inferior outcomes in terms of disability, pain and quality of life at the 1 year follow-up compared with the group starting rehabilitation 12 weeks after LSF [55].

In the most recent study published in 2014, 130 LSF patients were randomly allocated to A) A 4-week postoperative exercise programme focusing on postural control, walking and ergonomic advice (booklet) or B) The 4-week exercise programme plus eight individual 1-hour CBT sessions with a psychologist[30]. The CBT intervention proved superior in terms of improving pain, disability and psychological parameters in the first year following surgery.

Overall, these five studies show that rehabilitation interventions using CBT, or elements hereof, produce superior outcomes for patients undergoing LSF. Further, it seems that preoperative initiation of the rehabilitation intervention

could be beneficial, but the literature on this matter is very limited within spine surgery. However, the notion that the preoperative timing is important is supported by findings within the field of hip and knee arthroplasty, where the effects of preoperative interventions, mainly in the shape of patient education or exercise programmes, have been investigated more extensively[32, 33, 59]. Here, the literature indicates beneficial effects of preoperative interventions in terms of increased knowledge levels, reduced preoperative anxiety, lower opioid use, shorter length of stay and reduced postoperative pain.

Table 1. Clinical studies

Reference	Design / N / follow-up	Diagnosis / fusion techniques	Intervention	Outcome measures	Results and conclusion
Christen-sen et al, 2003 [54]	RCT / 2 yrs follow-up A: Video (n=29) B: Back-café (n=26) C: Exercise (n=26)	Isthmic spondylo-listhesis, degeneration after decompression. PLF with instrumentation 360-degree fusion	A. Video instruction of exercises. B: 3 back-café meetings with physio and peer patients and exercises as video group. C: Supervised exercise for 8 weeks.	Low Back Pain Rating Scale Return to work	The back café-group was better at performing daily functions and had higher return to work rate than the video- and the exercise group. Video and back-café group had less pain than exercise group
Nielsen Et al, 2010[31]	RCT / 6 mos follow-up A: Prehabil-itation (n=30) B: Usual care (n=30)	Degenerative diseases with LBP and radiating pain PLF with/without instrumentation	A: Preoperative training, information, optimised nutrition,, intensified postoperative mobilisation. B: Usual care	Brief Pain Inventory, Rolland Morris, Sit to Stand test, Timed Up and Go, 15D test Length of stay	The prehabilitation group had shorter length of stay and faster recovery of milestones. No difference between groups on quality of life or functional mobility after 6 months
Abbott et al, 2010[29]	RCT / 2- 3 yrs follow-up A: Exercise (n=54) B: Psycho-motor therapy (n=53)	Spinal stenosis, spondylosis, spondylol-isthesis, DDD TLIF PLF with/ without instrumentation	A: 12 week home-based exercise programme B: 3 outpatient CBT sessions and 12-week home-based program me.	ODI, Low back pain, EQ-5D, SF36, Self-Efficacy Scale, Back Beliefs Questionnaire, Coping Strategies Questionnaire	The experimental group achieved significantly better results in terms of disability, self-efficacy, outcome expectancy, fear of movement and work resumption 2-3 years after surgery.

Table 1. Clinical studies (continued)

Reference	Design / N / follow-up	Diagnosis / fusion techniques	Intervention	Outcome measures	Results and conclusion
Oestergaard et al, 2012 and 2013 [55, 60]	RCT with 1 year follow-up A: 6-week group (n=41) B: 12-week group (n=41)	Degenerative disc disease or spondylolisthesis grade I-II PLF with instrumentation TLIF	A: Group-based exercise programme initiated 6 weeks after surgery B: Same as group A but initiated 12 weeks after surgery	ODI Dallas Pain Questionnaire, Return to work, 6 minute walk test, Aastrand Fitness test.	Inferior outcomes on disability and pain were observed for the 6-week group. No difference between groups was present for return to work and physical performance
Monticone et al, 2014 [30]	RCT with 1 year follow-up A: Exercise therapy (n=65) B: Cognitive-behavioural therapy (n=65)	Degenerative or isthmic spondylolisthesis and/or stenosis. Fusion techniques not described	A: 4 week exercise programme focused on postural control, walking and ergonomic advice. B: 8 CBT sessions with psychologist, exercise program as group A.	ODI, Pain Catastro-phising Scale, Tampa Scale for Kinesio-phobia, Numeric Rating Scale, SF36.	The CBT intervention superior to the exercise intervention in reducing disability, dysfunctional thoughts, pain, and enhancing quality of life

4.4.2. Health economic studies in lumbar spinal fusion rehabilitation

The studies described in Chapter 4.4.1. provide important information about the clinical effectiveness of the trial interventions, but they do not allow us to establish whether the interventions represent good value for money. To answer that question, a health economic evaluation is essential as a supplement to a clinical trial[61]. In the field of LSF surgery three studies have explored the health economic consequences of different rehabilitation programmes. These evaluations are based on the studies by Christensen et al [54], Nielsen et al [31] and Oestergaard et al[55].

Reporting on the cost-effectiveness of Christensen's study, Soegaard *et al* found that the experimental "back-café" intervention was both clinically superior and more cost-effective than the video intervention and the intensive physiotherapy [58]. Seen from a hospital perspective, the video intervention was by far the least costly; but in a societal perspective this intervention turned out to be the most expensive during the 2-year follow-up due to a large use of general practice and physiotherapy.

A smaller scale cost-analysis including in-hospital costs and productivity costs was performed to supplement the clinical study by Nielsen et al [56]. Prehabilitation was found to be less costly due to a shorter length of stay and a shorter sick leave period during the 6-month follow-up, and at the same time the two groups achieved comparable outcomes for quality-adjusted life years.

The most recent economic evaluation of the study by Oestergaard et al showed that initiating rehabilitation after 6 weeks as compared with 12 weeks after LSF was both less effective and more costly [57]. An overview of the studies is given in Table II.

Table II. Health economic studies

Reference	.Design	Effect parameter	Types of cost	Results /conclusion
Soegaard et al, 2007 [58]	CEA* N = 90 Follow-up: 2 years	Dallas Pain Questionnaire, Low Back Pain Rating Scale	Costs in primary and secondary healthcare sector, patient costs and productivity costs.	The back-café group achieved superior clinical effects and were also the least costly. There was up to 100% probability of the back-café intervention being more cost-effective compared to both supervised exercises and video instruction of exercises
Nielsen et al, 2010 [56]	Cost-analysis N = 60 Follow-up: 6 months	Quality of life survey tool (15D)	Pre- and postoperative costs in primary health care sector, in-hospital costs (without surgery) and productivity costs.	An intervention with preoperative training and information and intensive postoperative mobilisation was less costly (€10,369 *versus* €12,488) and produced similar quality of life outcomes (0.91 QALY *versus* 0.90) than usual care for LSF patients.
Oestergaard et al, 2014 [57]	CEA* and CUA** N = 82 Follow-up: 1 year	Oswestry Disability Index, Quality-adjusted Life years (EQ-5D)	Costs in primary and secondary healthcare sector, patients costs and productivity costs	Initiating rehabilitation 6 weeks after LSF produced inferior outcomes and at a higher cost than initiation after 12 weeks. Thus, there was less than 15% probability of early initiation of rehabilitation being cost-effective for LSF patients

*CEA = cost-effectiveness analysis
**CUA = cost-utility analysis

4.5. Summary of background

The past two decades have seen a significant rise in the rates of LSF in patients suffering CLBP due to degenerative spinal disorders. Few published studies have investigated the potential of rehabilitation to improve the surgical outcome for this study population, but rehabilitation programmes using cognitive-behavioural therapy (CBT) are recommended. Moreover, initiation of interventions preoperatively seems to have beneficial effects by reducing bed days and hospital costs. In the field of LSF, no study has examined a preoperative rehabilitation intervention using a CBT approach. Extant literature recommends that a health economic evaluation be conducted as a supplement to clinical studies in order to provide decision-makers with the necessary information when considering the use of scarce resources in health care.

5. Aims and hypothesis

The overall aim of the thesis was to develop and evaluate a preoperative CBT intervention on outcomes of LSF surgery for CLBP. The thesis has four objectives:

Paper I:

Objective: To describe the theoretical basis and the details of the preoperative CBT intervention developed for the present study in accordance with the international recommendations regarding research using complex interventions.

Paper II:

Objective: To examine the effect of a preoperative CBT intervention on in-hospital pain, analgesic use, mobilisation and discharge.

Hypothesis: Participating in a preoperative CBT intervention will have a positive effect on acute postsurgical pain, will facilitate mobilisation during hospitalisation, and will reduce length of stay compared to usual care for patients undergoing LSF.

Paper III:

Objective: To examine the effect of a preoperative CBT intervention on disability, pain, pain coping and return to work.

Hypothesis: Participation in a preoperative CBT intervention will lead to decreased disability and pain, improved pain coping and faster return to work compared to usual care for patients undergoing LSF.

Paper IV:

Objective: To examine the cost-utility and the cost-effectiveness of a preoperative CBT intervention from a societal perspective.

Hypothesis: Participating in a preoperative CBT intervention will improve quality of life and reduce sick leave and use of the healthcare system compared to usual care for patients undergoing LSF.

6. Materials & methods

6.1. Ethical issues

The study was conducted in agreement with the Helsinki Declaration, and was approved by the local Ethical Committee (journal no. M-20110047). Permission to collect and analyse register data was granted by the Danish Data Protection Agency (journal no. 2011-41-5899) in accordance with The Act on Processing of Personal Data. The trial was registered in Current Controlled Trials ISRCTN42281022.

6.2. Study design

The study design, the study population, the interventions, the outcomes and the statistical analysis of the studies forming the basis of Papers I – IV are described collectively in the following section.

The study was a randomised controlled trial with follow-up at 3 months, 6 months and 1 year. Patients were allocated by computer generated block-randomisation (by hospital) to either usual care (control group) or a preoperative CBT intervention in addition to usual care (CBT group) in a 1:2 ratio. Blinding of the patients was not possible due to the type of intervention. Paper IV constituted a health economic evaluation conducted alongside the randomised trial. This evaluation included both a cost-utility analysis (CUA) and a cost-effectiveness analysis (CEA).

6.3. Patients

In the period October 2011 to June 2013 eligible patients were recruited from the Orthopedic Department of Aarhus University Hospital and the Elective Surgery Centre at the Regional Hospital of Silkeborg. The inclusion criteria were 1) a primary diagnosis of degenerative disc disease, stenosis or spondylolisthesis grade 1-2, as assessed by the spinal surgeons; 2) fusion for a maximum of 3 adjacent vertebrae, 3) age 18 – 64 years, and 4) competence in

the Danish language. Patients were excluded in case of less than 4 weeks to surgery from the time of inclusion, more than 80 km driving distance from the hospital or in case of psychiatric, inflammatory or malignant diseases.

Eligible patients were provided with verbal and written information about the study by the nurses in the ambulatory. If agreed, the patients received a phone call on the following day to get more detailed information about the study and the conditions of participation. Patients accepting participation received a consent form to sign, and a baseline questionnaire to complete. The patients were subsequently allocated to either the CBT group or the control group. The health personnel responsible for informing and including the patients were not otherwise involved in the study.

6.4. Interventions

Control group

Patients in the control group received the standard course of treatment, implying preoperative information about the upcoming operation including the anaesthetic procedure, medication, the postoperative rehabilitation and physical restrictions following surgery. Information was given by the operating surgeon, nurses and physiotherapists. Postoperatively the patients participated in the standard physical rehabilitation offered in their municipality, typically taking place in rehabilitation centers or local physiotherapy clinics. This was initiated 12 weeks after surgery and consisted of 8-12 weeks supervised training either individually or in groups. In some municipalities the rehabilitation programme also included brief information regarding pain and ergonomics.

CBT group

In addition to the standard course of treatment described for the control group, patients in the CBT group participated in a preoperative CBT intervention, described in full detail in paper I [62]. Briefly, the intervention consisted of six sessions, each of three hours duration. Patients attended four sessions prior to

surgery, and another two sessions three and six months postoperatively. The sessions took place at the hospital, where most of the patients underwent surgery. The health professionals delivering the intervention were a psychologist, an occupational therapist, a physiotherapist, a spine surgeon, a social worker and a previously operated patient. The health professionals participated in a brief training program aimed at learning the CB model and developing basic CBT skills. The content of the intervention was standardised, although some flexibility was allowed to respond to participants' needs. The key elements of the contents of each session were summarised in a patient handbook handed out the patient's first attendance. The patients' active participation was emphasised, and patients were encouraged to discuss their own worries and problems. Adherence with the intervention was defined a priori as attendance in a minimum of 3 sessions. A brief overview of the contents of the sessions is given in Table III on the following page.

Table III: Session overview

Session	Contents
A (preoperative)	• Physical and psychological reactions to stress • The link between thoughts, feelings, bodily reactions and behaviour. • What to expect of the operation and the postoperative period.
B (preoperative)	• The fear-avoidance belief model and the importance of physical activity in reducing pain. • Pleasant activity scheduling and activity pacing. • Ergonomics – restrictions an working posture following surgery.
C (preoperative)	• The link between thoughts, feelings, bodily reactions and behaviour. • Negative thoughts and their role in maintenance of a vicious circle. • Active and passive coping strategies.
D (preoperative)	• How to cope with pain in relation to family, friends and work. • The experiences of a previously operated patient. • Legislation and procedures in the authorities when being on sick leave and in relation to work resumption.
Follow-up (3 months post-op)	• Reflection of how patients have used the acquired cognitive techniques and coping strategies postoperatively. • Using pacing techniques to restart daily activities, hobbies and work. • Goal setting for the next three months
Follow-up (6 months post-op)	• Reflection of how patients have used the acquired cognitive techniques and coping strategies during the past 3 months • Discussion of achievements of previously set goals and setting new goals. • Coping with flare-ups. • Returning to work and how to cope with barriers.

6.5. Clinical evaluation (Paper II and III)

In the following section the outcome measures and the statistical handling for Paper II and Paper III are described. The methods of the health economic evaluation (Paper IV) are described separately in section 6.6.

6.5.1. Outcome measures

For each patient the following baseline characteristics were registered: gender, age, smoking status, working status, diagnosis, type of surgery and previous surgery.

Paper II:

Primary outcome:

- Back and leg pain (Numeric Rating Scale)

Secondary outcome:

- Mobility (Cumulated Ambulation Score)
- Use of rescue analgesics during hospitalisation
- Length of hospitalisation

For the primary outcome the patients reported their average back pain and leg pain on a daily basis on the first seven postoperative days using the numeric rating scale of 0-10 (best-worst) [63]. The median pain level was calculated from these scores.

The Cumulated Ambulation Score (CAS) was used for measuring postoperative mobility[64]. The CAS measures the level of mobility in the following three activities 1) getting in and out of bed, 2) sit-to-stand from a chair, and 3) walking. Each activity is assessed daily on a scale from 0-2 (0=Not able to, 1=Able to, with assistance, 2=Able to safely, without assistance (walking aid allowed)), summing up to a daily score of 0-6 points. The assessment was carried out on the first three postoperative days by the physiotherapists attending the patient.

Information about use of rescue analgesics (analgesics beyond the standardised analgesic protocol) was retrieved from the medical records system. Due to great variability in analgesic medications and dosages, the data were converted into daily morphine-equivalent doses to enable comparison between the groups [65].

Data on the length of hospitalisation in terms of number of days were retrieved from the medical records system.

Paper III:

Primary outcome:

- The Oswestry Disability Index

Secondary outcomes:

- Coping Strategies Questionnaire
- Fear-Avoidance Beliefs Questionnaire
- Low Back Pain Rating Scale
- Weeks of sick-leave after surgery

The questionnaires were administered by mail at baseline and three times after surgery (3 months, 6 months and 1 year).

The *Oswestry Disability Index* (ODI) was used to evaluate the disease-specific pain-related disability of the patients[66]. It comprises 10 questions concerning the following activities: pain intensity, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life, and travelling. Each question has six different response alternatives, with the scores of 0-5. The sum of the response scores is calculated (0-50), and presented as a percentage of 0-100% where 0% represents no pain-related disability. The Danish version of the ODI 2.0 has been found to have a high degree of validity and reliability [67, 68].

The Coping Strategies Questionnaire (CSQ) was used for assessing the patients' current use of coping strategies in relation to pain [69, 70]. The questionnaire is a 31 item self-report inventory, where patients rate to which extent they use a given coping strategy on a 7-point Likert scale (0=never,

6=always). The catastrophising subscale of the CSQ (CSQ-CAT) was used for assessing the patients' use of catastrophic thinking as a coping strategy in relation to pain. This subscale consists of 6 questions, summing up to a score of 0-36 points with higher scores representing higher levels of catastrophising. The CSQ-CAT subscale has been found to be reliable and valid measure of catastrophising in a Scandinavian setting [71].

The Fear-avoidance Beliefs Questionnaire (FABQ) was developed with the aim to investigate fear-avoidance beliefs among LBP patients in the clinical setting [72]. It consists of two subscales, the Physical Activity subscale (FABQ-PA) with a score of 0-24 points, and the Work subscale (FABQW) with a score of 0-42 points. For both subscales a higher score represents a higher level of fear-avoidance belief. The FABQ has been validated in Danish population of LBP patients [73].

The Low Back Pain Rating Scale (LBPRS) was developed and validated in Denmark, with the purpose of monitoring the outcome of clinical trials with LBP patients [74]. It consists of three scales measuring back and leg pain, disability, and physical impairment. For the purpose of this study only the pain index subscale was used, comprising measures of back and leg pain intensity on a 0-10 scale (best-worst) using the following three questions: the pain intensity at the time of examination, the average pain intensity within the past two weeks and the worst pain experienced within the past two weeks. Separate scores are calculated for back and leg pain.

Days of sick leave were measured using the Danish Register for Evaluation of Marginalization (DREAM). The database is administered by the Danish Ministry of Employment and includes information on all public transfer payments for all Danish citizens registered on a weekly basis since 1991[75]. The data on sickness benefits retrieved from the DREAM database is considered a valid measure of sick leave spells lasting at least 15 days [76].

6.5.2. Statistical analysis

The ODI was used for the power calculation. A difference of 15 points has been suggested as the minimal clinical important difference for surgical

populations[66]. Based on earlier studies the standard deviation was set to 20 points [26, 29]. Assuming a significance level of 0.05 and a power of 80% a total of 66 patients were needed in a 44/22 ratio. Allowing for a drop-out rate of 20% at least 80 patients had to be included. The patients were analysed according to their randomisation group, regardless of compliance with the intervention, according to the intention-to-treat principle.

All data was entered twice in EpiData version 3.1 (Aarhus University, Aarhus, Denmark), and any divergence was corrected according to original data. STATA version 13.0 (Stata Corp, College Station, TX) was used for statistical evaluation.

Paper II: Due to the non-parametrical nature of the primary outcome, self reported pain, the groups were compared using the Wilcoxon rank sum test. A difference of two points was considered clinically relevant [77]. For comparison of secondary outcomes (mobility, medication and hospitalisation), which were all of a non-parametrical nature, the Wilcoxon rank sum test or the chi squared statistic were used as appropriate.

Paper III: As for Paper II non-parametrical statistics was chosen for analysis due to the ordinal properties of both the primary parameter, the ODI, and the secondary outcome measures. The differences from baseline to each follow-up are thus presented with medians (with 25th and 75th percentiles), and comparison of differences between the two groups were made using the Wilcoxon rank sum test. Comparison of return to work rates during the first year was performed using a Kaplan Meyer survival analysis.

6.6. Health economic evaluation (Paper IV)

The following section describes the included cost variables, outcome measures and statistical methods used for the health economic evaluation. A brief introduction to the two approaches used for evaluation in the present thesis, the cost-effectiveness analysis (CEA) and cost-utility analysis (CUA), is given in Box I [61].

Box I. Cost-effectiveness analysis and cost-utility analysis

The *CEA* is an evaluation in which the costs and the consequences of alternative interventions are expressed as cost per unit of health outcome. The consequences are measured in natural effects or physical units, deemed relevant for the given treatment.
The *CUA* corresponds to the CEA, but uses 'utilities' as a measure of consequence instead of physical units. The utilities are expressed in 'quality adjusted life years' (QALY), a measure comprising both length of life and subjective levels of well being.
In both CEAs and CUAs the cost-effectiveness of one treatment alternative over another is expressed as the incremental cost-effectiveness ratio (ICER). The ICER is calculated using the formula ICER = $(C_A - C_B) / (E_A - E_B)$, where C_A is the cost of the intervention of interest; C_B is the cost of the comparator; E_A and E_B are the effects (consequences) of the new intervention and the comparator, respectively. Thus, the ICER summarises the results of the economic evaluation in one single parameter, which is the ratio of the additional costs per additional unit of effect or utility.

6.6.1 Costing

A societal viewpoint was adapted. Here all possible activities and resource consumption contribute to overall costs, regardless of their relatedness to the interventions. In economic terms, costs are defined as marginal, opportunity costs. The time frame was fixed by the date of index surgery to the date of index surgery + 365 days (1 year postoperatively). All costs are expressed in 2014-EUR. Costs and effects were not discounted, due to the time frame of 1 year.

Intervention costs. The costs of the intervention comprised the following parameters; 1) Resources used for training of the staff managing the intervention; 2) Working hours of the staff, including non-contact time (i.e. time used to set up the sessions, administration and record-keeping, and support/supervision time), multiplied by the gross salaries for each staff member. Gross salaries were calculated on the basis of published pay scales from relevant trade unions; 3) Consumables and educational materials for the

patients. The costs of 1, 2 and 3 were divided evenly between the 59 patients of the CBT group.

Primary health care sector. The National Health Service Registry (NHSR) [78] was used for gathering data regarding the patients' visits to GPs, medical specialists and therapists, valued using activity-based tariffs that are used to reimburse these providers.

Secondary health care sector. Secondary health care utilisation, in terms of the number of services and the national average Diagnosis- Related Grouping (DRG) tariffs, was extracted from The National Patient Register[79, 80].

Medication: Prescription medicine was recorded uniquely per patient in the Danish National Prescription Registry [81] and was valued using market prices.

Productivity losses. The human capital approach was used. For those who were part of the labour force at baseline the number of weeks of sick leave was obtained from the DREAM database described in chapter 6.5.1.[75]. Age- and gender-matched average gross salaries from Statistics Denmark were used to value production losses.

Patients' costs. The patient costs covered the following parameters: 1) time spent on participation in the CBT intervention, including transportation time, valued using age- and gender matched average gross salaries. Transportation time was estimated by assuming that 1 km of transportation took 1 minute; 2) Transportation expenses were calculated by the transportation distance (kilometers) multiplied by the official Danish mileage allowance; 3) The use of informal health care (e.g. help from family and friends) and 4) expenses for over-the-counter medication and personal aids. 3) and 4) were assessed using a modified version of the Dutch cost diary[82].

6.6.2. Outcome measures

Primary outcome:

- Quality-adjusted life years (QALY)

Secondary outcome:

- ODI

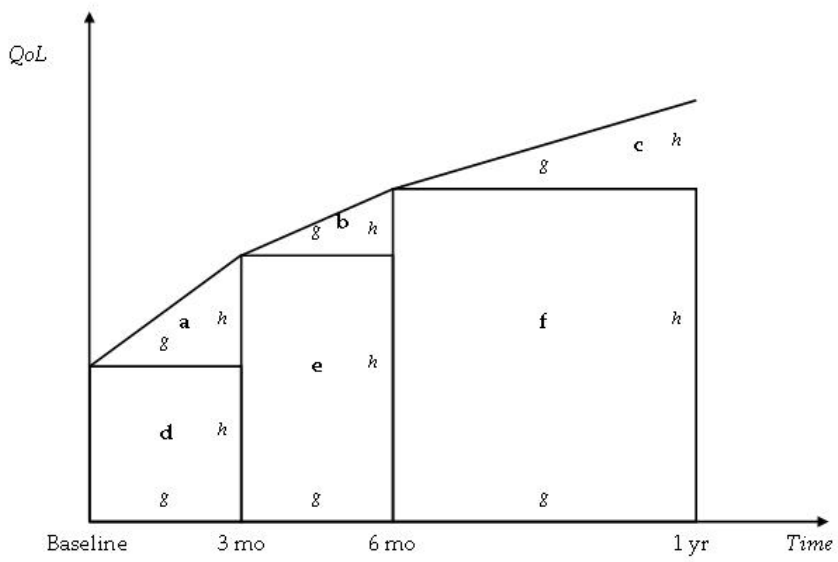
For calculation of QALY the patients' EQ-5D scores for baseline and follow-ups at 3 months, 6 months and 1 year were used[83]. The EQ-5D comprises five dimensions, which are mobility, selfcare, usual activities, pain/discomfort and anxiety/depression. Each dimension has three levels (no problem, some problems, extreme problems) resulting in a total of 245 potential health states. The scores fall on a scale of -0.624 to 1.0 (perfect health) including the scores of -0.293 for "unconscious" and 0.000 for "dead". The instrument has been validated in Danish, including the construction of Danish preference values [84]. Calculation of the QALY was performed using the following formula:

QALY=((baseline EQ-5D + 3 month EQ-5D)/2 x 3/12) + ((3 month EQ-5D + 6 month EQ-5D)/2 x 3/12) + ((6 month EQ-5D + 1 year EQ-5D)/2 x 6/12)

This corresponds to calculating the area under the curve as illustrated in Figure 3.

The secondary outcome measure, ODI, has been described in chapter 6.5.1.

Figure III: Calculation of quality-adjusted life years (QALY) using area under the curve.



6.6.3 Statistical analysis

Handling of missing data

For the cost data 100% response was acquired through registries, except for primary health care and prescription medication where data was missing for four patients (2 in each group). For the patient-reported outcomes the ODI suffered missing responses from five patients and the EQ-5D from six persons at 1-year follow-up. With the high response rate, the results for the responders formed the main analysis. To assess the potential importance of the missing data a sensitivity analysis was performed using the following strategies: 1) missing values were imputed using qualitative information given by the patients about their reasons for drop-out; 2) missing values were imputed using last observation carried forward.

Handling of skewed data

Cost data are often right skewed, as they cannot have a negative value and at the same time have no logical upper boundary. Further, a small proportion of patients often have very high costs, skewing the data further. We therefore applied the bootstrap method to estimate the mean costs with 95% confidence intervals[85]. The basic idea of bootstrapping is that inference about a population from sample data can be modeled by resampling the observed data any given number of times. Thus, by randomly drawing a large number of samples from the observed data, an estimate of the mean, variance, and confidence intervals can be built. In the present study non-parametric bootstrapping using 10,000 replicates was applied to form confidence limits for both costs, resource use, and clinical outcomes in the present study.

Cost-utility and cost-effectiveness analysis

The cost-utility and cost-effectiveness of the intervention was assessed by calculating the incremental cost-effectiveness ratio (ICER). The ICER is defined as the ratio between the mean cost difference between the two groups and the mean effect difference between the two groups (see Box I)[61]. Based on the

bootstrapped replicates of the estimated ICER, cost-effectiveness acceptability curves were drawn to show the probability that the CBT intervention is cost-effective compared to the control intervention for a continuum of hypothetical threshold values of willingness to pay for the given outcome (i.e. QALY or ODI) [86].

7. Results

As the study population forming the base of all papers were the same, their baseline characteristics will be described collectively. After presentation of the baseline characteristics the key results of paper II, III and IV will be presented separately. More detailed information is provided in the original papers in the appendix.

7.1. Patient characteristics

During the recruitment period of October 1st 2011 to July 1st 2013 a total of 648 patients underwent LSF surgery. Of these 221 patients fulfilled the inclusion criteria and were informed of the study, with the most common inclusion criteria not fulfilled being age (48% of all surgeries). After applying the exclusion criteria 157 remained, and of these 96 agreed to participate. The major part of those declining participation did so due to severe pain making them unable to drive to and from the hospital, in case of allocation to the intervention group. At the time of surgery another six were excluded due to changed or cancelled surgery. The patient flow during the 1-year follow-up is presented in the flowchart in Paper III. By random, surgery type was unevenly distributed between groups with more patients having TLIF surgery in the control group (Table IV). During the follow-up period three patients in the CBT group underwent spine surgery again. One underwent additional decompression (11 months after index surgery), one underwent re-fusion (8 months after index surgery), and one was re-operated just two weeks postoperatively due to a deep infection at the surgical site.

Table IV. Baseline characteristics of the study population. Numbers are n (%) unless otherwise stated

	CBT group (n=59)	Control group (n=31)
Male	23 (39)	16 (52)
Age (year ± SD)	51.4 (9.2)	47.7 (8.9)
Smoking	20 (32)	10 (30)
Working status		
Employed	32 (54)	15 (48)
Unemployed	11 (19)	11 (36)
Disability pension	9 (15)	5 (16)
Early retirement	7 (12)	0 (0)
Primary diagnosis		
Spondylolisthesis	16 (27)	7 (23)
Disc degeneration	32 (53)	17 (52)
Stenosis	6 (10)	7 (23)
Surgical procedures*		
PLF	41 (69)	12 (39)
TLIF	17 (29)	19 (61)
Uninstrumented	1 (2)	0 (0)
Decompressed	51 (86)	25 (81)
Previous spine surgery		
Spondylodesis	2 (3)	1 (3)
Decompression	7 (11)	1 (3)
Fusion levels		
One	36 (62)	20 (69)
Two	19 (32)	8 (27)
Three	4 (7)	3 (10)
Disability (ODI)		
Mean (SD)	40.7 (13.2)	40.8 (15)
Pain (LBPRS)		
Back,median (IQR)	7.0 (5.3;8.0)	7.2 (6.0;8.0)
Leg, median (IQR)	6.3 (4.3;7.7)	6.3 (3.7;8.3)
Quality of life (EQ-5D)	0.655 (0.389;0.723)	0.627 (0.356;0.723)

PLF: posterolateral fusion; TLIF: transforaminal interbody fusion; ODI: Oswestry Disability Index;LBPRS: Low Back Pain Rating Scale; EQ-5D: EuroQol 5 Dimensions

7.2. Hospitalisation (Paper II)

In Paper II we attempted to investigate the physical condition of the patients during hospitalisation in terms of pain, analgesic use, mobility and length of stay.

Both groups reported moderate levels of back- and leg pain intensity during the first postoperative week. The CBT group reported a median back- and leg pain of 5.4 points (4.0; 6.5) and 3.0 points (0.8; 5.1), respectively. This was comparable to the back pain of 5.3 points (4.0; 6.1) and leg pain of 3.1 points (1.1; 5.0) reported by the control group.

Regarding mobility more of the patients in the CBT group were mobile without assistance on the three assessed activities 1) getting in and out of bed; 2) sit to stand from a chair and 3) walking during the early postoperative phase (Figure III). This difference was significant ($P<0.05$) for all activities on the 3rd day and for independent walking on the 2nd day.

Figure II.I Mobility in the first three postoperative days after LSF for patients in the CBT group and the control group. Columns illustrate the percentage of patients capable of performing 3 different activities independently on each of the first 3 postoperative days. Red dots represent significant difference between groups (P<0.05)

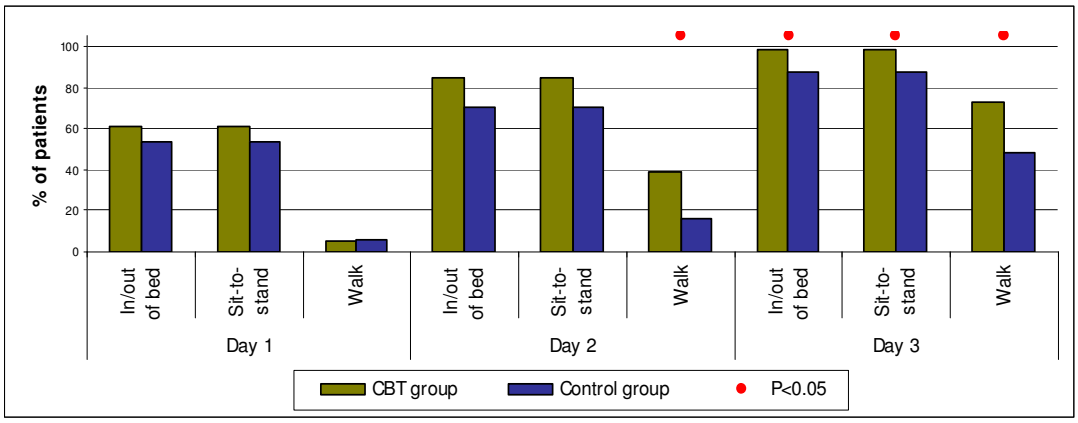
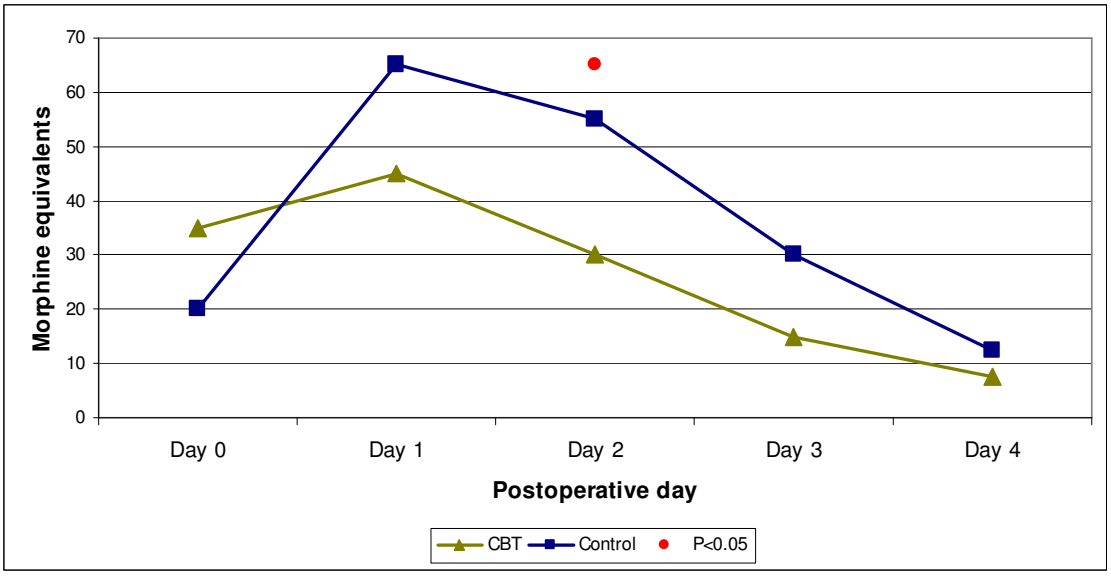


Figure IV shows the intake of rescue analgesics in the two groups during hospitalisation. There was a tendency for the intake of rescue analgesics to be lower in the CBT group but this difference was only significant on the 2nd postoperative day ($P = 0.021$). The total intake during hospitalisation was comparable between groups, with the CBT group requiring 142.5 morphine equivalents (70; 275) compared to 196.8 (145; 345) in the control group ($P = 0.2$).

Length of stay was correspondingly similar in the two groups, with the CBT group being hospitalised for 5 days (4; 6) and the control group for 4 days (4; 6) after their LSF operation.

Figure IV. Intake of analgesics during hospitalisation after LSF for patients in the CBT group and control group. Units in morphine equivalents. Day 0 is day of surgery.



7.3. One year after surgery (Paper III)

In Paper III we looked at the changes in disability, pain, pain coping and return to work during the first year after surgery.

For the primary outcome, the ODI, a large difference was seen between the groups early in the recovery phase. Thus, the CBT group reported a significant median reduction already after 3 months of -15 ODI points (-26; -4), compared to a median change of 1 point (-14; 8) in the control group (P = 0.003). The CBT group managed to maintain this large reduction throughout the first postoperative year, whereas the control group improved more slowly, to a small reduction of -6 points (-26; 4) at 1 year follow-up, leading to an insignificant difference between groups (P =0.082) Table V presents the self reported disability in the two groups at the different time points during the first postoperative year.

The two groups achieved significant and comparable reductions of more than 2 points in back and leg pain during the first postoperative year (Table V). Despite the larger disability reduction seen in the CBT group, the

groups did not differ in their self reported back and leg pain at any point of time during the 1 year follow up.

Table V. Change in disability, back and leg pain severity during the first year after lumbar spinal fusion surgery.

	CBT group		Control group		
	Change from baseline Median (IQR)		**Change from baseline Median (IQR)**		**Difference**
		n		***n***	***P-value***
ODI					
3 months	-15 (-26;-4)	55	1 (-14;8)	26	0.003
6 months	-18 (-24;-7)	55	-4 (-16;4)	25	0.056
1 year	-14 (-26;-5)	56	-6 (-26;4)	28	0.082
Back pain					
3 months	-3.0 (-4.3; -1.3)	54	-2.6 (-4.3; -0.3)	26	0.41
6 months	-2.3 (-4.0;-1.7)	55	-2.3 (-4.7;-0.7)	25	0.94
1 year	-2.5 (-4.3; -1.0)	54	-2.7 (-5.0; -0.3)	27	0.81
Leg pain					
3 months	-3.2 (-5.3;-1.3)	54	-2.3 (-4.7;-0.3)	26	0.23
6 months	-2.8 (-5.0;-1.3)	55	-2.0 (-5.7;-0.3)	25	0.43
1 year	-2.8 (-4.7; -1.3)	54	-1.3 (-6.0; -0.3)	27	0.70

Figure V (next page) shows the return-to-work rates for the two groups, for the 69 patients being part of the labour force at baseline. The two curves, representing the rate of return-to-work for each group, indicate that the return-to-work rates are similar between groups. For both groups, less than 50% in each group had returned to work 1 year after surgery.

Figure V. Return to work after lumbar spinal fusion.

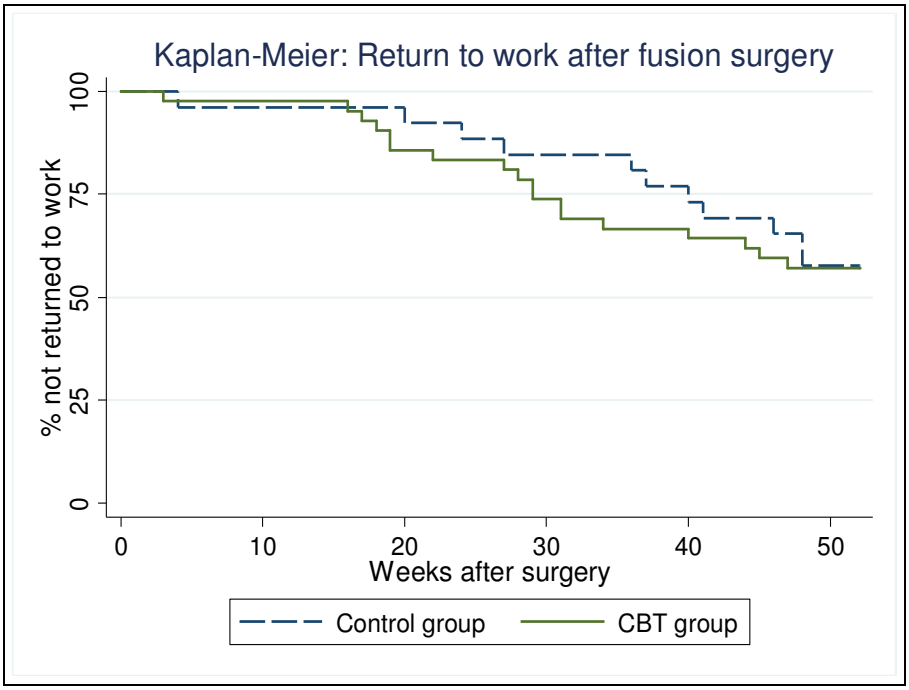


Figure VI and Figure VI (next page) illustrate the changes in the patients' levels on the catastrophising subscale of the CSQ (Figure VI) and the physical activity subscale of the FABQ (Figure VII). The CBT group showed no improvement on these variables from baseline to time of surgery, following participation in 4 preoperative CBT sessions. Following surgery an improvement was seen in both groups on the two parameters up until the 3-month follow-up. From 3 to 6 months the control group reported an increase in both variables whereas the CBT group remained at a low level, leading to a significant difference between groups at 6-month follow-up on both catastrophising (P = 0.04) and fear-avoidance beliefs (P = 0.01). Towards 1 year the scores of the two groups evened out again.

Figure VI. Level of catastrophic thinking during the first year after lumbar spinal fusion surgery.

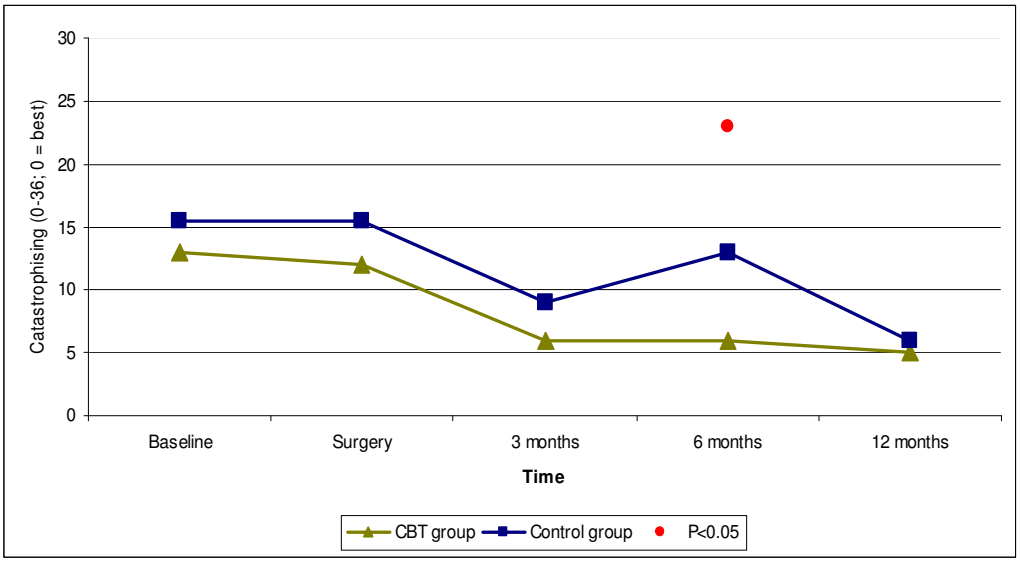
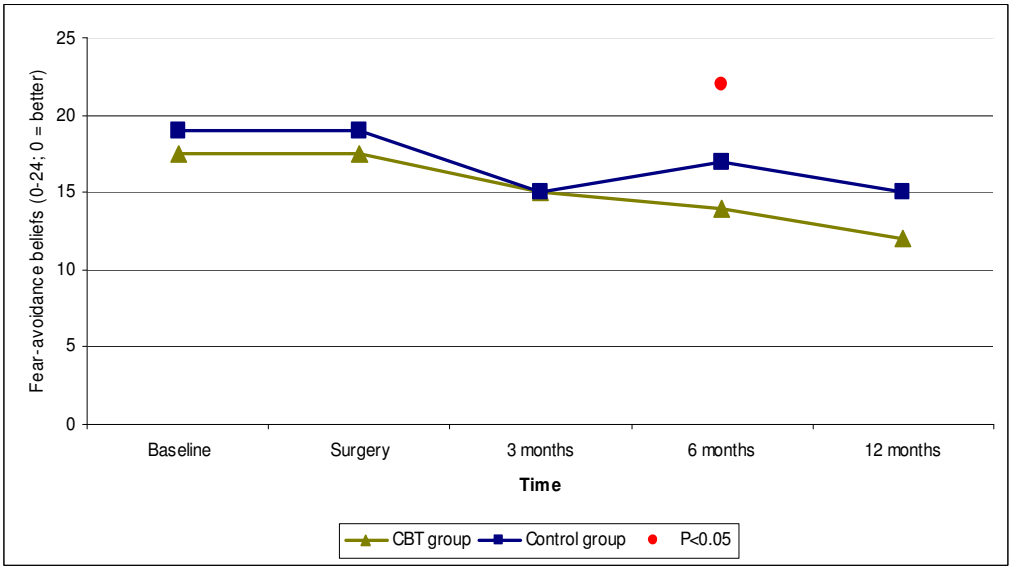


Figure VII. Level of fear-avoidance beliefs (subscale physical activity) during the first year after lumbar spinal fusion surgery.



7.3.1. Adherence with CBT intervention

Ten patients (16%) attended less than the required three sessions. Various reasons for non-adherence were given, e.g. could not take time off work as expected (n=3), driving to and from hospital caused too much pain (n=2), on maternity leave prior to surgery (n=1), serious illness of close relative (n=1) and other personal reasons (n=3). For the remaining 49 patients 7 patients (12%) participated 6 sessions, 17 (29%) in 5 sessions, 17 (29%) in 4 sessions and the remaining 8 (14%) in 3 sessions.

Supplementary analysis: As-treated:

The 10 non-adherent patients did not differ in their baseline characteristics except for being a little younger (47 versus 52 years on average). However, their ODI reduction at 1 year follow-up was small compared with the adherent patients (-5 points (-8;-4) *versus* -18 points (-28;-18)), diluting the effect of the CBT intervention on the ODI score. An "as-treated" analysis (with non-adherent patients analysed in control group) resulted in a significant difference between groups at 1 year on the ODI of -18 points (-28; -8) *versus* -5.5 points (-18; 4) ($P = 0.003$).

7.4. Health economic evaluation (Paper IV)

In Paper IV we aimed to assess the cost-utility and cost-effectiveness of the CBT intervention compared to usual care in a societal perspective.

Resource use and costs

In terms of resource utilisation the two groups did not differ significantly on any of the measured parameters except for resource use related to the intervention. This amounted to an additional €630 per patient for the intervention costs, an average of €610 for production loss (due to participation time), and €116 for transportation expenses. The results for resource utilisation are presented in Table VI, and the appertaining costs are presented in Table VII. The major cost in both groups was those produced by sick leave after surgery. In the CBT group this accumulated to €29,314 (22,615; 36,014) which

was not significantly different to the production loss in the control group of €31,883 (22,154; 41,680). The other large cost parameter was the costs in the secondary health care sector, primarily caused by the price of LSF surgery and hospitalisation. This mounted up to an average cost of €19,401 (17,678; 21,125) in the CBT group compared to €18,354 (17;434; 19,502) in the control group. Despite the extra costs of the intervention and related resource use the total costs did not differ between groups, with an estimated average difference in favour of the CBT group of €89 (-11,902; 12,080).

Health outcomes

During the first year the CBT group achieved an average QALY of 0.710 (95% CI: 0.670; 0.749), which was significantly better than the control group's of 0.636 QALY (95% CI: 0.573; 0.687) (P = 0.045). This difference was mainly produced by a significantly larger improvement in EQ-5D scores at 3 month follow-up reported by the CBT group (mean difference 0.095 (95%CI: 0.008; 0.193; P = 0.034) (data not shown).

As described in chapter 7.3 and table V, the reductions in disability (ODI) was significantly larger in the CBT group after 3 months and 6 months, but at 1 year follow-up this difference was no longer significant although improvements were still in favour of the CBT group.

Table VI. Use of resources in the first year following lumbar spinal fusion surgery. Values are mean units per patient with 95% confidence intervals.

	CBT group (n = 59)	Control group (n = 31)	Difference
Primary health care			
General practitioner	16.5 (13.6; 19.5)	17.4 (14.1; 20.7)	- 0.9 (-5.3; 3.6)
Medical specialist	1.3 (0.6; 2.0)	1.3 (0.3; 2.2)	0.0 (-1.1; 1.1)
Physiotherapist	6.2 (1.9; 10.6)	6.2 (0.9; 11.5)	0.0 (-7.5; 7.5)
Secondary health care			
Bed days	7.7 (5.9; 9.5)	6.8 (4.8; 8.9)	0.9 (-1.7; 3.5
Outpatient visits	7.8 (6.1; 9.6)	7.5 (4.9; 10.2)	0.3 (-2.6; 3.4)
Emergency room	0.12 (0.04; 0.2)	0.16 (0.03; 0.3)	- 0.04 (-0.2; 0.1)
Medication (no. of packages)	28.0 (21.4; 34.6)	21.6 (13.4; 29.9)	6.4 (-4.1; 16.9)
Production loss			
Weeks of sick leave	32.1 (27.2; 36.9)	31.1 (23.2; 38.9)	1.0 (-8.7; 10.7)
Patient costs			
Transportation (km)	410 (341; 473)	0	410 (344; 477)
Intervention hours	18.2 (16.0; 20.4)	0	18.2 (16.0; 20.5)

Table VII. Costs of resource use in the first year following lumbar spinal fusion surgery. Values are mean costs in 2014 Euro with 95% confidence intervals

	CBT group (n = 59)	Control group (n = 31)	Difference
Intervention costs	630 (630; 630)	0.00	630 (630; 630)
Primary health care			
General practitioner	262 (209; 316)	248 (184; 311)	15 (-69; 98)
Medical specialist	42 (16; 69)	54 (12; 96)	-12 (-62; 39)
Physiotherapist	122 (17; 226)	93 (16; 204)	28 (-118; 175)
Secondary health care			
Admissions	19,401 (17,678; 21,125)	18,354 (17,434; 19,502)	1,048 (-917; 3,012)
Outpatient visits	1,751 (1,372; 2130)	1,820 (1129; 2,618)	-69 (-926; 788)
Emergency room	7 (0.5; 13)	16 (3; 29)	-9 (-24; 5)
Medication	252 (143; 361)	161 (93; 245)	91 (-36; 218)
Production loss			
Weeks of sick leave	29,314 (22,615; 36,014)	31,883 (22,154; 41,680)	-2,568 (-14,493; 9,356)
Patient costs			
Transportation	116 (97; 135)	0.00	116 (97; 135)
Prod. loss (interv.)	610 (535; 684)	0.00	610 (535; 684)
Total costs	52,492 (45,361; 59,622)	52,580 (42,786; 62,374)	-89 (-12,080; 11,902)

CUA and CEA

Figures VIII and IX show the cost-effectiveness acceptability curves resulting from the CUA and CEA for both the complete cases and the sensitivity analyses. The CUA (Figure VIII) showed that at a threshold of willingness to pay of €40,000 for an additional QALY there is a probability of 70% that preoperative CBT is cost-effective compared to usual care. Figure IX illustrates the corresponding probability for a gain of 15 ODI points. There is approximately 90% probability that preoperative CBT is cost-effective at thresholds €10,000 and above for an additional gain of 15 ODI points. For the imputation strategy of *last observation carried forward* the probability was lower, 75% *versus* 90% at a threshold of €10,000, increasing to 90% at a threshold of €40,000.

Figure VIII. Cost-effectiveness acceptability curve illustrating the probability that preoperative CBT is cost-effective at given thresholds of willingness to pay for one additional QALY gain.

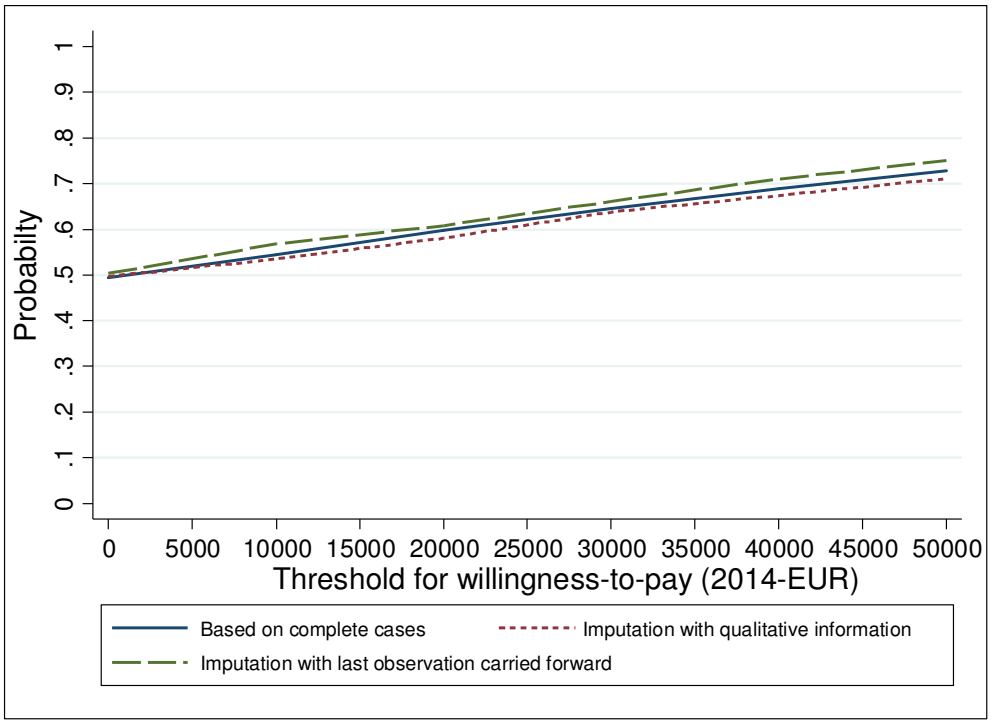


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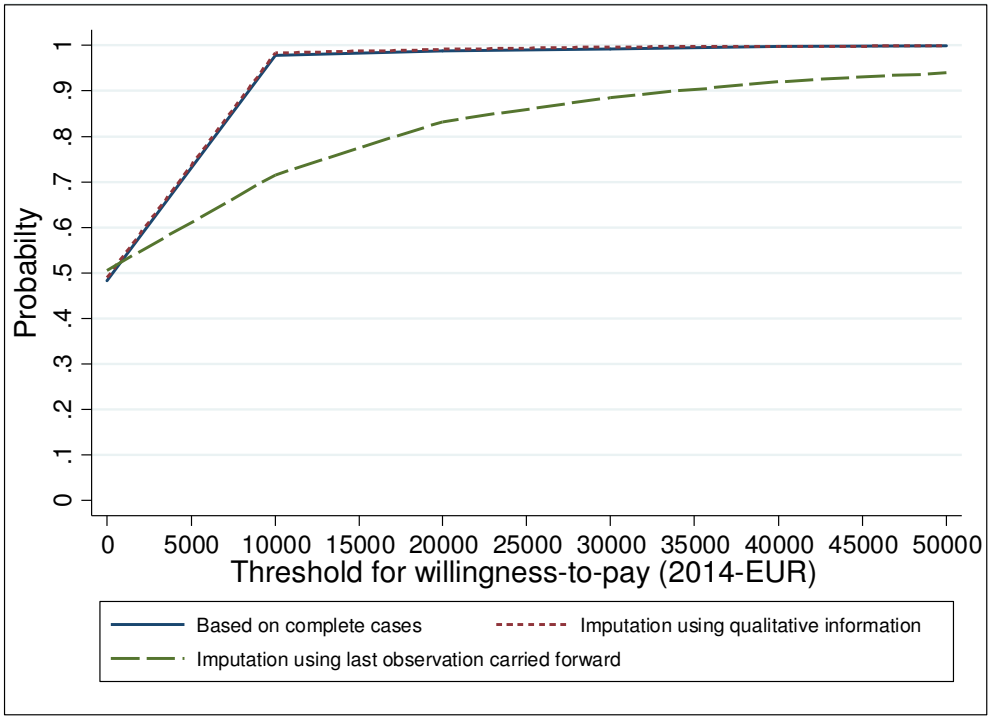
Figure IX. Cost-effectiveness acceptability curve illustrating the probability that preoperative CBT is cost-effective at given thresholds of willingness to pay for an additional gain of 15 ODI points.



7.5. Summary of results

In *Paper II,* we found that more patients in the CBT group were mobile without assistance during the first three postoperative days, and they also seemed to require less analgesic than the control group. Preoperative CBT did, however, not seem to influence post-surgical back and leg pain or length of stay. In *Paper III,* we found that patients in the CBT group achieved larger disability reductions 3 and 6 months after surgery compared to the control group. At 1 year follow-up this difference had evened out due to improvements in the control group. The faster improvements in disability did not translate into faster resumption of work, with less than half of the patients in both groups having resumed work after 1 year. Self-reported back and leg pain was comparable between groups. In terms of catastrophic thinking and fear-avoidance beliefs, the two groups had significant and equal reductions from baseline to 1 year follow-up apart from an increase on both outcomes in the control group from 3 to 6 months, leading to a significant difference between groups at 6 month follow-up. In *Paper IV,* we found preoperative CBT to be more effective in terms of QALY gain and disability reduction, and at the same time cost neutral when considering the overall health care sector and labour market perspective. Our results were largely unaffected by the sensitivity analyses performed, confirming the robustness of our findings.

8. Discussion

The aim of the present thesis was to design a preoperative CBT intervention based on best available knowledge and evidence and evaluate its effects on outcomes after LSF during a 1-year follow-up period. The designed CBT intervention is built up from a number of components which may act both independently and interdependently, and it can therefore be labelled a complex intervention [87]. This implies that certain methodological steps were taken in the design and evaluation of the study to avoid the intervention becoming a black box (i.e. we only now what goes into and comes out of the box, but have no knowledge of the interplay of the components *inside* the box). First of all, we provided a thorough description of the design, the rationale and the theoretical underpinnings of the intervention in Paper 1, in order to make readers able to compare and apply the results from our study to other theories, studies and settings. Further, in Paper II and Paper III we attempted to shed light over some of the theoretical pathways outlined in the Background and in Paper I, by performing measurements at several intermediate time points to allow for a more detailed analysis of which changes precede others. Finally, Paper IV provides a societal perspective to aid decision-making in the field of rehabilitation for patients undergoing LSF.

In the following chapters the strengths and limitations of the study will be described. More in depth discussion of the strengths and limitations can be found in the original papers. Following this, our findings will be discussed in the light of the theoretical assumptions on which the intervention was based and in the context of comparable studies. Further, the feasibility of the CBT intervention and the patients' perspective will be outlined.

8.1 Strengths and limitations

A general strength of the study was the randomised design, minimising the risk of confounding and selection bias. The use of validated outcome measures together with response rates of above 90% at 1 year follow-up is another strength of our study, enhancing the validity of our findings.

National Registers were used for the collection of cost data for the primary and secondary health care sectors, sick leave from work and prescription medication. Data in these registers are recorded in a prospective manner and have a high level of validity and completeness [75, 76, 78-81]. This makes them ideal for research purposes, and reduces the risk of recall bias, and we consider this a large strength of our health economic evaluation.

A potential weakness of our study was the uneven distribution of surgery types (PLF and TLIF) in the two groups with relatively more patients in the CBT group undergoing PLF. However, several studies have compared the two surgical approaches and have found no indications that TLIF is superior to PLF or vice versa [51, 88-90].

Another limitation of our study pertains to the issue of blinding, an almost unavoidable limitation of complex interventions. Thus, the blinding of patients was impossible and a positive expectation could influence the outcome of preoperative CBT in a positive direction. The application of an attention control in the control group, for example telephone calls during follow-up, would have strengthened the validity of our results by equalising the attention effect in the two groups.

For pragmatic reasons we set a time frame of 1 year for our study. This limited follow-up period entails a risk that relevant costs due to changes in productivity and clinical outcomes are missed. Others have found quality of life improvements to be maintained up to 4 years after surgery at no extra costs [91]. This could possibly have a positive impact on the clinical and health economic evaluation of our study, and warrants an extended follow-up period.

We did not attempt to keep a check on the postoperative rehabilitation as the patients belonged to 16 different municipalities, each managing the postoperative rehabilitation individually. The minimum standard offered is an 8-week exercise programme but some municipalities also offer a few hours of pain management or counselling in regard to work resumption. However, the randomised study design ensured an even distribution of the various types of rehabilitation in the two groups.

It was originally planned to use both the work subscale and the physical activity subscale of the FABQ. However, the major part of the patients found it difficult or irrelevant to answer the questions pertaining to the work subscale after surgery, because many of them had not returned to work, or had been given restrictions in relation to work after the operation. We therefore reported only the physical activity subscale of the FABQ in Paper II.

8.1.1. Costing

A possible shortcoming of the health economic evaluation was the omission of potentially relevant costs. This pertains to the costs related to short term sick leave and to the use of informal health care (i.e. help from family and friends or private domestic care). We attempted to measure both of these parameters by the use of cost diaries, but the compliance was very poor. The DREAM database does not contain information on sick leave spells shorter than 15 consecutive days, and we were therefore not able to assess if preoperative CBT could have an influence on short term sick leave during the first year. For the use of informal health care, a large number of patients in both groups (CBT 78%, control 61%) stated that they used help from family and friends at some point during the first 6 months. This indicates that the use of informal health care could be associated with relatively large costs, and we recommend that further attempts be made to retrieve this information in future studies.

The calculated intervention costs were probably a low estimate, seeing that the staff wages were not likely to represent the normal salaried cost of staff, and because no overhead costs were paid. An additional sensitivity analysis was performed allowing for an inflation of 20% for the intervention costs, resulting in an insignificant difference between groups of €19 (95% CI: -11,755; 11716), now in favour of the control group. Thus, the inflation of intervention costs did not change the results of the CUA and CEA.

8.2. Comparison with underlying theory and supplementary analyses

The CBT intervention was based on the assumption that many patients undergoing LSF due to CLBP have a high level of pain catastrophising and fear-avoidance beliefs, and our CBT intervention therefore emphasised the identification and altering of negatively distorted thoughts and beliefs about pain. On this basis we hypothesised that improvements in catastrophising and fear-avoidance beliefs would happen concurrently with, or even precede, changes in disability and pain, and that these changes would take place primarily in the CBT group. This was not the case, however. Instead, the change in fear-avoidance beliefs and catastrophising was almost similar in the two groups (shown in Figure VII and Figure VIII). These findings are in line with the findings of a prospective cohort study of 141 patients undergoing spine surgery for CLBP[92], where patients undergoing spine surgery followed the standard course of treatment at the hospital without any formal use of CBT. Still, an overall reduction in the patients' fear-avoidance beliefs from pre- to postoperatively (12 weeks) was found. In our study, the only difference between the CBT group and the control group was seen at 6 month follow-up, where the control group showed an deterioration in both psychological parameters. These findings could indicate that the patients in the control group were not prepared for the temporarily increased pain commonly experienced with the commencement of the postoperative rehabilitation (which takes place from 3 to 6 months after surgery), and therefore becoming increasingly worried about their pain. The patients in the CBT group were well-informed about this expected pain increase during exercise and how to cope with it.

We chose to explore the association between baseline psychological risk factors and 1-year outcomes on ODI and return to work in the present study population. The patients were stratified into high risk and low risk groups according to their baseline levels on the catastrophising subscale of the CSQ and both subscales of the FABQ (physical activity and work, respectively). Where no established predictive cut-off value exists the median baseline values were used as the cut-off value (i.e. 14 points for catastrophising

and 18 points for the FABQ physical activity subscale). For the work subscale of the FABQ the suggested predictive value of 27.5 points was used[93]. For disability reduction we found that patients in the CBT group performed equally well, independent of their baseline level of catastrophising, whereas patients in the control group did worse if they were in the high risk group. This finding was replicated for the work-subscale of the FABQ but not for the physical activity subscale. For return to work the CBT group and the control group were collapsed as the CBT intervention had no effect on this outcome. It was seen that significantly more patients with high levels of fear-avoidance beliefs (both subscales) and catastrophising had not returned to work one year after LSF (69% - 74%, depending on scale). This finding is in agreement with the findings of others [24, 94].

In Paper II we aimed to assess the influence of preoperative CBT on pain during hospitalisation as our primary outcome. According to the existing literature a high level of acute postsurgical pain (APSP) negatively affects the risk of developing chronic pain after surgery [11, 12, 95]. We performed a supplementary analysis with the aim to explore whether a high level of APSP (>5 points) was predictive of more pain and disability one year after surgery in the present study population. As we had found no significant difference between the CBT and control groups on pain and disability at 1-year follow-up we collapsed the two groups for stratification into groups of high APSP (n = 38) low APSP (n = 46). For back pain reduction at 1-year follow-up a tendency was seen of patients with high APSP performing worse than patients with low APSP (median reduction of 2 points (0.3; 4) *versus* 3 points (0.9; 5), respectively). For disability reduction a large difference was seen between the groups, as those with a high APSP reported a reduction of 7 points (2; 16) compared with a reduction of 16 points (5;28) in those with low APSP.

8.3. Comparison with other studies

In Paper II we attempted to investigate the effect of preoperative CBT on the acute postoperative phase. Nielsen et al, comparing the effect of a preoperative

intervention with usual care, reported on back pain, recovery milestones during hospitalisation (e.g. mobilisation to bedside, personal hygiene, walking, stair climbing) and length of stay[31]. In consistency with our results they found patients in the prehabilitation group to reach recovery milestones faster and found no difference between groups in terms of average and worst pain. In contrast to our study the prehabilitation group had a shorter length of stay. However, as their experimental intervention entailed not only a change of timing (from post- to preoperative), but also a different analgesic procedure, optimised nutrition and intensified postoperative mobilisation, it is impossible to differentiate the effects of the preoperative timing from any effects of the other components of the intervention.

Our findings on disability in Paper III were not as convincing as the results of the rehabilitation studies by Abbott et al[29] and Monticone et al[30] where baseline ODI scores of 44 and 49, respectively, fell to below 20 points after one year in the groups receiving CBT. This may partly be due to our broader inclusion criteria. Furthermore, in Abbott's study the contents of the exercise packages differed between the intervention group and control group, making it difficult to isolate the effect of the CBT from that of the altered exercise programme[29]. In our study we deliberately chose to leave all other parts of the surgical course of treatment and postoperative rehabilitation unchanged, to better be able to isolate the effect of the CBT intervention.

Looking at the results for work resumption less than 50% in each group had returned to work one year after surgery. We consider this a rather disturbing result, but nevertheless a rate that corresponds well to the return-to-work rates reported by others. Thus, two Danish studies reported return-to-work rates of 35% and 50% at one and two years after LSF, respectively [57, 58], whereas Abbott et al reported a return-to-work rate of 73% after 2-3 years[29], supporting an extended follow-up period as mentioned in Chapter 8.1.

In Paper IV we calculated a difference between groups of 0.071 QALY (95% CI: 0.001; 0.139) in favour of the CBT group, which is well above the minimal important difference of 0.03 QALY suggested in the literature[96]. However, if the primary objective is to influence resource allocation, then the

changes in QALY alone may be of limited interest without knowing the cost of that change (i.e. the incremental cost per QALY gain)[61]. In Denmark a threshold for willingness-to-pay per QALY has not been established, but the National Institute for Health and Clinical Excellence in Great Britain has set an upper threshold for reimbursement approval for procedures of £30,000/QALY (approximately €40,000)[97]. At this threshold the probability of preoperative CBT being cost-effective was 70% in our CUA, supporting the use of preoperative CBT in this study population. Another key issue to be recognised is the importance of patients maintaining improved health outcomes over time, as this has the potential of decreasing the cost per QALY calculated after one year. Thus, if the improvement is sustained for two years at no additional costs, then the cost/QALY would be only half the cost per QALY calculated at year 1. The results of the 4-year follow-up of the Spine Patient Outcomes Research Trial highlights the importance of this matter[91]. Here the benefit of fusion surgery over nonsurgical treatment seen at 2-year follow-up was also present four years after surgery, reducing the cost per QALY from $115,600 at two years to $64,300 at four years.

8.4. Feasibility of the intervention

Of the patients allocated to the CBT group 10 (17%) did not adhere to the intervention for various reasons. Several of the remaining 49 patients found it difficult to attend all of the preoperative sessions, in particular those living at some distance from the hospital. Approximately 30% attended all four preoperative sessions, while the remaining attended three sessions (43%) or two sessions (27%) prior to surgery. On this basis we suggest that one of the preoperative CBT sessions be placed after surgery (i.e. three sessions before and three sessions after surgery), where the patients found it easier to attend. The as-treated analysis (with the non-compliant patients analysed as controls) indicated that a good effect is achieved with the majority of the patients participating only three times before surgery (see Chapter 7.3.).

A large number of severely pain-disabled patients refused participation in the study, giving the transportation to and from the preoperative CBT sessions as the reason for refusal. It should be considered whether a different design of the intervention would be better suited for the part of the study population being most disabled by their back and leg pain, for instance by the use of internet based CBT programmes (iCBT). A recent RCT comparing an iCBT intervention to a face-to-face CBT group intervention for non-specific chronic pain found iCBT to be both less costly and at least as effective as the face-to-face intervention in terms of improvement in pain coping, pain intensity and quality of life [98].

8.5. The patient perspective

We chose to undertake a small qualitative study, as a supplement to the main study, to gain more information on the patient perspective [99]. The aim was to explore the lived experiences among patients undergoing LSF and to illuminate possible differences concerning pain coping strategies between patients in the CBT group and the control group. A research nurse, not otherwise involved in the study, conducted individual interviews with five patients from each group five to eight months after their operation. The patients all characterised the phenomenon of undergoing LSF as requiring a difficult adaptation process that was marked by ambivalence. They found it challenging to have to redefine themselves as human beings after surgery, setting new and realistic future goals, but at the same time felt relieved when they reached a state of acceptance of their situation postoperatively. This indicates that not only the coping strategies related to the pain condition *per se* is of importance, but also thoughts and beliefs *specifically* related to the operation and its consequences is a strong presence. Further, another common issue described by the patients was the need of recognition and support in relation to their CLBP problem and the required surgery. Based on this observation we consider it an advantage that the intervention was managed at the hospital by health professionals who were familiar with the LSF procedure.

In terms of different use of pain coping strategies it was also found that the CBT group tended to minimise pain by resting before pain onset whereas the control group reacted to pain by resting after its onset. This was a coping strategy presented to the patients during the CBT intervention, indicating that the patients were able to turn the learned strategies into action. The use of this active coping strategy in the CBT group may have contributed to the larger disability reductions and superior quality of life reported by the CBT group early in the postoperative period.

8.6. External validity

In the present study we chose to recruit patients from both a general hospital and a university hospital, and further to include patients with both disc degeneration, stenosis, spondylolisthesis, and previous spine surgery. We believe this represents the general basic LSF candidates seen in most spine ambulatories, thereby increasing the external validity of our results.

A risk of selection bias was introduced with the patients refusing to participate, as described in previously. This is a typical selection bias seen in intervention studies, i.e. that participants are less disabled than non-participants. This limits the generalisability of our results to a subgroup of less disabled CLBP patients undergoing LSF.

Our findings on sick leave and return to work can primarily be generalised to the Danish labour market. Legislation governing the labour market differs between countries, even between countries with which we often compare ourselves (e.g. Norway, Sweden and Holland), and the incentive to return to work may vary accordingly.

9. Conclusion

In the present thesis the effects of a preoperative group-based cognitive-behavioural intervention was compared to usual care in a study population of patients undergoing lumbar spinal fusion. The effect was studied within a biopsychosocial framework for understanding chronic low back pain.

Paper II: A significantly larger number of patients in the CBT group achieved independent mobility during the first three postoperative days, and the CBT group also tended to have a lower intake of rescue analgesics. The preoperative CBT intervention had no influence on self reported pain during hospitalisation, nor did it affect length of stay.

Paper III: Patients in the CBT group had achieved significantly larger disability reductions at 3- and 6- months follow-up, but the difference between groups had evened out after one year. There was no difference between groups with regards to self reported pain and work resumption. For catastrophising and fear-avoidance beliefs the two groups overall followed a similar pattern of improvement, except for a temporary worsening reported by the control group at 6-months follow-up.

Paper IV: We found preoperative CBT to be more effective and cost neutral when considering the overall health care sector and labour market perspective. Our results remained largely unaffected by the sensitivity analysis performed, confirming the robustness of our findings.

10. Perspectives and future research

In 2010, a disease management programme for low back pain was introduced in Central Denmark Region. The programme describes the pathway through the health care system from the first time a patient seeks help for low back pain at their general practitioner and until the patient is discharged after surgery. According to this programme, patients referred to hospital for a specialised multidisciplinary assessment should receive a CBT intervention if deemed necessary. However, at the present moment there is no established CBT intervention available at the hospitals managing the diagnosing and surgical treatment of these patients in Central Denmark Region. With the CBT intervention developed for this study we offer a detailed description of the intervention to be implemented in a hospital setting with a complete intervention manual for the health professionals, a work book for the patients, and the suggested set-up and budget to go with it. With a few adjustments, as discussed in Chapter 8.4., we recommend that the hospitals seek to implement this intervention. This implementation process should be monitored with regards to the rate of uptake of patients, the stability of the intervention (e.g. through supervision and/or video recording of sessions) and any broadening of patient groups (e.g. widening the age criteria or surgical groups) [87]. For patients who are too disabled by pain to manage the drive to and from the hospital, the possibility of adapting the CBT intervention to a primarily internet based version should be investigated. With the successful entry of telemedicine in the health care system, this should be an achievable target.

In continuation of the implementation process a consideration should be made, regarding the identification of subgroups of patients who will gain the most from CBT interventions. The literature suggests that more consistent and favourable results may be achieved when targeting treatment towards psychosocial risk factors primarily when these risk factors are at high levels, rather than providing comprehensive interventions regardless of psychological risk factors [100, 101]. Based on this we find it relevant to investigate the use of a stratification algorithm in a hospital setting for identifying patients at most need for the preoperative CBT intervention.

We did not find preoperative CBT to have an effect on return to work as expected, despite the significant improvements in disability seen in the CBT group already after three months. This could indicate that other strategies are required, aimed more specifically at work resumption. Whether the improvements in disability seen at three months can make the patients capable of returning to work already at this time, perhaps with shorter working hours or relevant restrictions, should be investigated further. Provided that the preoperative CBT intervention is implemented, an additional intervention targeting work-resumption could be initiated between three and six months after surgery, building on the effects of the CBT intervention. In a societal perspective this would be most relevant to investigate seeing that the largest cost of both the CBT group and the control group was the cost of productivity loss.

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Appendix

Appendix I

Rolving N, Oestergaard LG, Willert MV, Christensen FB, Blumensaat F, Bünger C, Nielsen CV. *Description and design considerations of a randomized clinical trial investigating the effect of a multidisciplinary cognitive-behavioural intervention for patients undergoing lumbar spinal fusion surgery.* BMC Muskuloskeletal Disorders. 2014, **15**:62

Appendix II

Rolving N, Christensen FB, Nielsen CV, Holm R, Bünger C, Oestergaard LG. *Effect of a preoperative cognitive-behavioural intervention on in-hospital pain, mobilisation and dicharge for lumbar spinal fusion patients.* Submitted for publication in European Spine Journal

Appendix III

Rolving N, Nielsen CV, Christensen FB, Holm R, Bünger C, Oestergaard LG. *Does cognitive-behavioural intervention influence the patients' disability, pain and pain behaviour after lumbar spinal fusion?* Spine. 2015, 40 (9)

Appendix IV

Rolving N, Sogaard R, Nielsen CV, Christensen FB, Bünger C, Oestergaard LG. *Preoperative cognitive-behavioural patient education versus standard care after lumbar spinal fusion: Economic evaluation alongside a randomized controlled trial.* Submitted for publication in Spine