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Exercise Intervention and Predictive Factors

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Impossible is nothing…..

Whatever you can do or dream you can, begin it!
Boldness has genius, power and magic in it.
(Johann Wolfgang von Goethe 1749-1832)

To my wonderful daughters
Johanna, Malin and Kajsa

ABSTRACT

Low-back pain continues to be one of the main problems for which subjects seek treatment in primary care. While the natural history of low-back pain is often considered to be good, many sufferers get further episodes that affect well-being as well as quality of life.

Aim: The main aim of the work presented in this thesis was to evaluate the efficacy of a graded exercise intervention in a sample of subjects with recurrent low-back pain still at work, and to investigate factors predicting future outcome of disability and pain.

Methods:One-hundred-and-eighteen subjects with recurrent low-back pain participated. In addition, *Study I* included 57 healthy age- and gender-matched controls. Pre-intervention, post-intervention, 6-month, 12-month (*Studies II, III, IV*) and 36-month (*Study III*) follow-ups evaluated pain, disability, physical health, fear-avoidance beliefs and self-efficacy beliefs. Self-rated questionnaires were used. Level of aerobic fitness was compared between the group with low-back pain and healthy controls (*Study I*), and a graded exercise intervention emphasizing stabilizing exercises was evaluated in comparison with either manual treatment (*Study II*) or daily walks (*Study III*). Predictive factors for a future outcome of disability and pain were investigated using multivariate regression analysis (*Study IV*).

Results: There was no difference in aerobic fitness level between subjects with low-back pain and healthy controls. In the group with LBP, regression analysis showed an association between a lower level of aerobic fitness and higher age, gender and lower levels of self-efficacy (*Study I*). In *Study II*, comparing a graded exercise intervention with manual treatment, a significant difference in favour of the exercise group regarding disability after the treatment was maintained in the long term. No significant difference emerged between the groups regarding pain. (*Study II*). In *Study III*, between-group testing showed significant differences in favour of the exercise group for perceived disability at 12-months, maintained at the 36-month follow-up. In addition, between-group results for pain showed greater reduction for the exercise group post-intervention than for the daily-walks group. Regarding secondary outcome, the results showed a significant group difference in favour of the exercise group in short- and long term regarding physical health and in self rated self-efficacy at 12- and 36-month follow-ups. Regarding fear-avoidance, no such differences emerged (*Study III*). Lower levels of self-efficacy, higher levels of perceived disability pain-level and pain frequency emerged as predictors of an unfavourable clinical outcome, and these predictors remained significant in the post-intervention models. (*Study IV*).

Conclusions: In conclusion, a graded exercise intervention emphasizing stabilizing exercises alleviated disability levels and improved physical health and rated self-efficacy more than manual treatment or daily walks did, in subjects with recurrent low-back pain and currently at work. The graded exercises also reduced recurrent need for treatment in the long term, indicating that the exercises had a preventive effect. Levels of aerobic fitness were comparable between the subjects with low-back pain and the healthy controls. However, lower levels of aerobic fitness were associated with higher age, gender and low self-efficacy in the sample of subjects with low-back pain. Importantly, higher levels of perceived pain, pain frequency and disability and a lower level of self-efficacy emerged as predictors of an unfavourable outcome of disability and pain in the long term, indicating that such early screening information might be useful for further management of patients with LBP.

SAMMANFATTNING

Ländryggsmärta är fortfarande en av de vanligaste orsakerna varför personer söker vård inom primärvården. Även om normalförloppet vid ryggsmärta oftast är gott så drabbas många personer av upprepade besvär, vilket påverkar såväl det allmänna välbefinnandet som livskvaliteten.

Syfte: Det huvudsakliga syftet med denna avhandling var att utvärdera effekten av ett träningsprogram med successiv stegring för icke-sjukskrivna personer med återkommande ländryggsmärta, samt att undersöka vilka faktorer som indicerar en sämre prognos avseende funktion och smärta.

Metod: Etthundra arton personer med upprepad ländryggsmärta deltog i studierna. Studie I omfattade också 57 friska kontrollpersoner som var matchade för ålder och kön. Skattad smärta, funktionsförmåga, fysisk hälsa, rörelserädsla samt tilltro till egen förmåga utvärderades med hjälp av frågeformulär före och efter avslutad behandling. Uppföljning gjordes 6, 12 *(Studie II, III, IV)* och 36 *(Studie III)* månader efter behandlingen. Jämförelse av konditionsnivå gjordes mellan gruppen med ryggsmärta (n=57) och den ryggfriska kontrollgruppen (n=57) (*Studie I).* Ett träningsprogram med successivt stegrade stabiliserande övningar utvärderades och jämfördes dels med manuell behandling *(studie II)* dels med dagliga promenader *(Studie III).* Faktorer som kan indicera sämre prognos för smärta och funktionsförmåga undersöktes med multivariat regressionsanalys *(Studie IV).*

Resultat: Resultaten visade ingen skillnad mellan gruppen med ländryggsmärta och den ryggfriska gruppen gällande konditionsnivå. I gruppen med ryggsmärta visade dock regressionsanalys ett samband mellan längre konditionsnivå och högre ålder, kön samt lägre grad av tilltro till egen förmåga *(Studie I).* I *Studie II* där träning jämfördes med manuell behandling sågs både efter avslutad behandling och vid uppföljning en signifikant större förbättring i upplevd funktionsförmåga hos träningsgruppen jämfört med gruppen som fick manuell behandling. Ingen skillnad kunde dock noteras beträffande skattad smärta. Resultat i *Studie III* visade, såväl efter 12 som 36 månader, en skillnad gällande upplevd funktionsförmåga till fördel för den stabiliseringstränande gruppen jämfört med gruppen som gick dagliga promenader. Även skattad smärta var signifikant lägre för stabiliseringsgruppen efter behandlingen, men skillnaden kvarstod inte i långtidsuppföljningen. Skattning av rörelserädsla visade ingen skillnad mellan grupperna vid något mättillfälle, men den upplevda fysiska hälsan och tilltron till egen förmåga visade en skillnad till stabiliseringsgruppens fördel vid långtidsuppföljningen *(Studie III).* Dålig tilltro till egen förmåga, upplevd sämre funktionsförmåga, smärtnivå och smärtfrekvens var faktorer som i den multivariata analysen visades vara viktiga prediktorer för en sämre prognos vid ryggsmärta vare sig de mättes före eller efter behandlingen *(Studie IV).*

Sammanfattning: Sammanfattningsvis så förefaller ett träningsprogram med successivt stegrade stabiliserande övningar förbättra skattad funktionsförmåga, fysisk hälsa samt tilltro tilll sin egen förmåga mer än manuell behandling eller dagliga promenader hos personer med återkommande ländryggsmärta och där de flesta är i arbete. Träningsprogrammet minskade också behovet av behandling i långtidsuppföljning vilket indikerar att programmet också kan ha en preventiv effekt. Faktorer som högre smärtnivå, ökad smärtfrekvens och bristande tilltro till egen förmåga förefaller tyda på en sämre prognos för god funktion vid ryggsmärta. Detta indikerar att det är viktigt att utvärdera prediktiva faktorer för att kunna identifiera patienter med risk för en sämre prognos, vilka kan komma att behöva vidare behnandling.

LIST OF PUBLICATIONS

The thesis is based on the following original papers. Each paper will be referred to by its Roman numeral (Study I-IV)

I **Rasmussen-Barr E**, Lundqvist L, Nilsson-Wikmar L, Ljungquist T.
Aerobic fitness in patients at work despite recurrent low back pain: a cross-sectional study with healthy age- and gender-matched controls.
J Rehabil Med 2008; 40:359-365

II **Rasmussen-Barr E**, Nilsson-Wikmar L, Arvidsson I.
Stabilizing training compared with manual treatment in sub-acute and chronic low-back pain.
Man Ther 2003;8:233-41

III **Rasmussen-Barr E**, Äng B, Arvidsson I, Nilsson-Wikmar L.
Graded exercise for recurrent low-back pain. A randomized controlled trial with 6-, 12- and 36-month follow up.
Spine 2009; 3:221-228.

IV **Rasmussen-Barr E**, Äng BO, Campello M, Arvidsson I, Nilsson-Wikmar L.
Factors predicting clinical outcome in recurrent low-back pain 12-and 36-months after an exercise intervention.
Submitted

Additional analyses have been added.

LIST OF ABBREVIATIONS AND DEFINITIONS

ANOVA	Analysis of variance
BMI	Body Mass Index
CI	Confidence Interval
FABQ	Fear-Avoidance Beliefs Questionnaire
GP	General Practitioner
IASP	International Association for the Study of Pain
ICC	Intraclass Correlation Coefficient
ICF	International Classification of Functioning , Disability and Health
LBP	Low Back Pain
MCIC	Minimal Clinically Important Change
ODI	Oswestry Low Back Pain Disability Questionnaire
OMT	Orthopaedic Manual Therapy
OR	Odds Ratio
RCT	Randomized Controlled Trial
SES	Self-Efficacy Scale
SF-36	The MOS 36-item Short Form Health Survey
VAS	Visual Analogue Scale
WHO	World Health Organization

Low-back pain	'low back pain, ache or discomfort, localized below the costal margin and above the inferior gluteal folds (with or) without referred leg pain'[126]
Non-specific low-back pain	'low back pain not attributed to recognizable known specific pathology'[47,103]
Pain	"an unpleasant and emotional experience associated with actual or potential tissue damage, or described in term s of such damage" [126]
Recurrent low-back pain	'low back pain that occurs again after an interval that was pain free' [29,212,216]

CONTENTS

1 INTRODUCTION

Low-back pain (LBP) continues to be one of the main problems for which sufferers seek treatment in primary care[12,23,40,45,149-151] and is considered worldwide to be associated with enormous costs, both in terms of direct health-care costs and losses in relation to work and disability[23] While the natural history of low-back pain is often considered to be good, many patients get recurrent episodes with consequences for well-being as well as for quality of life.[1,26,187,188,205] For most patients in primary care LBP is considered to run a recurrent course, not acute or chronic in the usual sense of these terms.[23,146,213,216] Pain is often expressed by the individual as the main reason for seeking care[59,4] even if the goal of the treatment is more often to reduce functional limitations caused by the pain. To date there is no "cure" for LBP, although an active physical approach has been advocated.[2,67,69,103] According to recent guidelines, an active approach, resuming normal activities and restoring function is the primary goal in LBP rehabilitation.[1,67,103] However, there is no clear consensus as to what type of exercise or active program should be prescribed[1,69,121,135] Recommendations for self-care in LBP and teaching the patient life-long habits might significantly control future episodes [138,187] Recently, there has been focus on exercises aiming to optimize the control of segmental motion and stabilization of the lumbar spine. These exercises differs from general exercises and endurance training by being graded, more body-specific and requiring from the patient more attention and precision of movement control.[157,160] Such a graded intervention may also affect psychosocial factors, importantly related to the persistency and recurrence of disability and pain. [44,211]

In the interaction between the physiotherapist and the patient with LBP, clinical judgment and expertise should be used *together* with current evidence, hereby choosing a treatment strategy that provides good function in the musculoskeletal system. Such a treatment strategy might prevent future recurrences of disabling pain and thus maintain the patient's current work status, considered important for health.[1,103,188] The present work was conducted to evaluate the effecacy of a graded exercise intervention emphasizing stabilizing exercises in short and long terms, and also to explore factors that might predict the future course of disability and pain in a sample of subjects with recurrent LBP, the majority at work.

1.1 PERSPECTIVES AND FRAMEWORK

According to the World Confederation of Physical Therapy (WCPT), physiotherapy is concerned with identifying and maximizing movement potential, with regard to prevention, rehabilitation and treatment.[178]

The present thesis concerns subjects with recurrent non-specific LBP, the majority at work, seeking physiotherapy treatment in primary care due to functional limitations and pain. The effect of LBP on the individual can be classified using the World

Health Organization's International Classification of Functioning, Disability and Health (WHO-ICF) model.[140] Non-specific LBP does not necessarily include structural changes by definition, but can cause loss of health status in the form of symptoms, disability and loss of function, limitation of activities and restricted participation.

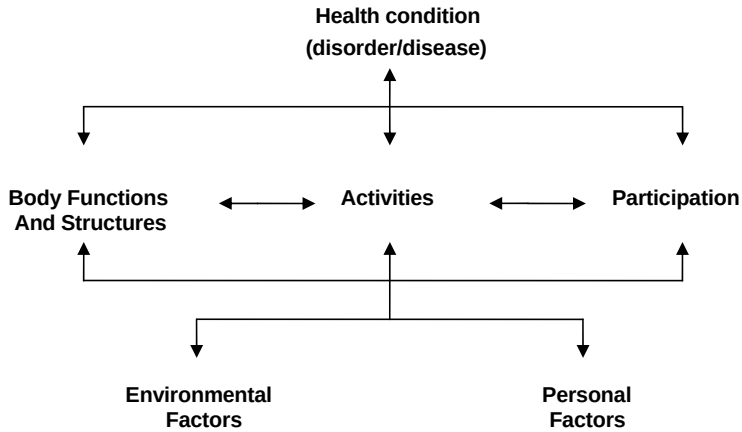


Figure 1. The ICF-model of functioning, disability and health

The ICF acknowledges that *every* human being can experience a decrease in health and thereby experience some degree of disability. The ICF thus recognises the experience of disability as a universal human one. Further, the ICF takes account of the social aspects of disability and does not see disability only as a 'medical' or 'biological' dysfunction. The WHO-ICF model has two main components (Fig 1). The first is functioning and disability, which is further divided into body functions and structures, activities and participation. Body function and structures are assessed in terms of change in physiological function and anatomical structure. Activity is the execution of a task or action, and participation is defined as involvement in life events. Functioning is the positive aspect of these components and disability is the negative aspect. The second main component of the WHO-ICF model includes a classification system to further describe environmental and personal contextual factors that can influence functioning and disability. In this thesis the ICF model is used to map dimensions of assessments and it is applied under methods and captures participation, activity, body function and structure and personal factors.

2 BACKGROUND

2.1 HISTORICAL PERSPECTIVE OF LOW-BACK PAIN

Low-back pain has been a problem for mankind throughout history. The oldest surviving text on the subject was written on papyrus about 1500 B.C. It is a series of 48 cases, the last of which was an acute back strain (as noted by Waddell 1996).[3,186] The relation between body and mind is fundamental to human existence and to medicine and was discussed as early as 427 B.C. by Plato:

"So neither of you ought to attempt to cure the body without the soul, and the reason why the cure of many diseases is unknown to the physicians of Hellas, is because they are ignorant of the whole which ought to be studied also, for part can never be well unless the whole is well."

From the sixteenth century a mechanistic approach of orthodox medicine became more dominant. Descartes (1596-1650) and followers divided human existence rigidly into mind and body, thus medicine dealt with the body and pain was a warning signal of disease. By 1800, physicians were beginning to look for a cause of back pain and suggested that it was 'rheumatic phlegm'. In the nineteenth century two key ideas laid foundations for our model approach to back pain; that it came from the spine and that it was due to trauma. In 1828 it was suggested for the first time that the vertebral column and the nervous system could be the source of back pain, which should be treated with rest. World War II saw an increase in LBP and, instead of being diagnosed as 'fibrositis' or a 'rheumatic condition' it was more likely to be attributed to 'strain'.[186] From then until some 10-15 years ago, LBP in primary care was considered a purely biomedical condition. There has since then been a transition from viewing LBP as a biomedical injury to viewing it as a multifactor biopsychosocial pain syndrome.[23,189] In addition, after many years of recommendations for rest and interruption of activities and work for subjects suffering from LBP, there is now growing evidence that an active approach, resuming normal activities, and restoring function is the primary goal in the rehabilitation of patients with LBP [1,67,103]

2.2 DEFINITIONS OF LOW-BACK PAIN

Musculoskeletal pain must not be seen as a disease but as a natural condition that most people experience at some time in life. Pain is a complex phenomenon associated both with emotional and psychological reactions. In all kinds of pain there are two components: subjective judgement of its intensity, localization and duration, and the emotional, discomfort and distressing experience that it brings[115] The consensus definition of pain developed by the International Association for the Study of Pain (IASP) as

"an unpleasant and emotional experience associated with actual or potential tissue damage, or described in term s of such damage" [126]

In this thesis, low-back pain is defined as

"pain, ache or discomfort, localized below the costal margin and above the inferior gluteal folds (with or) without referred leg pain" [126]

The term LBP refers to a large heterogeneous group of clinical and etiological entities. It has been estimated that 5-15% of occurrences have a clear pathoanatomical diagnosis.[35-38] The rest are considered to have non-specific LBP, a variety of pathological and pathophysiological conditions.[47,89,196] It is estimated that up to 10% of non-specific LBP cases will end in more persistent pain and disability. [47] An European guideline [2] for the management of non-specific LBP recommends the use of a triage or screening, to exclude specific spinal pathology , and the assessment of prognostic factors. The term "red flags" is in the clinical examination and screening of the patient used for signs and symptoms that are frequently associated with specific LBP (e.g. infection, tumour, osteoporosis, inflammatory process, fracture or radicular syndrome).[103] In the assessment of prognostic factors (e.g. emotional problems, work related problems and inappropriate pain behaviour) that may increase the risk of developing persistent pain; the term "yellow flags" is used[103] The goal by triage is to maximize the benefit of treatment and avoid unnecessary over or under treatment .[197]

This thesis concerns subjects with recurrent *non-specific LBP*. Non-specific LBP was defined as

"not attributed to recognizable known specific pathology (e.g. infection, tumour, osteoporosis, inflammatory process, fracture or radicular syndrome)"

and recurrent LBP was defined as

"pain that occurs again after a pain-free interval"[29,212]

There have been several attempts to classify this large group of LBP into more homogenous sub-groups.[43,118,148] Could sub-groups be identified, such a classification might assist in the choice of a treatment strategy, and this has been identified as a top priority for primary care research.[23,24]

Sub-classification by duration is commonly applied, e.g. acute pain for 0-3 weeks with pain and disability from onset, sub-acute pain for 4-12 weeks and more than 12 weeks for chronic or persistent pain.[131,212] Recurrent pain has been defined in several ways, [124,131,192,193,212,213,216]

e.g. patients seeking help after at least one month, going on sick-leave after at least one month still working; or a new episode after being symptom-free for six months. LBP in primary care is considered to run a recurrent or intermittent course, not acute or chronic in the usual sense of these terms.[23,213,216] Persistent and recurrent pain are not to be considered as a static condition.[124]

2.3 BACK PAIN – PREVALENCE AND RISK FACTORS

The overall life prevalence of musculoskeletal pain in the population varies between studies but is uniformly high.[11,59,88] A survey of long-lasting pain reported that 19% of all adult Europeans had long lasting pain of moderate to severe intensity that seriously affected the quality of their social and working life.[26] Almost half suffered from back pain. About 60-65% of the Nordic population is likely to experience LBP within a 12-months period.[108] In a working population in Sweden, life prevalence is reportedly 69%, 12-months prevalence 47 % and point-prevalence 18 %.[88] The Swedish National Public Health Report (2005) indicated an increase in the prevalence of back and neck pain during the previous decade and in outpatient attendance for back and neck patients.[172] These patients are commonly seen by general practitioners and physiotherapists in everyday practice. Most patients will improve rapidly after the onset of LBP, and improvement is seen up to three months after onset.[40,147] However, six months after an episode, 60-70 % will have experienced recurrences, 16% will be sick listed and as many as 60-80% will experience recurrent pain after 12 months. Thirty-three percent will have intermittent or persistent pain of moderate intensity and about 20% a poor functional outcome.[40,72,147,215,216] Picavet & Shouten[151]reported in a Dutch prevalence study that of 65% of sufferers with LBP reported recurrent pain; 48% mild and 17% severe recurrent pain.

The determination of risk factors for LBP is a difficult task as the origin and cause of LBP and disorders are complex, being affected also by psychosocial factors.[83,103,194]
A Dutch study[149] reported that being a woman, low educational level and work status were risk factors for LBP. Physical factors such as work load, whole-body vibrations, frequent bending and twisting of the trunk, frequent heavy lifting, and static work postures have all been proposed as risk factors associated with LBP.[82,119,131] A review[116] of work-related psychosocial factors and LBP concluded that high job demands, low job satisfaction and low work support were considered risk factors for LBP. Waddell & Burton[188] asserted that remaining in work is beneficial for physical and mental health and well-being.

2.4 ANATOMY AND KINEMATICS OF THE LUMBAR SPINE

The basic anatomical and functional unit of the vertebral column is the intervertebral joint and the two synovial facet joints.[18] The spine is inherently unstable. Its overall mechanical stability, especially in dynamic conditions and under heavy loads is provided by the passive elements and the precisely coordinated surrounding muscles.[143] Lucas (1970)[114] hypothesized that a buckling failure of the lumbar spine, without support of muscles, occurs with compressive loading of as little as 90N. Lucas' model[114] argues that antagonistic muscle activity is required to maintain the lumbar spine in a mechanically stable equilibrium[35,38,58] The muscles situated near the body surface and far from the midline are considered to be highly effective motor agents whereas those adjacent to the spinal column are mainly concerned with maintenance of segmental and body posture.[161] Bergmark[15] proposed in a biomechanical model that the lumbar spine is stabilized by an activation of "the local muscle-system": segmentally inserted muscles and the "global muscles system" i.e. muscles which transfer the load directly between the thoracic cage and the pelvis. Stability depends on the system but also on the task being performed. Stability of the lower back in relation to perturbations can be expressed as a robustness of the system to cope with different disturbances.[158] Stabilizing exercises are proposed to make the spine more robust thus reducing risk of injury.[158]

2.5 LOW-BACK PAIN MECHANISMS

Many spinal structures probably play a role in pain production, and all innervated structures in the spinal motion segment are possible sources of pain.[130] Several distinct types of pain exists; nociceptive pain, inflammatory pain, neuropathic pain and functional pain. *Nociceptive* pain is transient pain in response to noxious stimulus, *inflammatory* pain is spontaneous pain and hypersensitivity to pain in response to tissue damage and inflammation, *neuropathic* pain is spontaneous pain and hypersensitivity to pain in association with damage to or a lesion of the nervous system, and *functional* pain is hypersensitivity to pain resulting from abnormal processing of normal output.[165,217] The nociceptive sensation may occur via inflammation, biomechanical loading changes and immunological factors.[144,145]

Panjabi[144] hypothesised that trauma or a repetitive micro-trauma may cause injuries of the spinal ligaments, disc annulus and the facet capsules, so affecting the embedded mechanoreceptors. The injured mechanoreceptors may then generate corrupted transducer signals, leading to corrupted muscle response pattern produced by the neuromuscular control unit, resulting in an abnormal loading due to changed motor behaviour and thus excessive loading of, and strain on, the facet joints. Other authors [92,167] have also suggested that the ligament mechanoreceptors have an important role in muscle coordination and in the reflex regulation of functional joint stability. This, by

contributing to pre-programming for muscle stiffness through reflex modulation of the γ-muscle spindle system. These abnormal conditions may persist and may over time lead to back pain.

The contribution of psychological factors to the development and maintenance of pain perception in LBP needs to be considered.[165] There is a cognitive response secondary to the pain sensation which will be drawn from the person's experience and other variables such as stress, passive coping strategies, depression, anxiety, anger and somatisation, which can all worsen the perception of pain.[183-185] Carlsson & Nachemson[131] summarized that "mechanical factors, plus global pain sensitivity plus psychosocial factors make up the degree of disability and pain the person experiences".When evaluating the patient it is necessary to understand the clinical findings in relation to issues of everyday functioning and social adjustments.

2.6 MANAGEMENTS OF LOW-BACK PAIN

Management and treatment of LBP may follow both a biomedical and a bio psychosocial model. A biomedical model assumes that there is a one-to-one relationship between the amount of damage and the pain. Management will then comprise localization and treatment of underlying pathology and structure in order to achieve a remedy or a cure.[42] A biopsychosocial model allows for interaction of the biological, physiological and social aspects of pain.[208]

Evidence-based guidelines for the treatment of LBP have been developed in several countries. A review of 11 of these guidelines concluded that the recommendations for management and treatment of LBP are quite similar.[99] Trials of different treatment modalities available for LBP have failed to determine what strategy is optimal and no single intervention is likely to be effective in treating the overall problem of non-specific LBP.[2] There is however convincing evidence that subjects with LBP should continue their everyday activities as much as possible,[1,2,103,131] and an active approach has indeed been recommended in the treatment of subjects with persistent LBP.[1,2,67,103]

2.6.1 Manual treatment and management

Orthopaedic manual therapy (OMT) is a specialized area within physiotherapy that is represented worldwide. Approximately 400 physiotherapists in Sweden have a postgraduate diploma in OMT according to IFOMT´s standards and more than thousands have been trained in OMT in postgraduate courses. The definition of OMT as presented by the International Federation of Orthopaedic Manipulative Therapists (IFOMT) is:

"Orthopaedic Manual Therapy (OMT) is a specialized area of physiotherapy / physical therapy for the management of neuromusculoskeletal conditions, based on clinical reasoning, using highly specific treatment approaches including manual techniques and therapeutic exercises. Orthopaedic manual therapy also encompasses, and is driven by, the available scientific and clinical evidence and the bio psychosocial framework of each individual patient"

Manual treatment is commonly used in primary care by physiotherapists; in combination with specific and functional exercises. Manual treatment comprises a variety of techniques; mobilisation, manipulations, massage and stretching. The effectiveness of mobilisation and manipulation are often summarized in reviews. Reviews present moderate/strong evidence that manipulative therapy can be effective for the relief of pain and improvement of function, at least in the short term.[18,33, 27] Inhibition of nociceptive stimuli by physical stimuli (e.g. massage, manipulation) is capable of activating endogenous nociceptive control systems via descending pathways and segmental inhibition ("gate theory") resulting in pain relief.[109,204]

In everyday practice a treatment goal is always discussed together with the patient after the clinical examination. It is this thinking, discussion and decision-making associated with clinical practice and evidence that enables the physiotherapists to take the best-judged action for individual patients.[91] Treatment may comprise a combination of manual methods and specific exercises and functional training both under the therapist's supervision and as self-management in order to avoid recurrences. The treatment strategy or approach in clinical everyday practice is more pragmatic than in the present context, where we decided to evaluate the efficacy of a graded stabilizing programme in comparison with manual treatment; not the two together. In this work the clinical examination and analysis of functioning, including the subjects studied was standardized using clinical tests applied in everyday practice by physiotherapists with a post-graduate diploma in OMT.[16,174]

2.6.2 Exercises

An evidence-based review[164] in Sweden of different treatment approaches for LBP concluded: "Stay active – back pain is common and usually not harmful". Evidence-based guidelines for an active approach have been developed in many countries. According to recent guidelines, there is moderate/strong evidence that exercise therapy is more effective in the reduction of pain and disability, than passive treatment and than care by a general practitioner.[1,2,66,67,69,103] Activity and back pain influence each other. Both total inactivity and some types of activity may cause LBP.[1,31] However, in the treatment of sub-acute, persistent or recurrent LBP, an active approach is recommended.[1,103,164] The term "activity" refers to mobility and activities of daily living, recreational and sport-related activities and occupational activities.[1] Exercise therapy may be defined as "*a series of movements specifically designed to condition or develop the body when performed regularly or to improve fitness as means of promoting health*".[1,69]

It is not clear if the efficacy of an exercise program is due to physical performance factors. There is conflicting evidence that exercises in the treatment of LBP lead to fiber type change or muscle hypertrophy (Käser et al 2001). The effects of exercises might be related to other factors such as improving self-beliefs. Supervision by a physiotherapist seems to improve the efficacy of an exercise programme[69,104,122,123] and the use of grading exercises together with a cognitive-behavioural approach appears to be advisable.[2] However, no single programme is optimal for all patients with LBP and there is conflicting evidence regarding where exercises have highest efficacy.[1,31,67,127,136] It is therefore, recommended that future research should focus on investigating specific exercise interventions strategies, among others stabilizing exercises, instead of general exercises and in well-defined low-back-pain populations.[29,68]

Graded stabilizing exercises

The treatment strategy termed 'stabilising exercises' is not a new entity.[162] One of the earliest references[162] reported that "the most successful exercise program avoids further strain to damaged structures while encouraging a posture of minimum stress to improve function and limit disability".

During the past decade there has been new focus on exercises aiming to optimize the control of segmental motion and stabilization/control of the lumbar spine. Bergmark[15] proposed in a biomechanical model that the lumbar spine is stabilized by activation of "the local muscle system" segmentally inserted muscles; Here, later experimental research has reported deficits in m. Transverus Abdominus (TrA) and m. Multifidus (MF) in subjects with LBP compared to healthy subjects.[10,73,74,79,80,84,87,182] Hides et

al.[75] reported a decrease of the cross-sectional area (CSA) of MF, in subjects with first-episode LBP. The recovery of of the MF CSA was not not automatic and differed between the groups investigated;the specific stabilizing training group recovered the CSA better than did the reference group.[75] In the long term that group also got less recurrent pain periods. In addition, altered motor control of the lateral abdominals seems related to the persistence of LBP.[80,94,182] At least in the early phases of management, stabilizing exercises targeting these muscles appear to be effective in reducing disability, pain and recurrence rate in LBP.[75,139] It has been argued, however, that it is important to involve a combination of several potentially lumbar spine stabilizers in an exercise programme.[93,94]

Stabilizing exercises differ from general exercises by being more body-specific and requiring more attention and precision from the patient.[159,160] To avoid recurrent LBP the importance of activating the stabilizing muscles in activities of daily life, especially those that set off pain, is underlined. The progression of the exercises is based on the patient's pain level and observed movement control and quality. Progression depends on weather or not the specific activation is integrated with the performance of the exercises and the postural control in a functional manner. Further progression of the intervention is always integrated with the kind of exercise, sport or activity that patients with LBP prefer or are used to. Being individually dosed and graded[110] into functional and loaded positions, the programme might also affect personal factors e.g. self-efficacy[44,211] and fear of movement.[190,210]

To date, few trials have investigated stabilizing exercises without integration of other modalities,[75,139,156] while others have evaluated stabilizing exercises integrated with education,[30,102,134] manual therapy,[30,60,129] manipulation,[30,55,102] and general exercises.[30,55] These trials report somewhat conflicting results (Table 1). The present aim was to evaluate the efficacy of graded stabilizing exercises without integration of other modalities.

Table 1. Selected randomized controlled trials investigating stabilizing exercises published 1997-2009.

Authors	Patients and duration	Intervention	Efficacy
Cairns et al [30] 1996	n=97 with recurrent LBP	A: SE+MT+GE+ edu B: MT+edu	After treatment A=B At 12-months A=B
Ferreira et al[55] 2007	n=240 with recurrent LBP	A:SE B: GE C: MT	After treatment A>B , C At 6 and 12 months A=B=C = ns
Goldby et al [60] 2006	n=346 LBP>3 months	A: SE+edu B: MT+edu + edu C: edu	After treatment A> B,C At 6 and 12 months A=B>C
Hides et al [75] 1996	n=41 First time LBP < 3 weeks	A: SE B*:* GP	After treatment A=B, A>B regarding cross-sectional area m. multifidus At 12 and 36 months; A= less recurrent pain
Koumantakis et al[102] 2000	n=55 with recurrent LBP	A: SE+GE+edu *B:* GE+edu	After: Pain A=B, Disability A>B At 3 months = ns
Moseley et al[129] 2002	n=57 LBP >2 months	A: SE+MT+edu B*:* GP	After treatment A>B At 12-months A>B
Niemestö et al[134] 2003	n=204 LBP >3 months	A: SE+MT+edu B: GP+edu	At 5 and 12 months A>B At 24 months = pain A>B
O'Sullivan et al[139] 1997	n=44 >3 months Spondylolisthesis	A: SE B: GE	After treatment and 30 months Pain and disability A>B
Rasmussen-Barr et al[156] 2003	n=47 with recurrent LBP >6 weeks	A: SE *B:* MT	After treatment pain A=B, disability A>B, At 3-months disability A>B
Rasmussen-Barr et al[157] 2009	n=71 with recurrent LBP >8 weeks	A: SE *B:* daily walks	After treatment pain A>B. disability A>B At 12 months disability A>B, physical health and self-efficacy A>B

LBP= low-back pain, > significantly better than reference group SE=stabilizing exercises, MT=manual treatment, GE=general exercises, edu=education, GP=general practitioner, ns=non significant

2.7 FACTORS INFLUENCING OUTCOME

Several trials have investigated possible prognostic factors for *disability* in LBP,[50,106,117] namely: gender (female),[50,106,117] long painduration,[50,108,179] fairly low exercise level,[13,50,155] fairly high pain level or frequency,[50,179] duration of current period,[13,117]co-morbidity[108,169,179] and well-being or mental health.[108,117,179] Prognostic factors of importance in predicting persistent *pain* may be pain severity,[61,98] disability,[61,98] smoking, fear-avoidance beliefs[112,44,63] and self efficacy.[44] Subjects with severe pain will continue to suffer from severe pain while those with mild or moderate pain, even if recurrent, run a relatively low risk of future severe pain.[70,110,214,122] Importantly, other mediators of disability such as psychosocial factors may also impede recovery.[112] Recent reviews of prognostic factors report that psychological, social and economic factors are important for both the onset and the persistence of LBP.[111,153]

Early identification of patients at risk of chronic low-back pain seems important, and research in this area has been recommended.[191,23,90] Early factors that will predict long-term outcome may be helpful when choosing treatment strategies and in identifying subjects at risk of an unfavourable outcome of disability and pain. The prognostic factors evaluated in this work are only self-reported variables. It has been suggested that self-reported variables best explain changes in disability compared with physical measures after exercise rehabilitation for LBP.[122]

Deconditioning

Physical activity, in general, is considered important for health, depression and pain experience, and greater aerobic fitness may increase tolerance of physical activity and contribute to better mood, sleep and relaxation.[128,142] A factor contributing to the recurrence or persistence of LBP, it has been suggested, is physical “disuse” or “deconditioning”.[25,200] There is no clear evidence that patients with LBP are less physically fit than healthy controls and several trials report conflicting results.[77,133,171,199,202,207] Factors that might contribute to the aerobic fitness level in subjects with LBP are activity level, work status, pain level and fear-avoidance behaviour.[85,125,166,200,201,206] The lower activity level, reported by subjects with LBP might be an important variable when evaluating disability in relation to aerobic fitness in patients with LBP.[201] The WHO-ICF recommends focus on patients’ function instead of on their restrictions; this would imply pinpointing a person's "daily activity level" rather than his/her "disability level".[198]

Fear-avoidance beliefs about physical activity

Fear-avoidance beliefs refer to the avoidance of movement or activities that are believed or expected to cause pain, injury or re-injury.[41,209] Patients with LBP describe how pain prevents them from performing normal activities, and may report a fear- avoidance behaviour.[209,210] It is hypothesized that a chain of reactions including catastrophising and avoidance can lead to disuse, disability and depression, creating a vicious circle.[209] Most research on fear-avoidance beliefs is conducted in patients with persistent LBP. However, patients with recurrent episodes of pain may also have rising fear.[166] Linton et al.,[113] showed fear-avoidance beliefs to be related to the inception of a recurrent LBP episode. Further, pain-related fear can reportedly be detectable even in a pain-free population.[28] Sub-groups of patients have been reported to use various strategies in how they react to recurrent episodes of pain; some catastrophising their pain, which leads to avoidance behaviour.[14] Graded physical activity might be beneficial in the treatment of fear-avoidance behaviour as graded exercises affect self-efficacy thus mediating fear-avoidance beliefs.[5,6,211] (Fig. 2)

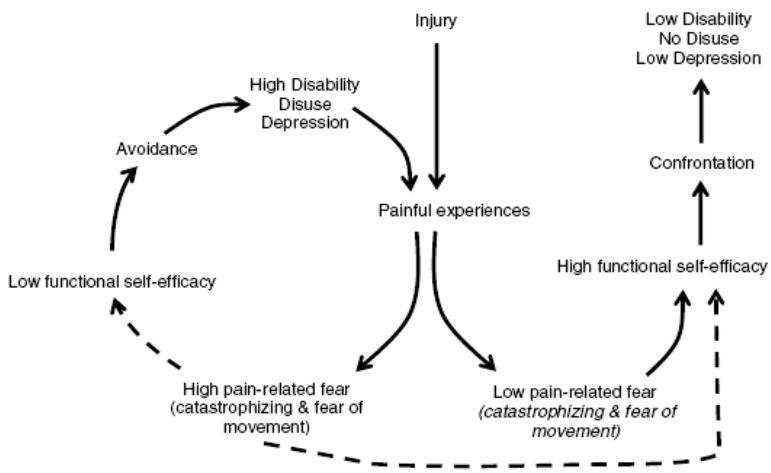


Figure 2. Revised fear-avoidance model incorporating the mediation role of self-efficacy (With permission from S.Woby)

Self-efficacy

Self-efficacy refers to the way how people set a goal and anticipate the likely outcome to guide and motivate their effort.[9] If a patient with LBP might finds motivation to engage in a situation, individual self-efficacy beliefs will influence the choice of activities, the amount of effort expected and persistence in the face of obstacles and adverse experience.[9] Self-efficacy is a better predictor of disability in relation to pain in recurrent LBP than e.g. fear-avoidance beliefs are:[44] it is also reportedly a mediator of pain-related fear (Fig.2).[211] How far patients are disabled by pain may depend on their self-efficacy: patients with a stronger self-efficacy more easily find strategies to prevent further recurrences.[14] These people believe, and are confident, that regular exercise prevents relapses.[14] Strong self-efficacy may also explain why subjects with disabling pain go on facing daily activities and working situations while weak self-efficacy is associated with e.g. helplessness and pessimistic thoughts.[8,44]

2.8 RATIONAL FOR THE THESIS

The rational for this thesis was to evaluate the efficacy of a graded exercise programme emphasizing stabilizing exercises for patients with recurrent LBP. These patients are commonly seen in primary care and seek treatment over and over again from different caregivers for their back problem. From my clinical experience as a physiotherapist, there was a good reason to believe that a graded exercise programme might be important in the management of these patients. Such exercises may reduce disability and pain and also be an important self-management strategy in order to avoid recurrent pain periods. For me, it was important to evaluate the efficacy of these exercises in randomized controlled trials, validating what was experienced in clinical practice. It was also thought that the supervising role of the physiotherapist, as relevant during the intervention period is an important aspect.

In the clinic it is also important to be able to identify patients at risk of an unfavourable outcome and to identify those patients that may not benefit from an exercise intervention and thus need additional back-pain management. Therefore the assessment and identification of prognostic factors before treatment is considered important to investigate and to implement in the clinic.

2.9 SUMMARY OF PROBLEM AREAS

General problems relevant to the present work are that:

- many people with recurrent LBP seek care over and over again implying that their functional limitation and pain affect their quality of life

- an active approach is recommended in the management of recurrent and persistent LBP but there is conflicting evidence as to what exercises that have the highest efficacy

- there is a lack of trials evaluating treatment or exercise interventions in different subgroups of LBP in the long term of more than one year

- it is essential to investigate factors predicting the course of disability and pain in the long-term. Such studies over more than one-year are scarce

3 OVERALL AIM

The main aims presented in this thesis were to evaluate the efficacy of a graded exercise intervention on disability and pain and to investigate factors predicting future outcome in subjects with recurrent low-back pain currently at work and in this group also to investigate factors predicting future outcome of disability and pain.

3.1 SPECIFIC AIMS

Specific aims were

to evaluate aerobic fitness level in subjects with low-back pain as compared to a healthy age- and gender-matched control group; and wheather the level of aerobic fitness in the subjects with low-back pain related to various illness- and health-related factors. *(Study I)*

to investigate the efficacy of a graded intervention emphaiszing stabilizing exercises in comparison with manual treatment in subjects with low-back pain, in the short- term and a long-term *(Study II)*

to investigate the efficacy of a graded intervention emphasizing stabilizing exercises in comparison with the instruction to take daily walks in the short- and long-terms *(Study III)*

to investigate potential independent factors that may predict an unfavourable clinical outcome of perceived disability and pain at 12- and 36-months following an exercise intervention *(Study IV)*

4 METHODS

4.1 DESIGN AND ETHICAL CONSIDERATIONS

This thesis is based on one cross-sectional study (*Study I*), two randomized controlled trials (RCT) (*Studies II and III*) and one predictive cohort study (*Study IV*). The study designs of Studies I-IV are presented in Table 2.

Table 2. Studies and their design, number of subjects, data collection and main outcome measures.

Study	Type of study outcome	Number of subjects	Data collection	Main
I	Cross-sectional	57 subjects with LBP* 57 healthy subjects	Questionnaire Ergometer test	Aerobic fitness Pain, disability Health related variables
II	Randomised controlled trial	47 subjects with LBP*	Questionnaire	Pain, disability General health
III	Randomised controlled trial	71 subjects with LBP*	Questionnaire	Pain, disability Health related variables
IV	Prospective Cohort study	71 subjects with LBP*	Questionnaire	Pain, disability

* LBP = Low-back pain

For all four studies, the subjects received written and oral information about the study and gave their informed consent before inclusion. Confidentiality and the voluntary nature of a questionnaire and physical measurement were stressed. They were informed that no data could be linked to any individual, that they could withdraw at any time without giving any reason, and that participation or non-participation would not affect their future care or treatment.

The studies were approved by the Regional Medical Research Ethics Committee, Karolinska Institutet, Stockholm.

4.2 STUDY SAMPLES

A total of 118 subjects with LBP and 57 healthy subjects participated in the studies reported in this thesis. The studies are based on two samples (n=47 and n=71). A healthy age- and gender-matched control group was in addition included in *Study I* (n=57). Subjects were recruited consecutively from LBP sufferers seeking care in private physiotherapy health care in Stockholm. They lived in urban or suburban parts of Greater Stockholm. Of the subjects, 23% (*Studies I, III, IV*) were referred by general practitioners, and the rest sought care on their own initiative or through recommendation (Table 3).

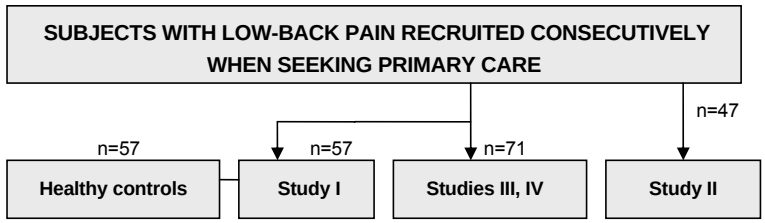
Studies I, III and *IV* were based on the same sample of subjects (n=71). They had recurrent LBP and were at work. *Study* II was based on subjects (n=47) with slightly different inclusion criteria, and included five subjects reporting sick leave and three reporting continuous instead of recurrent LBP on inclusion.

Inclusion criteria
Men and women aged 18-60 years, still at work despite ongoing recurrent LBP (>8weeks) *(Study II* > 6 weeks, n=5 on sick leave) but with at least one pain-free period during the previous year. LBP was defined as pain, ache or discomfort, below the costal margin and above the inferior gluteal folds, without referred leg pain[126] In *Study II*; pain could be referred to the knee or knees (n=6).

Exclusion criteria
First-time LBP, pain radiating to the leg or legs with or without overt neurological signs, pregnancy, known lumbar disc hernia or fracture, back surgery, diagnosed inflammatory, joint disease, known severe osteoporosis, known malignant disease.

The subjects were clinically examined by physiotherapists (n=12) with postgraduate diploma in orthopaedic manual therapy (OMT), all with more than 15 years of specialization. The examination was performed in the same manner for all subjects. The subjects had mechanically-induced LBP with pain on active movement (e.g. extension, flexion, and lateral flexion), paravertebral tenderness and a positive Springing test of at least one lumbar segment. The clinical tests used have previously been tested for acceptable inter-examiner reliability.[16,174] While the two samples were recruited with somewhat different inclusion criteria, they exhibit similar demographic and clinical data (Table 3). Figure 3a and b show the two samples' baseline data on the Disability Rating Index.[163]

Table 3. Recruitment pathway, demographic and clinical data of subjects with LBP and controls participating in Studies I-IV.



	Study I		Studies III, IV	Study II
	Healthy Controls	Subjects with LBP		
	n=57	N=57	N=71	N=47
Women/men (n)	28/29	28/29	36/35	35/12
Age (yrs)*	38 (11)	38 (11)	40 (12)	38(11)
Height (m)*	1.75 (0.09)	1.75 (0.09)		
Weight (kg)*	74 (14)	76 (16)		
BMI (kg/m^2)*	25 (4)	25 (4)		
Previous treatment (% of group)			74	74
Physical activity level (once per week) (% of group)	79	61	60	64
Physical health (SF-36) (0-100) **			75 (40-95)	
General health (VAS) (0-100)**			32 (18-51)	30(20-43)
Pain duration (yrs) **		10 (1-37)	10(1-38)	4 (1-20)
Duration of current pain (>12 weeks) (% of group)		38	47	42
Pain (VAS) (0-100)**		35 (20-60)	35(10-84)	33(21-49)
Perceived disability (ODI) (0-100) **		22 (12-28)	20(12-28)	14(10-24)
Perceived disability (DRI) (0-100) **			31(13-46)	33(16-48)
Self-efficacy beliefs (0-64) **		49 (39-56)	48 (39-56)	
Fear-avoidance beliefs (FABQ)				
FABQ Work (0-42) **		11. (5-18)	12 (5-19)	
FABQ Activity (0-24 **		12 (8-16)	13 (8-16)	

*mean (SD),**md (25th-75th) VAS=Visual Analogue Scale, ODI=Oswestry low-back pain disability questionnaire, DRI=Disability Rating Index

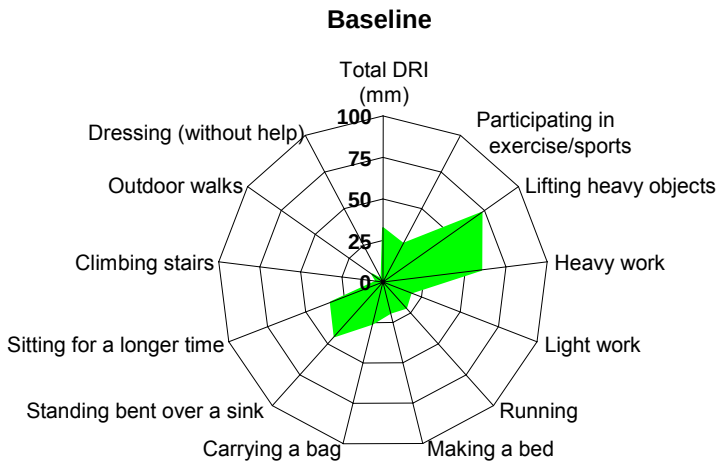


Figure 3a. Perceived disability as measured at baseline with the Disability Rating Index in Study II (n=47). The diagram describes the ten factors that make up the total DRI Score (mm).

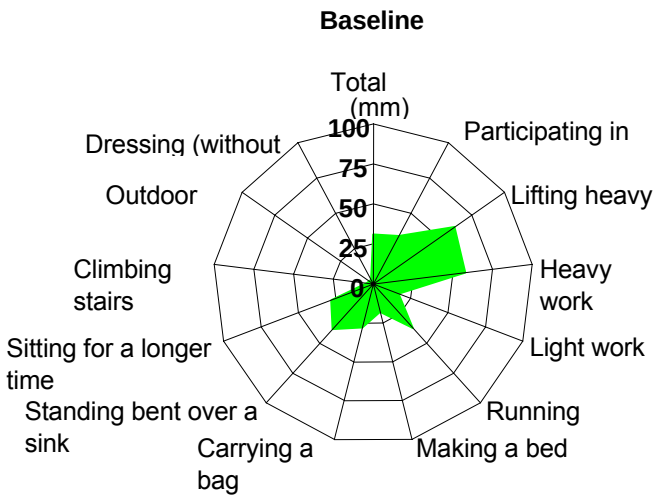


Figure 3b. Perceived disability at baseline as measured with the Disability Rating Index in Study III-IV (n=71). The diagram describes the ten factors that make up the total DRI Score (mm).

Non-responders and withdrawals

Five subjects withdrew from *Study II* immediately after inclusion because they preferred other treatment or training outside the trial. One subject in the manual therapy group was diagnosed with lumbar hernia during the intervention. Ten subjects did not answer the questionnaires or reminders at the 3- and 12 months follow-ups, giving a total dropout rate of 26% if the subjects that completed the intervention are included. Regression analysis showed no difference regarding baseline values between non-responders and responders. Concerning *Study III* withdrawals and drop-outs are presented in Fig 4. A total of 90 percent answered the 6-month follow-up, 86 percent the 12-month follow up and 79% the 36-month follow-up.

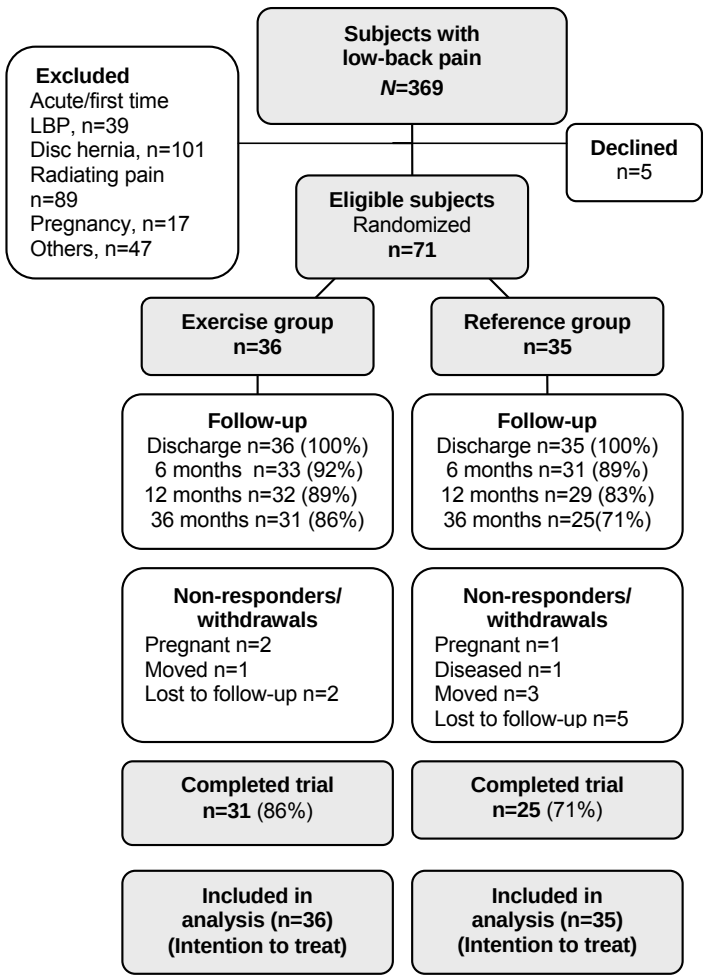


Figure 4. Flowchart of subjects, non-responders and withdrawals in Study III.

4.3 MEASUREMENTS

A general questionnaire was completed by all subjects with questions on back ground variables, demographic data, job satisfaction, medication, exercise habits, sick-leave, pain frequency, well being, previous treatment, previous outcome of treatment, expectation of current treatment.[168] The subjects completed the general questionnaire and the instrument (Table 4) as described hereunder on inclusion. After intervention and at 6-, 12- and 36-month follow-ups the same questionnaire and instruments were mailed and returned to the "Low-Back Pain Project" in pre-paid envelopes. The general questionnaire has been used in previous LBP research.[50,51,168]

Table 4. The ICF model, used to map dimensions of assessments

ICF components	Instruments	Study
Impairments		
Perceived pain	Visual Analogue Scale	I, II, III, IV
	Borgs CR-10 Scale	I
Activity Limitation/Participation		
Perceived disability	Oswestry LBP Questionnaire	I, II, III, IV
	Disability Rating Index	II
Exertion/Fatigue	Borgs RPE-Scale	I
Aerobic fitness	Ergometer test	I
General health	Visual Analogue Scale	I
Physical health/General health	Short Form – 36	I, III, IV
Physical Activity Level	Question*	I, III, IV
Personal Factors		
Self-efficacy	Self-efficacy Scale	I, III, IV
Fear-avoidance beliefs	Fear-avoidance beliefs Questionnaire	I, III, IV

* "How often do you exercise?"

Visual analogue scales

Visual analogue scales (VAS) were used to assess perceived pain.[86] The VAS used was a 100-mm horizontal line anchored on the left "no pain" and on the right "unbearable pain". Validity and reliability have been sufficiently tested for patients with LBP.[17,33] Furthermore, pain –frequency was measured on a 5-point scale included in the general questionnaire. . Patients also reported whether they had more than one pain focus, in response to a question also included in the general questionnaire.

Borg's Category Ratio-10 Scale

Before and after each cycle test the patients rated their perceived pain using Borg´s CR-10 Scale.[20] This category scale is used for ratings of pain intensity with certain ratio properties. It has ten scale steps plus an additional possibility to rate "maximal pain" (=11-12).

Oswestry Low-back Pain Disability Questionnaire

The Oswestry Low-back Pain Disability Questionnaire (ODI) covers 10 domains.[54] It is designed to assess how pain affects various activities of daily living (pain level, personal care, lifting, walking, sitting, standing, sleeping, sex life, social life and travelling). Higher scores mean greater activity limitation. Total possible score is 100. The scale is designed to assess disability in LBP patients and is recommended as a functional scale for back-pain.[100] Depending on the score, the patients can be categorized minimal- or no disability (0-20%), moderate disability (20-40%) or severe disability (40-100%). Fisher and Johnson conducted a detailed validation of the questionnaire. [57] The ODI has been tested for good reliability.[53,57,100,101]

Disability Rating Index

The Disability Rating Index (DRI) consists of 12 visual analogue scales of which patients to rate their ability to perform daily physical activities.[163] The 12 activities are dressing (without help), outdoor walks, climbing stairs, sitting for a fairly long time, standing bent over a sink, carrying a bag, making a bed, running, light work, heavy work, lifting heavy objects and participating in exercise/sports. The scales range from 0 mm (without difficulty) to 100 mm (not at all). The mean score of the 12 ratings is used as a disability-rating index, DRI. A higher index means more difficulties. DRI is considered to be a robust, practical clinical and research instrument with good responsiveness and acceptability for assessment of disability caused by impairment of common motor functions. It has high reliability and validity.[163]

Borg's RPE Scale

During the bicycle test in *Study* I, the subjects rated their perceived exertion and fatigue using Borg's RPE Scale.[20] The scale runs from 6 (no exertion at all) to 20 (maximal exertion). The RPE scale is constructed to show a linear relation ship with exercise intensity and many studies show a high association between pulse and rated exertion.[21]

Ergometer test

A sub maximal Åstrand bicycle test[20,22] is performed to predict maximum oxygen consumption (VO_2ml x kg $^{-1}$ x min $^{-1}$). Maximum oxygen consumption (VO_2max) is

estimated from the known linear relationship between heart rate and oxygen consumption at sub maximal workloads. The test result is expressed as ml VO_2ml x kg $^{-1}$ x min $^{-1}$. The subject cycle on a cycle ergometer for six minutes or until steady-state is achieved. The subjects start cycling with a workload of 0.5 W/kg at a constant rate of 60 rpm. The resistance is gradually increased. The resistance is based on the subject's heart rate during the first two minutes, to achieve a steady-state heart rate of at least 120 beats, a value which represents the limit for possible calculation of VO_2ml x kg $^{-1}$ x min $^{-1}$ It has been reported that validity and reliability of the test is good.[95 81]

General Health

General health was measured with a horizontal visual analogue scale (0= best imaginable to 100=worst imaginable). This scale was included in the general questionnaire used in previous research on subjects with LBP.[50,51,168] The general health scale was used in study II.

Physical health

The Short Form-36 Health Survey (SF-36) is a generic health survey not designed for any special patient category, but recommended in studies of back pain.[175] The results are presented as sum scores (0-100) for eight subscales (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotion, mental health) each with a different number of questions. In *Study I* two of the eight subscales were used; general health (GH) and physical functioning (PF). In *Study III* and *IV,* the summa score physical health (PCS) comprising several of the eight sub scores, was used. In PCS the subscale physical functioning (PF), show the strongest relation, but also the subscales role physical (RP), bodily pain (BP) and general health (GH) are strongly related to the summa score PCS. A high score means better health or better physical functioning. The SF-36 has been sufficiently tested for reliability and validity.[175,176]

Physical activity level

This question is included in the general questionnaire which has been used in previous research on subjects with LBP.[50,51,168]

How often do you perform physical activity? Physical activity was graded in four steps: *1* – I never perform physical activities, *2* – I perform physical activities a few times every month, *3* - I perform physical activities once a week, *4* – I perform physical activities more than once/week.

Self-efficacy

The self-efficacy scale (SES) assesses self-efficacy beliefs specially related to eight basic physical activities: walking, running, carrying bags, standing (in line), cycling, sitting in an armchair, sitting at a table, working in a forward-bent position.[52] Within each category the subject was asked to rate, on a eighth point scale, for how long (< 2, 2-5, 5-10, 10-15, 15-25, 25-35, 35-45., >45 minutes) he thought he was able to endure the activity. A high score indicates a strong belief in one's self-efficacy. Total possible score is 64.

Fear-avoidance beliefs

The modified fear-avoidance beliefs questionnaire (mFABQ) is a 16-item, two-factor, self-report questionnaire developed to focus on patients' beliefs about how work (7 items; sum score 42) and physical activity (4 items; sum score 24) affect their pain.[28,190] In study I both scores were used and in study II and IV the sum score on physical activity was used. Higher sum scores indicate more fear-avoidance beliefs.
The mFABQ showed good validity and reliability.[62]

4.4 INTERVENTIONS

Following the clinical examination, eligible subjects received a new appointment, which was administrated by the secretarial staff at the clinic. The initial clinical examination lasted for 60 minutes for all included subjects. All subjects were informed on inclusion that physical activity is beneficial for LBP, but not what activity that is considered best. All subjects received information on the importance of continuing normal activities, and basic advice on e.g. lifting, resting, and sitting. The treatment period was for six weeks in *study II* and for eight weeks in *study III.*

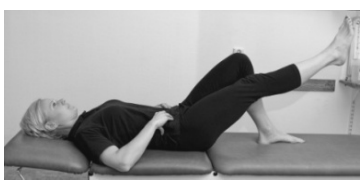
4.4.1 Ergometer test

In *Study I* a sample of subjects (n=57) tested their aerobic fitness level in comparison with a healthy age- and gender matched control group (n=57). The controls were consecutively included. The subjects with LBP (n=57) and healthy controls (n=57) underwent an ergometer test[7] on two occasions with an interval of two days. Test one was used in the statistical analysis. One test leader, a physiotherapist, was responsible for all tests. The subject cycled on a calibrated cycle ergometer with a fitness computer (Monarch Ergomedic 829E, Sweden) for six minutes or until steady-state was achieved. The test leader asked the subjects to try their hardest, but to take their pain and fatigue into account. The subjects started cycling with a workload of 0.5 W/kg at a constant

rate of 60 rpm. The resistance was gradually increased. The resistance was based on the subject´s heart rate during the first two minutes, to achieve a steady-state heart rate of at least 120 beats, a value which represents the limit for possible calculation of VO_2ml x kg $^{-1}$ x min $^{-1}$. [20,22] The subjects rated their perceived exertion and fatigue during the test using Borg's RPE Scale.[20] Before and after each test the patients rated their perceived pain using Borg´s CR-10 Scale.[20] If the subject perceived pain or symptoms from cardiovascular or pulmonary difficulties, the test was stopped. Time, perceived pain, exertion and reason for stopping the test were recorded. The subjects were instructed not to eat or smoke, or to perform excessive physical activities, for at least two hours before the test.

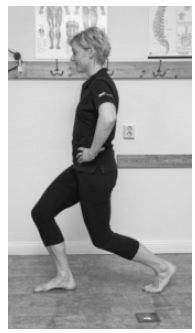
4.4.2 Exercise interventions

The subjects in *study II* and *III* were instructed in a similar way regarding the initial phase of the exercise protocol emphasizing stabilizing exercises. The subjects were informed of how the stabilizing muscles act, as hypothesized, in healthy people and in those with LBP.[73, 78-80,160] The PT demonstrated how the muscles act as stabilizers. It was explained that the "deep inner muscle corset" (i.e. the local muscle system) and the "outer corset" (i.e. the global muscle system)[15] are both important for maintaining good functional stability of the spine. The importance of re-learning activation of the deep inner corset was emphasized. To avoid recurrent LBP, the importance of activating the stabilizing muscles in activities of daily-life, especially those that set off pain, was underlined. The PT individually supervised and used clinical judgment in the progression of the graded stabilizing exercises. The progression of the exercises was based on the patients' pain level and observed movement control and quality. In contrast to strength training, the programme used low-load endurance exercises. The first stage consisted of specific exercises to address the stabilizing muscles, following the protocol described by Richardson & Jull,[159] with instructions to gently draw in the anterolateral abdominal wall (i.e. TrA isolated from the other abdominal muscles) together with a tightening of the MF in different non-postural positions, together with relaxed breathing. A bio-pressure unit was used in the learning process (Stabilizer™, Chattanooga Group, Hixon, TM). In *study II* and *III* the device was used to provide biofeedback to assist in the in the learning process of a correct activation of the deep abdominals. The unit has been studied for intra-tester reproducibility but is considered to have a low reliability.[173]



In *Study II*, the physiotherapist individually instructed and controlled the graded home training program once/ week for six weeks (Appendix I). In the subsequent phase, the protocol gradually progressed to performing the exercises posturally

more upright and to functionally-loaded positions/exercises. The subjects in *study III* were once/week during eight weeks supervised by a physiotherapist in the gym. The subjects performed the graded home training program and in addition graded exercises with moderate resistance via pulleys in standing and seated positions to increase the demand on the stabilizing muscle system and to train the "local" and "global" muscle system [15] together (Appendix II).



A natural spine position both during the exercises and in daily life was emphasized, avoiding pain-generating postures. The patients were encouraged to perform the low-load exercises at home every day both in *Study II* and *III*. The home-training programme was designed to take approximately 15 minutes. In *Study II* the subjects had a training diary to control compliance. The subjects were instructed to maintain the programme indefinitely to avoid recurrence of pain. It was emphasized that while adherence with a home-training programme is important, the most important thing is to incorporate activation of the stabilizing muscles and in daily life.

In *Study II*, the reference group received manual treatment including a combination of muscle stretching, segmental traction and mobilization according to findings from the clinical examination. No manipulations were used. The subjects were recommended to continue with usual activities.

In *Study III* the reference group, were informed of the benefits of daily walks as physical activity.[127] They were instructed to take a 30-minute walk of every day. The walk could be divided into two parts of 15 minutes. They were instructed to walk at the fastest pace that was convenient and did not set off pain. If their pain persisted or increased they should slow down. They should continue with other usual activities. They were also given general home exercises but with no follow-up instructions. The daily walks taken were recorded in a diary which was returned to the PT at the last visit. The subjects were informed that if the pain increased or if they had any questions they were free to call their PT.

4.5 PREDICTIVE FACTORS

To be able to investigate potential independent predictive factors in a pre- and post-intervention model that might predict an unfavourable clinical outcome in the long term of 12 and 36 months a multiple regression analysis's were performed.

The main dependent variable disability was measured with Oswestry Low Back Pain Disability Questionnaire (ODI)[54] and the other dependant variable perceived pain was

measured with visual analogue scale (VAS).[86,214] Such dependant variables have previously been studied[13,50,96,108,169] and the importance to study predictive factors on data from longitudinal RCT using comparable statistics on group level has been emphasized.[105] The dependant variables were driven by binary variables; perceived disability as >20% [54] (yes/no) and perceived pain as >20 mm[86,214] (yes/no).

Predictive factors (independent variables)
The following possible predictive factors were evaluated; *age*, (tertiles;18-31, 32-42, 43-60) and gender (man/woman, *expectation of treatment* (no expectations/to be completely restored), *reduction of physical activity* as compared with before current pain episode (reduction /no reduction), *job-satisfaction* (no/yes), *co-morbidity with neck-pain* (yes/no), *current pain duration* (>12 weeks/8-12 weeks), *similar pain* more than 5 years (yes/no), *pain-frequency* (continuous/seldom) and *well-being* (poor/good). Perceived pain was measured with VAS[86,214] (tertiles;>53, 25-53, 0-24), fear-avoidance belief regarding physical activity, (>13/ <13), [97] and self-efficacy was measured with the Self-efficacy Scale (tertiles; >52, 41-52, 0-40).[52] Perceived disability was measured with ODI (>20/<20).[54] To assess physical health, SF-36 was used (tertiles; >43, 37-43 0-36).[175]

4.6 STATISTICS

All outcome data derived from the questionnaires in *Studies I-IV*, i.e. rated, self assessed variables was analyzed by using non-parametric tests. However, descriptive data was presented (e.g. age, height, weight, BMI) as mean (standard deviation) and ordinal data is presented as median and range or percentiles (25^{th}-75^{th}).The Student *t* test, the Mann-Whitney *U* test and $\chi 2$ testing were used to assess potential baseline group differences regarding continuous, self-assessed and proportional data, respectively.

Friedman's ANOVA was used to control for potential within-group effects (*Studies II, III*. Between-group testing (Mann Whitney *U* test) was run on score differences from baseline on each follow-up occasion (*Studies II, III)*. A p-level ≤ 0.05 was considered statistically significant in all studies. The specific statistics used for each and one of the included studies are presented in Table 5.

Table 5. Statistical methods applied in the different studies.

Statistics applied	Study I	Study II	Study III	Study IV
Non-parametric				
Mann-Whitney *U* test	•	•	•	
Friedmans Anova		•	•	
Chi-square test ($\chi 2$)			•	•
Parametric				
Student *t*-test	•			
Regression				
Spearman's rank correlation coefficient	•			•
Logistic regression				•

Study I

To compare predicted aerobic fitness (VO_2max) between the patient group and the control group, Student's *t* test for unpaired observations with a normal distribution of the data was used. In the group with LBP the relation between the dependant variable, predicted aerobic fitness level (VO_2max) and the investigated variables was investigated with a regression analysis. Spearman's rank correlation coefficient (r_s) was used, with the following descriptive terms: -0.25 = little if any correlation; 0.26-0.49 = low correlation, = 0.50-0.69 moderate correlation; 0.70-0.89 high correlation and 0.90-1.0 very high correlation.[48] A multiple linear regression analysis was performed to define the contribution of independent variables investigated to the dependant variable. The most related variables ($p \leq 0.05$) from the univariate analysis were further analysed in the multiple regression analysis.

Study II

The Mann Whitney *U* Test was used on baseline data to account for group differences on entry to trial and in 'change' scores for each measure (difference between individual baseline and follow-ups). A $\chi 2$ testing was used to compare 'improved' cases in the two groups after the treatment period and at the 3- and 12-months follow-ups. An 'improved' subject was here defined by a minimal clinical significant change (MCIC); ≥ 10mm (VAS, DRI) and ≥10 % (ODI).[141] The $\chi 2$ test was also used to assess differences in recurrent treatment periods between the groups.

Study III

Between-group testing (Mann-Whitney *U* test) was conducted on score differences from baseline on each follow-up occasion. A MCIC of ≥ 10 % as measured with ODI and ≥ 15mm as measured with VAS was determined.[17, 141] The subjects were, after treatment, and at follow-ups dichotomized by MCIC in perceived disability and pain. To assess between-group differences in MCIC, $\chi 2$ testing was used. An intention-to-treat procedure was followed (last-observation-carried-forward).

Study IV

The Spearman rank-correlation coefficient was in used to screen whether strong co-linearity (defined as $r > 0.5$) existed between the baseline independent variables. Univariate logistic regression analyses with the dependant variables were performed with all predictive factors, where odds ratios (OR) were calculated to reflect the strength of the associations, together with the 95% confidence-intervals (95% CI). All predictive factors that were $p \leq 0.10$ at the univariate screening were entered in the multivariate backward step-wise logistic regression model. Here, pre- and post intervention variables was analysed for the dependant variables disability and pain at the 12- and 36-months. Both univariate and multivariate regression analyses were adjusted for the effects of the exercise intervention as compared to daily walks. The pre-intervention model included possible early predictive factors as measured at entry of the study. In the post intervention model the health-related variables pain-frequency and well-being as measured after the intervention was in addition included in the multivariate analysis together with the significant predictive factors ($P \leq 0.10$) at entry of the study. In the multivariate analyses the significance level was set to $p \leq 0.05$.

5 RESULTS

5.1 STUDY I

Ergometer test

All subjects (n=114) in both the patient group (n=57) and the control group (n=57) completed the two sub maximal cycle tests. An acceptable limit of agreement was found between the two tests. There was a significant group difference in VO_2max for women with LBP compared to women among the healthy controls (p = 0.029), but there were no overall difference between the two groups when analyzing men and women togehter. There was a difference in activity level (once/week) between the LBP group and the controls (p<0.001). Sixty-eight percent of the LBP patients reported a decline in physical activity level after the onset of LBP.

In addition to the limit of agreement between the two ergometer tests an intra class correlation coefficient (ICC) was calculated in order to investigate the reliability between the tests. The ICC was .95 (CI .90-.97) which refers to a good reliability.[48]

Associations between aerobic fitness level and variables

The multiple regression analysis in the sample of subjects with LBP (n=57) showed that lower aerobic fitness level was significantly associated with higher age, gender, lower level of self-efficacy and BMI (Table 6). Gender aspects were further investigated with age, BMI and self-efficacy as independent variables. Men strongly associated higher age with lower aerobic fitness level (VO_2max) while in women the lower level of aerobic fitness was associated with a higher BMI and a lower level of self-efficacy.

Table 6. Multiple linear regression analysis for predicted aerobic fitness level (VO_2max) as dependent variable and gender, age, pain (VAS), perceived disability (ODI), self-efficacy beliefs (SES) and body mass index (BMI) as independent variables in the sample of subjects with LBP (n=57); men and women separately.

	r^2	Gender	Age	VAS	ODI	SES	BMI
All *(n=57)*	.45						
Standardized β		-0.30	-0.38	-0.05	-0.05	-0.34	-0.24
Significance (p)		0.006*	0.001*	0.67	0.73	0.03*	0.04*
Women *(n=28)*	.48						
Standardized β			-0.26			0.50	-0.40
Significance (p)			0.08			0.001*	0.007*
Men *(n=29)*	.51						
Standardized β			-0.62			0.24	0.03
Significance			0.001*			0.14	0.85

*p ≤ 0.05 VAS = Visual Analogue Scale, ODI=Oswestry Low Back Pain Disability Questionnaire, SES=Self-efficacy-scale, BMI=body mass index

5.2 STUDY II

Within group analysis
Analysis of difference within each group immediately after the treatment period, revealed significant improvement in the exercise group regarding assessed pain ($p<0.001$), functional disability levels (DRI; $p<0.001$, ODI; $p<0.001$) and assessed health ($p<0.05$). Disability levels assessed with the ODI in the reference group showed as well a significant improvement ($p=0.01$) after the treatment period, though this was not maintained in the long term. At the 3- and 12-month follow-ups the exercise group had maintained its improvement with regard to the assessed variables while the reference group showed no such significant improvement either after the treatment period or at the 3- or 12-month follow-ups.

Between group analysis
When comparing change-scores of outcome measures between the groups, Mann-Whitney *U* test showed a significant difference in favour of the exercise group with regard to functional disability (DRI) after the treatment ($p=0.04$), maintained in the long term. However, no significant difference was seen between the groups directly after the treatment period regarding pain, disability levels assessed with ODI, or health. Neither were there effects on 3-month follow-up, nor at 12-month follow-up. Directly after the intervention there was no difference in improved cases between the groups regarding minimal clinically important change (MCIC). However at 3-month follow-up there were significantly more improved cases in favour of the exercise group with regard to; pain ($p=0.002$), general health ($p=0.02$) and functional disability (DRI; $p=0.03$). At both follow-ups more subjects in the reference group reported recurrent treatment periods than in the exercise group; at the 3-month follow-up, 8 (50%) *vs* 2 (11%) had undergone new treatment periods and at the 12-month follow-up 7 (50%) *vs* 2 (11%) respectively. However, after the treatment period there was no difference ($p=0.37$) between the groups regarding assessed satisfaction with manual treatment or stabilizing exercises.

An additional analysis was performed using an intention-to-treat (ITT) approach. This was applied by using LOCF (last-value-carried-forward). Within group analysis showed in the main the same results as above. Between groups analyses showed again the same results as above but revealing in favour of the exercise group a greater differences between the groups when handling the data with the ITT-approach.

5.3 STUDY III

Within group analysis

Regarding primary outcome, Friedman's within-group ANOVA revealed that both groups significantly improved over time concerning physical disability ($p<0.01$) as well as for pain ($p<0.001$). For secondary outcome, Friedman's ANOVA revealed improvement over time concerning physical health in both groups ($p<0.001$) but for fear-avoidance and self-efficacy beliefs, there were improvements only in the intervention group ($p<0.001$).

Between group analysis

Between-group testing (Mann-Whitney *U* test) showed significant differences in favour of the exercise group for perceived disability at the 6-month and 12-month, maintained at the 36-month follow-up (Fig.5). In addition, between-group results for pain showed greater reduction for the exercise group post-intervention. However, no such between-group differences were seen in the long-term (Fig 6). Regarding secondary outcome, the results showed a significant group difference in favour for the exercise-group in short- and long term concerning physical health and assessed self-efficacy after 12 and 36 months. Regarding fear-avoidance, no such differences emerged.

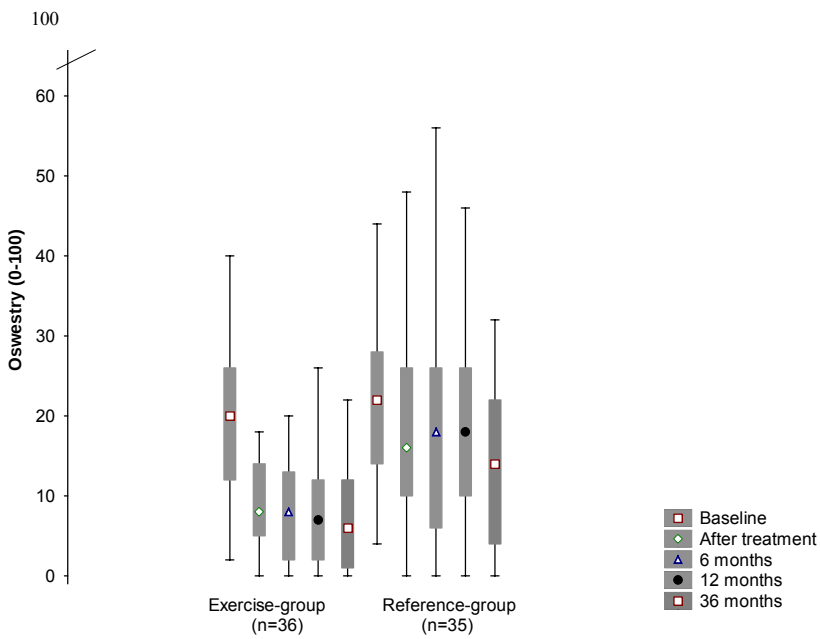


Figure 5. Outcome of disability as measured with Oswestry (ODI) at baseline, after treatment and at 6-, 12-, 36-months follow-up for exercise- and reference-group (md (25^{th}-75^{th})).

Minimal clinically important change

Regarding minimal clinical important change (MCIC); 53% of the subjects in the exercise group and 34% in the reference group showed a clinical important change (≥15mm) in pain (p=0.11) after the intervention. Regarding perceived disability, 44% of the cases in the exercise group and 31% of the cases in the reference group showed an MCIC (≥10 points) (p=0.26) after the intervention. At the 12-month follow-up 53% of the cases in the exercise group and 26% in the reference group showed an MCIC regarding perceived disability, a result that was not significant between the groups. At the 12-month follow-up 55% of the exercise-group and 26% of the reference group had reduced their pain level by 50% or more (p=0.01).

In the exercise group, there was 96% attendance at the PT sessions, and in the reference-group, 71% adherence with the daily walks. Long-term adherence with training at the 12- and 36-month follow-ups was 78% and 61% in the exercise group versus 57% and 51% in the reference-group, respectively (p=0.01, p=0.41). Twenty-two percent in the exercise group and 46% in the reference group reported a recurrent need for new treatment periods at the 12-month follow-up (p=0.03), while at the 36-month follow-up the proportions were 36% and 40%, respectively (p=0.73). At baseline there was no difference between the groups' expectations of the intervention. After the intervention, the exercise group was significantly more satisfied.

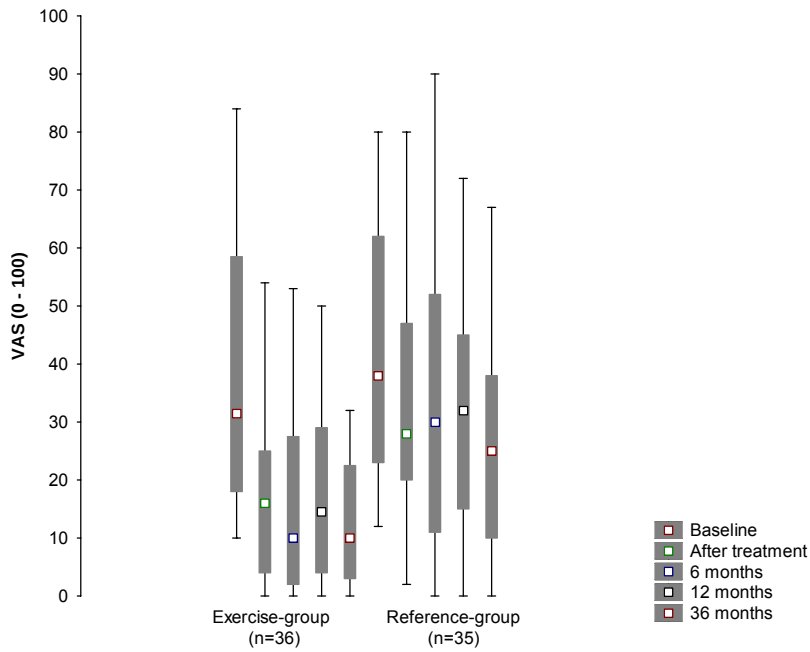


Figure 6. Outcome of pain as measured with Visual Analogue Scale (VAS) at baseline, after treatment and at 6-, 12-, 36-months follow-up for exercise- and reference-group (md (25^{th}-75^{th})).

Effect size (*d*) was calculated after the intervention and at all follow-ups. *d* is defined as the difference between the means. Cohen[36] defined effect sizes as "small, *d* = .2," "medium, *d* = .5," and "large, *d* = .8". The effects size (*d*) over time favoured the exercise group for perceived pain; after the intervention it was considered large (0.81) and at follow-ups; medium (0.64, 0.76 and 0.69). For perceived disability, the effect size favoured the exercise group and was considered medium both after the intervention and at the follow ups (0.67, 0.64, 0.73, and 0.77).

5.4 STUDY IV

At the 12-month follow-up, 33% of the subjects reported a disability level of >20% as measured with ODI, and 50% of a pain level >20 mm as measured with VAS. At the 36- month follow-up, 25% reported a disability level >20% and 44% a pain-level >20mm respectively (Table 7).

Table 7. Outcome in perceived disability (ODI) and perceived pain (VAS) at different time points (% of group).

	Baseline	After treatment	12 months follow-up	36 months follow-up
ODI				
0-20	45	78	68	75
21-40	38	18	27	24
41-100	17	4	6	1
VAS				
0-20	24	44	50	56
21-40	32	37	28	32
41-100	44	19	22	12

Values are percentage of group (%). ODI =Oswestry Low Back Pain Disability Questionnaire, VAS,=Visual Analogue Scale

The following independent variables did not emerge as significant predictors in the nivariate level for any of the dependent variables: gender, age, similar pain the last 5 years, job-satisfaction, expectation with treatment, reduced physical activity level and fear-avoidance beliefs.

Predictive factors for disability (≥ 20) at 12 and 36 months

Using univariate logistic regression analysis, seven possible predictive factors for disability at 12 months emerged ($p \leq 0.10$):self-efficacy, perceived pain, pain frequency, perceived disability, physical health, well-being and co-morbidity with neck pain. Regarding perceived disability at the 36-month follow-up, five possible

predictive factors emerged: perceived disability, physical health, perceived pain, and self-efficacy and current pain duration.

In the multivariate *pre intervention* model two predictive factors emerged for 12 months outcome; self-efficacy and perceived disability. With the 36 months outcome, the same two factors emerged as predictors. In the *post intervention* model three predictive factors emerged for disability at 12 months; pain level, self-efficacy and pain frequency and at 36 months follow up self-efficacy and disability emerged as predictors.

Predictive factors for pain (≥20) at 12 and 36 months

At the *univariate* level, five possible predictors emerged *(*$p \leq 0.10$) regarding perceived pain at the 12-month follow-up, self-efficacy, pain level, well-being, lower levels of physical health and co-morbidity. Further, for perceived pain at 36 months, four possible predictive factors emerged; pain-frequency, self-efficacy, pain level, and physical health.

In the *pre intervention* multivariate model, two predictive factors emerged for pain, at 12 months follow up; pain level and self-efficacy and regarding pain at 36 months follow-up three predictive factors emerged; pain-frequency, pain-level, and level of physical health. In the *post intervention* model pain-frequency emerged as predictive factor for pain at 12- and -36 months follow-up and in addition for 12 months outcome pain level emerged as a predictive factor.

The Nagelkerke R^2 was calculated and used to describe the approximate proportion of the variation in the response that was explained by the model (Table 8). The Nagelkerke R^2 increased from 0.35 from the pre intervention model to 0.55 in the post intervention model regarding the outcome of disability at 12 months follow-up. Regarding perceived pain; Nagelkerke R^2 increased from 0.33 to 0.45. Regarding the follow up of 36 months no changes were seen between pre and post intervention models.

Table 8. Nagelkerke R^2 for the two predictive models (pre and post intervention) at 12 and 36 months follow-ups.

Predictive models	**Nagelkerke R^2**	
	Pre intervention	Post intervention
ODI 12 months pre- intervention	0.35	0.55
ODI 36 months pre intervene tion	0.36	0.35
VAS 12 months pre intervention	0.33	0.43
VAS 36 months pre intervention	0.19	0.15

ODI=Oswestry Low-back Pain Disability Questionnaire, VAS=Visual Analogue Scale

Table 9. Multiple logistic regression analysis (final) with significant prognostic variables (p<0.10) at baseline (*pre-intervention model*), and variables at baseline combined with variables after intervention *(post-intervention model*) to predict an unfavourable outcome at 12- and 36-months follow-ups.

	Outcome at 12-months follow-up						Outcome at 36-months follow-up					
	Pain			Disability			Pain			Disability		
Baseline	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Pre-intervention model												
VAS 25-53 vs <23	4.80	(1.32-17.36)	0.016									
VAS >53 vs>23	7.57	(1.85-29.95)	0.004				3.89	(1.10-13.68)	0.03			
Pain frequency (daily vs seldom)							7.99	(1.69-37.77)	0.008			
SES <41 vs >52	3.24	(0.93-11.26)	0.05	5.94	(1.62-21.73)	0.007				4.20	(1.03-17.00)	0.04
ODI <20 vs >20				5.24	(1.28-21.34)	0.02				7.34	(1.29-41.58)	0.02
Physical health 37-43 vs >43							0.17	(0.04-0.68)	0.01			
Post-intervention model												
Pain frequency (daily vs seldom)	8.33	(2.21-31.36)	0.001	7.73	(1.65-35.55)	0.009	4.50	(1.58-12.77)	0.004			
VAS 25-53 vs <25	6.65	(1.54-28-71)	0.01	9.83	(1.44-67.14)	0.02						
VAS >53 vs <25	20.35	(3.77-109.7)	0.001	11.82	(1.52-91.92)	0.02						
SES< 41 vs >52				9.78	(2.10-45.47)	0.004				4.20	(1.03-17.89)	0.04
ODI >20 vs >20										7.34	(1.29-41.58)	0.02

VAS= Visual Analogue Scale, ODI=Oswestry Low Back Pain Disability Questionnaire, SES=Self-efficacy Scale

6 DISCUSSION

The research presented in this thesis has focused one one sub-group of non-specific LBP sufferers, namely those with recurrent low-back pain, the majority currently at work. These subjects are commonly seen in primary health care settings. They seek treatment over and over again from a variety of caregivers. Even if currently at work, their functional limitation and pain presumably affect their quality of life and well-being. They are actively seeking are care or are referred by a general practitioner.

Today, more than ever it is considered important to prevent first-time or recurrent LBP from becoming persistent and disabling. Further, patients with LBP should be encouraged and supported to remain at work, since work status is reportedly associated with factors as health status, well-being, aerobic fitness and pain levels.[37,188]

Research in the area of LBP has been advocated [2,66,67] and should be conducted in populations seeking care and therefore best represent subjects with LBP. It is also recommended that future research should focus on investigating specific exercise interventions strategies instead of general exercises and in well defined low-back pain populations.[67] There is a consensus of an active approach in the treatment of LBP[164] but there are conflicting results where and what exercises have the highest efficacy.[69,120,135] The overall aim of this work reported in this thesis was to evaluate the efficacy of a graded individualized exercise programme emphasizing stabilizing exercises and to investigate prognostic factors in order to optimize treatment for subjects that seek care for their LBP.

6.1 STUDY SAMPLE

The study sample within the framework of this thesis consisted of consecutively enrolled subjects seeking care at an outpatient' physiotherapy clinic in central Stockholm. The sample was well defined and may be considered homogenous. The subjects had recurrent LBP with localized mechanical LBP. Except for five persons in *Study II*, the subjects were currently at work when included. One-quarter of the sample were referred mainly from general practitioners. The present subjects were residents of Greater Stockholm. Subjects who remain in primary health care, as in the present thesis, may be expected to be less disabled than patients who are referred to specialized secondary settings.[44] Few clinical trials distinguish between subjects at work and those who are not, which makes it harder to interpret the outcome. [77,102,123,134,177]

6.2 EXERCISE INTERVENTION

Two randomized controlled clinical trials (*Study II,III*) investigated a graded exercise programme emphasizing stabilizing exercises . The first trial investigated the efficacy of a graded home training programme supervised by a physiotherapist once/week for

six weeks (*Study II)*, while the other study used a graded exercise intervention integrated with more functional and loaded exercises in the gym, but still supervised by the physiotherapist (*Study III*).

With respect to inter-group variability the exercise-group reduced disability significantly in short term in both studies. In addition there was a significant difference in the long term in favour of the exercise group in *Study III*, while such results emerged only for pain in the short term (*study III*). The secondary outcome rated physical health, self-efficacy and less need for recurrent treatment periods were improved in favour of the exercise group while no such effects emerged for fear-avoidance beliefs (*Study III*). The effect size off the graded exercises in comparison with daily walks was medium to large (*Study III*).

Our results are comparable to those of trials evaluating stabilizing exercises as an isolated factor in specific sub-groups of LBP.[76,139] Other clinical trials evaluating these exercises[30,55,60,102,129,134] used a more pragmatic approach combining the stabilizing exercises with other modalities. This may explain, at least partly, the discrepancies among the studies. The present studies aimed to investigate the efficacy of the exercises not in combination with other modalities.

In *Study II* the results of the graded exercise intervention were compared with those of a more passive approach (manual treatment) and in *Study III* with a more general active approach; daily walks. The main difference in the approaches between the two studies are that in *Study II*, both the exercise and the reference group got the same attention from the physiotherapist while in *Study III* the reference group only met twice; week 2 and week 8. The reference group (*Study III*) was instructed to take daily walks which were reported in a training diary. One might assume that the difference in attention from the physiotherapist between the groups in *Study III* might have affected the outcome and thus need to be considered when interpreting the results. Factors such as the patients' expectations[34] , the therapists' enthusiasm and expertise,[137] need to be considered in the interpretation of the results. In addition exercises supervised by a physiotherapist are reported to be important for the outcome.[69,122]

The more body-specific exercises (*Study III*) probably also made a difference. A general exercise program i.e. daily walks does not aim to train specific activity patterns; they might not alleviate the disability in the same way as body-specific stabilizing exercises do. Further, general exercises do not change the activity pattern of the stabilizing muscles, as recently reported.[65] Comparing the approach in *Study II and III,* we intended in *Study III* to integrate the graded exercises together with functional more

loaded exercises in which both "local" and "global" muscles work together.[15] This has previously been proposed to be important in an exercise protocol.[93,94]

The present exercises were intended to change the activity pattern of the stabilizing muscles. The theory of the protocol is that repeated voluntary activation of a muscle induces plastic change in the nervous system, leading to a modification of the automatic recruitment of the trained muscle during the performance of functional tasks.[182,195] However, few clinical trials present evidence of such a change. Recent laboratory studies evaluating an isolated voluntary contraction of TrA in patients with LBP showed an improvement in motor control six months after the intervention.[181,182] Hall et al.[65] reported that non-specific "core" exercises targeting the abdominals did *not* change the activity pattern of TrA. These laboratory studies, however, include few subjects; and the importance of whether changes in trunk-muscle activity are a cause or an effect of LBP is not known. We did not control for a possible change in muscle activity pattern using ultrasound or electromyography but aimed, rather, to investigate the patients' own ratings of pain and disability after an exercise intervention based on this hypothesis. It is, however, not clear that reduced pain and disability following stabilizing exercises is associated with changes in the muscle activity pattern: other underlying explanations are possible. [56]

Behavioural-cognitive treatment emphasizes modification of a behavioural process assuming that pain and disability are influenced not only by somatic factors.[203] While the present subjects in both trials were being gradually coached in exercises and function, a behavioural change might have occurred. Exercise protocols should focus on improving functional abilities using a graded approach,[44,110] and the use of such an approach seems advisable in LBP.[2] There is also growing evidence that self-efficacy is a mediator of both pain and fear-avoidance associated with disability.[44,211] One might therefore assume that, in the exercise group (*Study III*), the enhanced self-efficacy beliefs were associated with the alleviation of disability.

There was no difference in the patients' expectation of the intervention between the groups either in *Study I* or *Study II* as measured before the intervention. However, as measured after the intervention a difference between the studies in satisfaction with the intervention was observed; in *Study II* both groups were as satisfied with the intervention while in *Study III* the reference group, was not as satisfied as the exercise group, implying that that the difference in attention by the physiotherapist in the two groups in Study III made a difference.

In both *Study II* and *Study III*, results showed that the subjects in the exercise group had fewer recurrent visits to care givers in the long term compared with the reference groups. This may imply that the graded exercise programme was a good self-treatment strategy used by the subjects. They were instructed to use the exercises indefinitely to avoid recurrences.

6.3 PREDICTIVE FACTORS

Lower level of aerobic fitness may contribute to the persistence and chronicity of LBP. No overall difference in aerobic fitness was shown between the subjects with LBP and the healthy controls (*Studyr I*). However, lower levels of aerobic fitness in the group with LBP were associated with higher age, with gender and with lower level of self-efficacy. To date there are inconclusive reports concerning LBP, aerobic fitness levels, physical activity levels and gender differences. Hoch et al[77] reported lower levels of aerobic fitness in a sample of women with LBP and proposed that a decline in exercise-frequency after the onset of LBP could be an explanation of this. Other studies have reported that men with LBP show poorer aerobic fitness than those with normative values.[132,171] Lower activity level is previously reported to be a possible predictor for future disability in LBP[50], however in our study (*Study IV)* investigating possible factors for an unfavourable outcome; activity level did not emerge as a predictor. This doesn't mean that a lower or reduced activity level is unimportant merely that in our study including other possible predictive factors; others were more important. This is also reported by Picaet &Shuit[152] who found no proof in a population based cohort that persons who are physically inactive are at risk for LBP. It is however discussed weather the association between activity and LBP is U-shaped; too much or to little activity generating an increased risk for LBP.[31,71]

Our results did not show an association between fear-avoidance beliefs and a lower level of aerobic fitness, which has previously been reported.[170] In addition, fear-avoidance beliefs did not emerge as a predictor for an unfavourable outcome *(Study IV)*.This might apply to the fact that the majority of our sample was currently working. One of the most important factors regarding levels of aerobic fitness (VO_2max) could be work status.[199] It is reasonable to believe that for patients with recurrent LBP currently working; at least the aerobic fitness level would be sufficient to meet the physical demands of the job.

The predictors emerging from the multivariate analysis, that were the most important for future disability were lower self-efficacy, and disability; and for future pain level; perceived pain and higher pain frequency. In the post-intervention model, combining pre-intervention measurements with the post-intervention variables pain-frequency and well-being, the same predictive factors emerged and in addition pain-frequency

and perceived pain for disability. This might confirm the importance of these predictors. As previously reported, self-efficacy might be an important mediator of both pain and fear-avoidance in disability in subjects with LBP.[5,44] Enthoven et al.[50] reported of important predictors at 5-years follow up, following an intervention; pain-frequency and rated disability emerged as predictors in addition to several other factors that did not emerged in the present study. There was however a difference between the study populations; 91% of their subjects reported an outcome of disability (>20 ODI) at baseline whearas the present study reported of 45% (>20 ODI).

Pain frequency emerged as an important predictor of disability at 12 months and of perceived pain at both follow-ups. Perceived pain at entry was also a risk of future pain, especially for those who scored pain in the higher third (>53 VAS) at entry. A higher pain-level at baseline is reportedly associated with higher future pain level.[154,169] Subjects with severe pain will continue to suffer from severe pain while those with mild or moderate pain, even if recurrent, run a relatively low risk of future severe pain.[110 214 70 122] Subjects with LBP seeking care might express pain as their main problem. However, physiotherapists should focus on an active approach aiming at restored function.

Lower self-efficacy emerged as a predictive factor for both pain and disability. This predicted future disability at the 12- and 36-month follow-ups in both models. Self-efficacy refers to the way a subject sets a goal and anticipates the likely outcome to guide and motivate his effort.[9] It is reportedly a stronger predictor of disabling LBP than e.g. fear avoidance is. [44,45] In addition, a recent study investigating level of self-efficacy in knee function concluded that a subject's self-efficacy appears to be an important factor in rehabilitation viewed as outcome associated with physical participation.[180] The extent to which subjects are disabled by pain may depend on their self-efficacy: subjects with a stronger self-efficacy more easily find strategies to prevent further recurrences.[40] These subjects believe, and are confident, that regular exercise prevents relapses.[14] A strong self-efficacy may also explain why subjects with disabling pain go on facing daily activities and working situations while low self-efficacy is associated with e.g. helplessness and pessimistic thoughts.[8,44] In addition, a passive coping strategy is reportedly associated with future disabling pain.[13,90]

6.4 METHODOLOGICAL CONSIDERATIONS

6.4.1 External validity

Since our subjects with LBP were recruited consecutevily when seeking primary care, external validity extends only to such subjects. The majority of the subjects sought care actively on their own initiative or on recommendations. One-quarter of the sample were referred mainly from general practitioners. In Stockholm a GP's referral is not needed to seek physiotherapy care. This might differ if compared to other primary care settings in Sweden or other countries. The subjects were included in the study by physiotherapists with post-graduate diplomas in orthopaedic manual therapy. A health care setting with all physiotherapists experienced in clinical examination of low-back pain disorders might not generalize to every clinical setting This might be considered a limitation to the present study. The majority of the subject were currently at work on inclusion (*Study II*; n=5 on sick-leave).

Regarding external validity of the outcome of randomized controlled trials evaluating a specific intervention there is a difference of the efficacy of the intervention as evaluated in the trial and the effectiveness. Efficacy indicates the capacity for beneficial change (or therapeutic effect) of the given intervention, while effectiveness relates to change under real-life condition. This implies that even if the graded intervention emphasizing stabilising exercises was efficacious in the present studies this does not necessary mean that the exercise intervention shows efficiency in other settings in clinical everyday practice.

6.4.2 Internal validity.

Design

The randomized controlled trials included in this thesis (*Studies II, III*) were performed in the clinical reality of an outpatient physiotherapy setting. A limitation to be considered is the randomization of subjects in *Study II* and *II.* Due to practical reasons the subjects were allocated alternately to either treatment group. However, analyses of demographic and clinical data at baseline, showed no significant difference between the group for which reason it may be assumed that that there were no important differences between the groups. The subjects were also stratified by gender.

Responders and non responders were investigated at baseline in both samples (n=47, n=71). The difference between responders and nonresponders was investigated in a multivariate analysis. In *Study II* no differences were shown, while in *Study III*, there was a difference in physical health between responders and non responders at baseline which must be considered when interpreting the results.

In *Study I*, a healthy age- and gender control group was included for comparison with the subjects with recurrent LBP regarding aerobic fitness level. The control-group was consecutively included. Of course the results in aerobic fitness level might vary depending on who is included in a control group: if normative values from the general population had been used instead, the results might have differed. A possible limitation of all studies may be lack of power. In *Study I*, it was considered sufficient to include a minimum of 25 subjects in each group. In *study II*, only a power of 60% was reached and the drop-out rate was high (26%). We therefore considered *Study II* a pilot study. In *Study III*, we hypothesised that the intervention group would lower its pain level by one-third more than the reference-group at 12-months follow- up. There is of course a chance that the differences between the groups for the outcome measures of interest used in *Study III* were not identified because of type II error. However, a recent trial,[122] presented a power calculation for a clinical study similar to ours and presented a power of 80% (alpha 0.05), including 60 subjects randomized into two different exercise groups. The inclusion of more subjects would have strengthened the power of all our studies. However, we considered the samples well defined in comparison to other clinical trials that include a variety of subject at different levels of pain and disability but also at different stages of sick leave, work or disability payment.

In both *Study II* and *III* we compared two different treatment strategies. To add a third group would have strengthened the results. However, as the trials were performed in the clinical reality of a physiotherapy setting this was not possible. In *Study IV* the small sample might explain the wide confidence interval for prediction, indicating that the precision of the odds ratio estimates is uncertain.

Methods

For all of our studies we used self rated measurements; a general questionnaire and several instruments that have been sufficiently tested for reliability and validity. Self-reported questionnaires are recommended as outcome measurement instruments in LBP.[19,46] Self-report measures are reported to best explain changes in disability compared with physical measures after exercise rehabilitation for low-back pain.[2,122] By using valid and reliable instruments recommended in LBP research we consider that we had a good and accepted research method. However, the additional inclusion of physical measurement might be discussed for future research. To be able to conclude whether a graded exercise programme emphasizing stabilizing exercises change muscle activity patterns, physical measurements are needed to complement self-rated variables.

When self-measured variables are studied as possible predictors of clinical outcome, time is often not taken into account. As LBP fluctuates over time, individual factors could regress to the mean.[107] In addition, subjects with recurrent LBP may follow their

own course, so that all measurements in relation to an intervention tend only to be points that the sufferer has reached. [39] As rated disability and pain may vary over time, collecting predictive data from at least two time points might be prognostically superior to information from a single time point.[9,32,49] We choose to include two health related variables as previously described in a post intervention analysis of possible predictors for an unfavourable outcome of disability and pain.[50] The post intervention models for 12 months follow up were stronger than the pre-intervention model. This would imply that it might be very important to evaluate variables collected after the intervention to be able to identify subjects at risk of an unfavourable course. To include well-being and pain-frequency in a post intervention model has been reported in previous research.[50]

The ability to detect clinically important changes over time is called responsiveness.[173] A statistically significant score change after an intervention does not necessarily mean that the change is clinically important.[64] To facilitate the comparison of results between groups a minimal clinically important change (MCIC) may therefore be used in the analysis in outcome studies. Different cut-off values have been proposed for VAS and ODI.[141] An improvement from baseline by 30% is suggested.[141] Different cut-off points have been discussed recently. Previous studies on MCIC have suggested a range of 2-29 points for VAS and a range of 4-15 points for ODI. Note that, we used different cut off values in our two RCTs (*Studies II* and *III*). Importantly, there are indications that an MCIC is smaller in less disabled subjects and larger in more disabled populations, meaning that the MCIC used in *Study III,* might be too high.

6.5 LIMITATIONS OF THE STUDIES

Before any conclusions were drawn from the studies in the present thesis, several study limitations were thouroghly discussed and considered.

Several of the limitations of the present studies are discussed in the text above. Concerning all studies the question of power might be considered. However, the samples investigated, even if small, were considered homogenous; the majority of the subjects currently at work and included with strict clinical inclusion criterias. In *Study I* the healthy control group were consecutively included. The size and the composition of the healthy control group might be a potentional weakness. If normative values should have been used instead maybe the results would have differed investigating the difference in aerobic fitness level between subjects with LBP and healthy controls. In *Study II,* drop-outs and non-responder rate was considered high; five initially and ten later. We therefore elected to consider study II a pilot study. In *Study III*, the fact that the exercise group got more personal attention from the physiotherapist than the reference-group, instructed to take daily walks, must be considered when interpreting the results. In *Study IV* investigating possible factors predicting an unfavourable outcome of disability we employed data previously used in a RCT. Irrespectively of

patients' initial status; we included all subjects in the univariate analysis. To increase outcome sensitivity, we could have included only subjects with a certain pain and disability level. However, we whished to include subject seeking care for their recurrent LBP, particularly since pain and disability might fluctuate in such populations.

6.6 GENERAL DISCUSSION

"Stay Active", concludes the Swedish Council on Technology Assessment in Health Care (SBU).[164] In addition several reviews and guidelines conclude that activity and resuming normal activity are important in the management of LBP.[2,69,103,127,164] Still, a population-based cohort study reported that low activity is *not* a risk factor for LBP.[152] In its prevention, however, there should be focus on the preventive possibilities that lie in specific physical activities. This requires more research on the role of the *quality* of exercises and physical activity rather than their *quantity*.[152]

Exercises for LBP are common in everyday clinical practice to prevent pain, improve functional limitations, gain strength and endurance and restore activities of daily living. Still there is a lack of knowledge concerning the association between treatment variables and changes in outcome. The positive outcome of exercises could be affected by factors such as the physiological processes accompanying physical exercises.

Maybe there should be more emphasis on the positive experience of physical exercise than on increased muscle strength. Here, a graded programme emphasizing stabilizing exercises seems to be an alternative and a contribution to the management of recurrent LBP. The fact that patients are directly exposed to activities during 'graded exposure' could partly explain why this mode is effective. Graded exposure might thus be an effective method of enhancing functional self-efficacy because it requires patients to engage in and successfully accomplish fearsome or difficult activities.[110,211] The present results show that graded exercises are more effective than general exercise such as daily walks. Not that daily walks of 30 minutes are unimportant for health; only that other, more body-specific, supervised exercises are more effective in reducing disability and pain levels in subjects with recurrent LBP.

Many such subjects seek different kinds of treatment, over and over again, from a variety of health care providers.[138] This 'over-treatment' may result in a 'validation' of their back problem, leading to even more consumption of clinical care.[138] Clinical experience shows that patients with LBP often expect a hands-on approach in the treatment of their pain, and of course manipulative therapy can be effective for the relief of pain, at least in the short term.[18,33,76] However, clinical experience also indicates that manual therapy has not met the challenge of alleviating persistent pain in the long-term. Minimising unnecessary visits to different caregivers for recurrent pain

is an important socioeconomic consideration. The present supervised graded exercise programme seemed to reduce the need for long-term recurrent care. This was perhaps because the subjects in the exercise group were instructed to go on with their exercises indefinitely to avoid recurrent pain; and also perhaps because they changed their habits and thus better controlled future pain episodes [138,187] However, lacking significant difference between the exercise group and the reference groups regarding recurrent visits to caregivers at the 36-month follow-up *(Study III),* one may discuss whether preventive, recurrent visits to the physiotherapist might be advisable. This is a question for future research.

The meeting between the subject with LBP and the physiotherapist may be considered important for the outcome of the intervention. The physiotherapist has great knowledge and uses clinical experience and evidence together, meeting the patient at an appropriate level of understanding. The physiotherapist mediates understanding to the patient by explaining pain mechanisms and the importance of performing certain exercises which might motivate the subject to adhere to the intervention. This "cognitive" approach may be important in changing the sufferer's behaviour and in reducing recurrent pain periods.

The present subjects with recurrent LBP reported mild-to-moderate disability and pain. They might be considered healthy despite functional limitations and pain, and seemed to benefit from an active approach. However, no intervention is optimal for all subjects with LBP. For this reason, evaluation of clinical predictors before and after an intervention may be very important. in the identification of subjects risking future disability and pain For these subjects, further treatment or management might be necessary. Also, it is advisable to implement and use present knowledge of predictors in our clinical work. And here, physiotherapists in primary care have a great responsibility, namely to use evidence together with clinical experience in the treatment of patients with recurrent LBP.

6.7 FUTURE RESEARCH

Management and treatment in non specific LBP is a challenging problem. The present work has identified areas in which more research is warranted.

There is a need for further studies

- to evaluate the efficacy of the present graded exercise intervention in more specified sub-groups in LBP, in comparison with other exercises; and to evaluate the long-term efficacy of the interventions

- to clarify related mechanisms between outcome of these graded exercises and motor control of the stabilizing muscles of the spine

- to implement knowledge of predictive factors in clinical work, so as to prevent future disablement resulting from further episodes of recurrent low-back pain

- in qualitative research: to use a different approach in the evaluation of what factors affect the outcome of an intervention

6.8 CLINICAL IMPLICATIONS

The studies included in this thesis report that a graded spervised programme emphasising stabilizing exercises is more effective than manual treatment and general exercises in the treatment of subjects with recurrent LBP, the majority at work. Based on these findings the message of this thesis is to implement this programme in everyday clinical practice for subjects with recurrent LBP, such as ours. The programme might not be appropriate for all subgroups in LBP. However, most patients with LBP need coaching in the avoidance of pain-generating postures and in spinal control. Importantly, the physiotherapist in clinical everyday practice has an important supervising role in the learning process of the graded exercise programme.

The ability to identify subjects with recurrent LBP at risk of an unfavourable outcome is important for the physiotherapist as an aid to recommending additional treatment strategies in order to avoid further episodeds of recurrent low-back pain. It is therfore advisable to implement current evidence of predictive factors in clinical everyday practise. Hence, the outcome of the present studies may offer important knowledge and evidence for physiotherapists working with patients with recurrent LBP in primary care.

7 CONCLUSIONS

- The present results show that a supervised, individualized graded exercise programme emphasizing stabilising exercises is more effective in reducing perceived disability, self-rated physical health and self-efficacy than manual treatment or daily walks is. The exercise intervention also reduced the need for recurrent treatment in the long-term indicating the exercises might be preventive.

- The aerobic fitness level in the group with low-back pain was comparable to that of healthy age- and gender-matched controls indicating that maintaining work status might be important for aerobic fitness. Among those with lower levels of aerobic fitness in the group with LBP the aerobic fitness level was associated with higher age, with gender (women) and with lower self efficacy.

- Higher levels of perceived pain, pain frequency and disability and a lower level of self-efficacy emerged as predictors of an unfavourable outcome of disability and pain in the long term in a sample of subjects with recurrent low-back pain, indicating that such early screening information might be useful for the further management of low-back pain.

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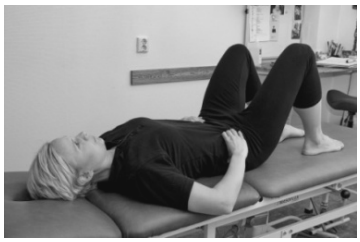
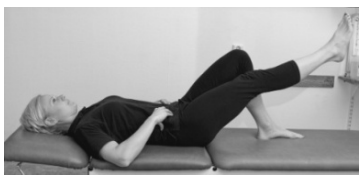
Appendix I

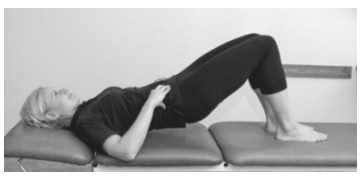
1 Draw in lower abdomen



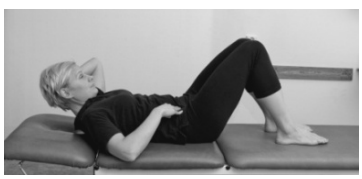
2 Knee out



3 Leg stretch

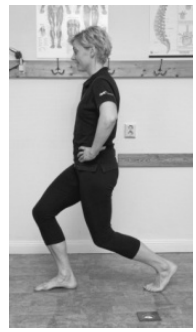


4 Bridging

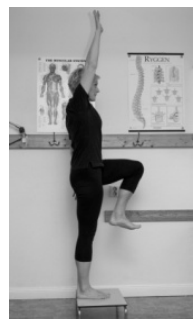


5 Small sit-up

6 The' pointed dog'



7 Fall out



8 Step-up

Appendix II

1

2

Step-up

pulley

3

Pulley

4

Leg-press

5

Pull-down

6

Dips