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Low back pain and widespread pain in primary health care: Early access to physical therapy, treatment and prognostic factors

by

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Göteborg 2011

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ISBN 978-91-628-8235-8

Cover illustration by Camilla Svensson

Printed by Geson Hylte Tryck, Göteborg, Sweden 2011

Abstract

Low back pain (LBP) and widespread pain (WP) are common and incur considerable costs to society mainly due to work disability. Identification of prognostic factors, intervention and early access to care seems important for influencing and preventing pain and disability in LBP and WP but further knowledge is warranted. The overall purpose of the present thesis was to obtain knowledge about a) prevalence and characteristics for WP in chronic LBP (CLBP), b) prognostic factors for activity and work status, c) the effect of function based intervention on health status and body functions in patients with WP or fibromyalgia, and d) the effect of early access to physical therapy for subacute LBP.

Study I

The purpose was to estimate the prevalence of WP according to the American College of Rheumatology (ACR) 1990 criteria in women with CLBP consulting primary health care and to evaluate differences in body function, activity, participation, environmental factors, health-related quality of life and other health-related aspects between patients having CLBP with or without simultaneous WP. One hundred and thirty patients with CLBP were included in this cross-sectional study. Twenty-eight percent of the CLBP patients fulfilled the ACR's criteria of WP. The CLBP+WP group showed significantly more severe impairments in body functions, more severe activity limitations, and participation restrictions ($p<0.05$). Moreover, the CLBP+WP group reported significantly more negative environmental impact in terms of private social support, lower health-related quality of life and other health-related aspects compared to the CLBP group ($p<0.05$).

Study II

This two-year prospective longitudinal cohort study of female patients with CLBP within primary health care investigated changes in body functions, activity, participation, environmental and other health-related factors. Prognostic factors were identified for activity and participation at the two-year follow-up. Ninety five percent (123/130) of the patients included in Study I were followed up at two years. Prognostic factors for later activity limitation (Roland Morris disability questionnaire (RMDQ)) and work ability (yes/no) were analyzed by multivariate regression analyses. Twenty eight percent (n=34) fulfilled the criteria of WP at the first assessment and 29% (n= 36) at the two-year follow-up. The 6-minute walk test (6MWT) predicted both future activity limitation and work ability. Other variables with predictive ability for activity limitation were the Örebro musculoskeletal pain screening questionnaire (ÖMPSQ) and Stress and Crises Inventory (SCI-93). Higher performance in the 6MWT, earlier work ability and lower scores in the Hospital Anxiety and Depression Scale, depression (HADS-D) predicted work ability after two years. These three factors were used to construct a nomogram for assessing the probability for future work ability.

Study III

The purpose was to evaluate the effect of pool exercise in patients with fibromyalgia (FM) or WP and to determine characteristics influencing the effects of treatment. A total of 134 women with FM and 32 with WP were randomized to a 20-session pool exercise and a 6-session education program or to a control group undertaking the same education program. The primary outcomes were the Fibromyalgia Impact Questionnaire (FIQ) total score and the 6MWT. The FIQ-total ($p = 0.04$) improved in the intervention group, with an effect size of 0.32. Patients who had participated in at least 60% of the exercise sessions improved in the FIQ-total (effect size 0.44), the 6MWT (effect size 0.43) and FIQ-pain (effect size 0.69) compared with controls ($p < 0.05$). The exercise-education program showed significant, but

small, improvement in health status in patients with FM and WP, compared with education only. Patients with milder symptoms improved most with this treatment.

Study IV

The purpose was to evaluate the effect of early access to physical therapy treatment for patients with subacute LBP compared to access with a four-week waiting list. Sixty consecutive primary health care patients with subacute LBP were randomized either to early access (EA) within two days for physical examination and individualized physical therapy treatment (n=32) or a control group (CG) with a four-week waiting list (n=28). The primary outcome measure was pain intensity (Borg's category scale for ratings of perceived pain). Secondary outcomes included ÖMPSQ, RMDQ, sick-leave, visits to health care and physical therapy. No significant differences in pain between the groups were shown at discharge. At 6 months, the reduction of pain was significantly greater in the EA compared to the CG (p=0.025) indicating that early access to physical therapy resulted in greater improvement in perceived pain at 6 months compared to later access.

Conclusions

The presence of widespread pain was found to negatively impact body function, activity, participation, environmental factors, health-related quality of life and other health-related aspects, and should therefore be assessed in female patients with chronic low back pain. Lower performance in walk test (6MWT), higher risk scores for future disability (ÖMPSQ) and more severe clinical stress symptoms (SCI-93) predicted activity limitation (RMDQ) at the two-year follow-up. Higher performance in walk test (6MWT), lower level of distress (HADS-D) and earlier work ability predicted future work ability. Probability of future work ability could be assessed by calculations based on these three factors (a nomogram). Education combined with pool exercise was found to improve the health status of patients with widespread pain or fibromyalgia and should be considered as an intervention alternative for these patient groups.

Early access to examination and individualized physical therapy treatment indicated clinical improvement for patients with subacute low back pain. An early physical therapist access model should be considered for the management of patients with low back pain in primary health care.

Keywords: Low back pain, widespread pain, fibromyalgia, physical therapy, primary health care, treatment, exercise therapy, education, early access, outcome assessment (health care) prognostic factors.

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ISBN 978-91-628-8235-8

List of publications

The present thesis is based on the following papers, which will be referred to in the text by their Roman numerals. Their copyrights belong to the journal or publisher which has granted permission for reprints in this thesis.

I. Nordeman Lena, Gunnarsson Ronny, Mannerkorpi Kaisa. Prevalence and characteristics of widespread pain in female primary health care patients with chronic low back pain. Submitted

II. Nordeman Lena, Gunnarsson Ronny, Mannerkorpi Kaisa. Prognostic factors for activity and work status in women with chronic low back pain consulting primary health care: a two-year prospective longitudinal cohort study. Submitted

III. Mannerkorpi Kaisa, Nordeman Lena, Ericsson Anna, Arndorw Maudh, and the GAU Study Group. Pool exercise for patients with fibromyalgia or chronic widespread pain: A randomized controlled trial and subgroup analyses. J Rehabil Med 2009;41:751-760

IV. Nordeman Lena, Nilsson Björn, Möller Margareta, Gunnarsson Ronny. Early access to physical therapy treatment for subacute low back pain in primary health care. A prospective randomized clinical trial. Clin J Pain 2006;22:505-511

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1. Abbreviations and definitions

1.1. Abbreviations

6MWT	Six-minute walk test
ACR	American College of Rheumatology
BRPE	Borg category scale for ratings of perceived exertion
BRPP	Borg category scale for ratings of perceived pain
CG	Control group
CLBP	Chronic low back pain
CWP	Chronic widespread pain
EA	Early access group
FIQ	Fibromyalgia Impact Questionnaire
FM	Fibromyalgia
HADS-A	Hospital Anxiety and Depression Scale (anxiety)
HADS-D	Hospital Anxiety and Depression Scale (depression)
HR	Heart rate
IASP	International Association for the Study of Pain
ICF	International Classification of Functioning, Disability and Health
LBP	Low back pain
LTPAI	Leisure time physical activity instrument
MFI-20	Multidimensional Fatigue Inventory
MOS-SSS	Medical outcome study- social support survey
PHC	Primary health care
PPT	Pain pressure threshold
RCT	Randomized controlled trial
RMDQ	Roland Morris Disability Questionnaire
SCI-93	Stress and Crisis Inventory-93
SF-36	36-item Short Form Health Survey
PF	*Physical functioning*
RF	*Role physical*
GH	*General health*
SF	*Social functioning*
RE	*Role emotional*
VT	*Vitality*
MH	*Mental health*
PCS	*Physical component summary score comprising: PF, RP, BP, GH*
MCS	*Mental component summary score comprising: VT, SF, RE, MH*
TP	Tender point
VAS	Visual analogue scale
WP	Widespread pain
ÖMPSQ	Örebro musculoskeletal pain screening questionnaire

1.2. Definitions

Low back pain	Pain and discomfort, localized below the costal margin and above the inferior gluteal folds, with or without leg pain[1,2]
Widespread pain	"Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain." [3]
Fibromyalgia	History of WP for at least 3 months. "Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites": *"Occiput*: bilateral, at the suboccipital muscle insertions. *Low cervical*: bilateral, at the anterior aspects of the intertransverse spaces at C5-C7. *Trapezius*: bilateral, at the midpoint of the upper border. *Supraspinatus*: bilateral, at origins, above the scapula spine near the medial border. *Second rib*: bilateral, at the second costochondral junctions, just lateral to the junctions on the upper surfaces. *Lateral epicondyle*: bilateral, 2 cm distal to the epicondyles. *Gluteal*: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle. *Greater throchanter*: bilateral, posterior to the trochanteric prominence. *Knee*: bilateral, at the medial fat pad proximal to the joint line." [3]

2. Introduction

Low back pain (LBP) and widespread pain (WP) are common and incur considerable costs to society mainly due to work disability.[1,4,5] As time is a key factor in work compensation systems the demands on healthcare systems have increased and efficient management by improving access to the appropriate care provider for the patients' health problem might be crucial. Moreover, early identification of prognostic factors and interventions are essential for influencing and preventing pain and disability.

My inspiration for writing this thesis started with the frustration of the constant difficulties in providing adequate appointments at the physical therapy department within primary health care (PHC). The department then introduced a Same-day-appointment scheduling model including direct access to a physical therapist with or without physician referral. This appointment model enabled the physical therapist to see patients not according to urgency but on the basis of the patients' perceived need on a same-day basis. The positive experience of this new model provided the inspiration to investigate the effect of early access to examination and individualized intervention by a physical therapist for patients with LBP in the critical subacute phase. It was through this study that I became involved in another study investigating education and pool exercise for patents with WP. Studying patients with WP raised questions of the presence and characteristics of WP in patients with CLBP and consequently the need to evaluate prognostic factors useful in a Same-day appointment model including self-referral to a physical therapist.

2.1. The etiology of pain

Several conditions are included in LBP and the suggested diagnostic triage of LBP is described below in more detail.[1,2,6,7]

LBP can have a biomechanical origin with nociception generating the pain. Various spinal structures such as paravertebral musculature, ligaments, facet joints, anulus fibrosus and spinal nerve roots have been suggested as the cause of pain.[8] Other pain sources are disc herniation and spinal stenosis.[8] It has been suggested that if nociceptive input continues over time it may result in functional, chemical and structural alterations in peripheral systems and at various levels within the central nervous system.[9,10]

Nociceptors are normally inactive and respond to potential tissue injury leading to inflammation. Inflammation may induce a peripheral sensitization with a decreased threshold and increased responsiveness of the peripheral ends of the nociceptors which are partly caused by changes in proteins. Further, this will lead to increased input to the spinal cord's dorsal horn. Impulses from the nociceptors are conducted by the afferent neurons (A-delta and C-fibers) to the dorsal horn, where transmission to the spinal cord neurons is conducted. From here, the signal is transmitted via the spinal cord neurons to the cerebral cortex. Transmission in the dorsal horn is influenced by descending signals from the brain, so-called central inhibition. This transmission can be facilitated by reduced central inhibition and an increased activation of N-methyl-D-aspartic acid receptors resulting in an increased sensitivity of the post-synaptic neuron. This process will lead to an increased central neural responsiveness, so-called central sensitization.[9-12]

In patients with chronic pain, other neurobiological alterations have been noted in the hypothalamic-pituitary-adrenocortical axis and sympathetic nervous system.[13,14] Disturbances in the neurohormonal system have been described as interacting with pain perception and suggested to be an effect of prolonged stress which chronic pain may induce.[14]

In conclusion, the dysfunctional modulation of central pain processes and its interaction with mental responses and environmental factors contribute to the development and

maintenance of signs and symptoms in patients with chronic pain such as WP or FM. Patients with CLBP have shown signs of central pain processes, where nociceptive input may be small or nonexistent.[15,16]

Irrespective of etiology, the patient's perceived pain is always subjective and should be received with understanding according to the International Association for the Study of Pain (IASP) defining pain as: "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[17]

2.2. The International Classification of Functioning, Disability and Health

LBP and WP are multifactorial and the biopsychosocial approach should be considered. The medical diagnosis (ICD-10) provides information about the disease or disorder but not the consequences. Therefore, a number of outcome measures for symptoms, functioning, disability and health have been developed. To promote standardization in clinical research of LBP, Deyo et al have recommended a set of measurements including pain, disability, overall health status, work disability and satisfaction with care.[18] Another assessment model of health is the International Classification of Functioning Disability and Health (ICF) which enables an overview of the complex interaction between functioning, disability and health.[19] (Figure 1) The ICF structures information around functioning, disability and contextual factors, comprising the following components: body function/structure, activity, participation and environmental factors. However, personal factors are not classified in the ICF. The ICF may facilitate better understanding of multifactorial disorders as LBP and WP and ease communication between different care providers, other professional groups and the patient. However, the classification according to the ICF is comprehensive making it difficult to use in the clinic or in research. Therefore, ICF Core Sets have been developed, representing problems in functioning for patients with common disorders such as LBP and WP. [20,21] However, further validation of these Core Sets is warranted.

The present thesis attempts to classify included measurements according to the ICF components but without an ICF evaluation. Some of the outcome measurements such as pain intensity (VAS) correspond with the ICF components and domains, while other measurements can be partly linked. The Roland Morris Disability Questionnaire (RMDQ) was used in the present thesis for self-reported activity limitation due to LBP.[22] Seventeen statements in the RMDQ are reported to be linked to the activity component of the ICF,[19,23] while one other study reported 20 of 24.[24] Health-status measurements used in the present thesis comprise several ICF components covering different domains and levels of accuracy. Therefore, these measurements are presented as health-related quality of life or other health-related aspects rather than classifying them to a specific ICF component.

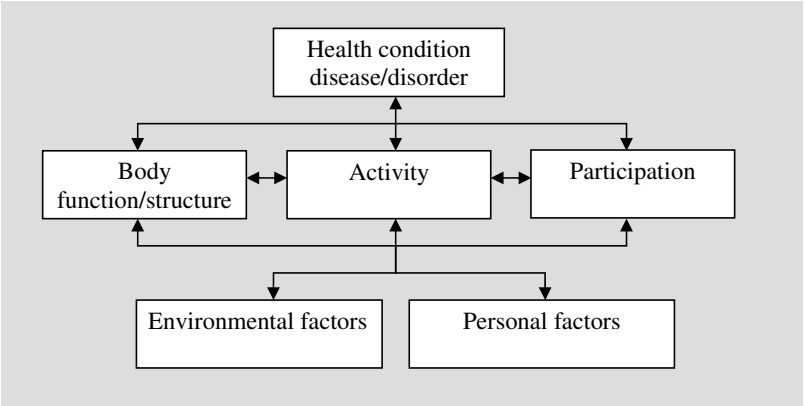


Figure 1. Interactions between the ICF components (WHO; 2001)

2.3. Low Back Pain

2.3.1. The prevalence of low back pain

A majority of the general population will suffer from LBP.[1,25,26] Reviews of prevalence data report life-time prevalence ranging between 49% and 84% and point prevalence between 12% and 33%.[26,27]

In studies of the general population, 31% were estimated to have chronic musculoskeletal pain.[28] Another study estimated the prevalence of chronic pain at 55% where 90% of these reported musculoskeletal pain.[29] CLBP was among the most common regions, estimated at 23% and 26% for women and 19% and 24% for men.[28,29]

2.3.2. The definition of low back pain and diagnostic triage

LBP is mostly defined as pain and discomfort, localized below the costal margin and above the inferior gluteal folds, with or without leg pain.[1,2,7]

There are several considerations to be taken when assessing a patient with LBP. Through history taking and clinical examination the use of a diagnostic triage classifying patients into three categories regardless of duration is recommended: 1) serious spinal pathology, 2) nerve root pain, or 3) non-specific LBP.[1,2,6,7,30] Serious spinal pathology is rare (1%) in patients with acute LBP consulting PHC.[31] However, to identify or exclude serious pathology is most important. There is a list of clinical features, so-called “red flags” consistent with pathology which is recommended when estimating if signs and symptoms require further investigation.[1] The category of non-specific LBP, generally described as non pathological, is determined by medical or technical assessment.[2] Most (85-90%) patients are found within this category.[8,27] Patients with non-specific LBP comprise a heterogeneous group of patients with a variety of LBP conditions. They are managed by various procedures based on history and clinical examination to classify patients into clinical subgroups to assist in the management of LBP.[32-36] However, since various diagnostic methods to establish etiology in individual cases, such as subgroup classification, are under investigation, the condition of LBP is often denoted as non-specific in clinical research to evaluate cohorts of patients.[32,37] The present thesis focuses on non-specific subacute or chronic LBP throughout the thesis.

Another important screening of patients with LBP is the identification of so-called “yellow flags” i.e. emotional, behavioral and cognitive factors hindering recovery.[1,2,38] There is a

consensus that psychosocial factors are important in the transition from acute to chronic LBP and are recommended to be identified early.[7,39]

Further classification is based on the duration of pain: acute LBP is usually defined as less than three weeks duration, subacute 3-12 weeks and CLBP longer than 12 weeks.[1,2] The term chronic is commonly used in the literature but in clinical practice long-term is preferable. Another variation is recurrent LBP with symptom-free periods. The definitions for chronic and recurrent LBP overlap.[40]

2.3.3. The course of low back pain

Acute LBP is generally described as having a favorable prognosis. Most individuals in the general population (up to 90%) with acute LBP recover spontaneously within four to six weeks regardless of treatment.[1,25,41] However, the population consulting PHC does not seem to have such a favorable prognosis. At the one-year follow-up a majority (63%-82%) continue to have persistent or recurrent LBP and 20%-45% had poor functional outcomes.[42-46]

Pain and disability are reported to decrease rapidly within the first month after the initial visit to PHC.[47] After 12 weeks (i.e. CLBP) recovery has been described as slow with a poor prognosis[1,6] and vague improvements in self-reported outcomes.[48] However, for most patients the experience is an episodic course of pain and disability and CLBP is recommended not be treated as a static condition.[2,40]

2.3.4. Prognostic factors for low back pain

Prognostic factors for the transition from acute to CLBP have been identified in all components of the ICF and in areas concerning personal factors and other health-related aspects.[42,44,49-54] Women have been shown to be at greater risk for CLBP[42] but gender differences are not fully understood.[55,56]

The few studies which have explored prognostic factors for recovery delay of CLBP report some similar risk factors as for the development from acute to CLBP.[57,58] Identified predictors for persistent CLBP (i.e. persistent pain, disability due to LBP and no return to work to previous capacity) are; previous sick-leave due to LBP, high pain intensity or high level of disability due to LBP, perceiving high risk of chronic pain, low education and immigrant status.[58] Other predictors are fear of pain and catastrophizing thoughts.[57] Various factors can impact disability in patients with CLBP such as body function, functional demands and environmental factors. Therefore, more knowledge of prognostic factors contributing to the recovery or recovery delay of CLBP is warranted.[57-59]

2.3.5. Treatment of low back pain

Clinical guidelines from various countries are available for the management of LBP in PHC[30,60] and the previously described diagnostic triage is recommended by all.[60] When LBP is considered as non-specific the overall aim of treatment for acute LBP is pain relief, improved function and prevention of recurrence or chronicity.[7] The consensus for the treatment of acute/subacute LBP is to provide information concerning etiology and symptoms, reassure a favorable prognosis, give advice to stay active and, if appropriate, pain relief medication. However, recommendations for initiating spinal manipulation, back-specific exercises and general exercise therapy diverge.[7,27,60] If the patient fails to return to activity and participation supervised exercise therapy, behavioral therapy and multidisciplinary treatment programs are suggested to be introduced.[7]

When LBP is considered chronic treatment aims to improve consequences and influence contributors of persistent pain.[6] Treatment options recommended are behavioral therapy, exercise therapy, education and multidisciplinary treatment programs.[6] Other treatments recommended are manual therapy.

Despite growing evidence for various treatment modalities more knowledge is needed for optimal timing and treatment choice to appropriate patients.[61-66]

2.4. Widespread pain

2.4.1. The prevalence of widespread pain

In studies of general populations, the prevalence of WP has been reported to be between 4.2% and 13%. Fibromyalgia (FM) is reported between 0.7% and 3.3%.[55]

In patients with LBP consulting PHC, 15% are reported to have WP simultaneously.[67] In secondary health care settings the prevalence of WP among patients with CLBP is reported to be 32% and 38%.[68,69] Irrespective of study-population, WP is more common in women than in men.[28,55,67-69] but the reason for gender differences as in CLBP is not fully comprehended.[55,56]

2.4.2. The definition and characteristics of widespread pain

In 1990, the American College of Rheumatology (ACR) introduced classification criteria for fibromyalgia, which have enabled patient homogeneity in clinical research. The ACR define widespread pain (WP) as pain present in both sides of the body, above and below the waist, and in the axial skeleton. The criteria for FM is long-standing WP (> 3 months) and tenderness for 11 of 18 tender points (TP).[3] It has been suggested that WP and FM represent overlapping disorders where FM is associated with more severe symptoms.[70]

WP can be present in various health conditions such as CLBP.[68,69] WP is often associated with allodynia and/or hyperalgesia in varying degrees,[3,15] impaired physical and mental body functions, activity limitations and participation restrictions.[71-73]

2.4.3. Treatment of widespread pain

A combination of pharmacological and non-pharmacological treatment is recommended for the treatment of patients with FM.[74] The non-pharmacological treatment recommended for patients with FM are supervised aerobic exercise[75] and education programs including self-management strategies with the purpose of enhancing self-efficacy for the management of FM.[76]

Self-management strategies combined with physical exercise treatment performed at low to moderate intensity have shown positive effects on overall health, physical function and pain.[77-81] Aerobic exercise improves overall health, physical function and possible pain and tenderness.[75]

A common recommendation for physical exercise treatment is that it should be of low or moderate intensity with a gradual progression avoiding exacerbation of symptoms.[75]

Cognitive-behavioral therapy is also recommended as a treatment option for the management of FM symptoms.[76] Other non-pharmacological treatments sometimes used are manipulation and massage or acupuncture. However, these need further evaluation.

Despite investigations of several treatment options for patients with FM optimal management is not known and more knowledge of who benefits most from specific exercise treatments is warranted.

2.5. Direct access to a physical therapist and the time factor

2.5.1. Self-referral to a physical therapist

Self-referral permits the patient to consult a physical therapist without a referral from a physician. Self-referral to a physical therapist has long been introduced in many countries[82-84] and was gradually introduced in Sweden until 2009. The purpose of enabling self-referral was to improve patient's choices, cooperation between care providers and increased cost-effectiveness.

In the literature, the term direct access to physical therapist has been used for various models such as when the physician utilizes a practice-based physical therapist[85] or in recent studies as self-referral.[82,84,86,87] Direct access (self-referral) is reported to be appropriate for the patient, physical therapist and physician.[84,88-90] The suggested advantage to patients is the possibility to independently choose a care provider and enable early access to physical therapy treatment.[84,89] Direct access, from the physical therapist's perspective is greater independence to examine and decide treatment[89-91] and from the physician's perspective a reduction of workload.[88,89] Previous studies have shown that direct access results in reduced costs, fewer physical therapy treatment sessions, physician consultations, prescriptions of X-ray, prescription of analgesics and secondary care referral.[82,84,88] Despite several advantages of self-referral to physical therapist the general population's knowledge of physical therapy as an independent profession is limited.[86,92] Moreover, the knowledge of the effect in patient outcome measures is limited.

Critics of direct access argue that the physical therapist may oversee serious pathology[90,91] and qualifications have been suggested necessary for a direct access model such as postgraduate experience and higher education.[91,93] To meet this criticism, studies have shown that a specialized physical therapist nearly always makes adequate decisions for critical musculoskeletal disorders[93,94] and achieves high clinical accuracy when compared to magnetic resonance imaging.[95]

2.5.2. Same-day appointment model

Direct access is described as delivering physical therapy treatment at a more appropriate time.[89] However, avoid delays in a self-referral system the clinic could offer a same-day, appointment-scheduling model as previously described.[96] This model offers the patients an appointment on the same day as requested regardless of urgency.[96]

Several advantages have been claimed with this advanced access model such as increasing care provider capacity by meeting the predicted demand for appointments on the day of need, increased continuity between patient and care provider and sustaining a balance between supply and demand of care.[96-98] The same-day appointment model enables the patient to get the care they want at the time they need it.[98]

2.5.3. Early intervention

In the literature the meaning of early intervention diverges and comprises; intervention initiated early in symptom duration,[99-103] or early in sick-leave duration[104] or when the patient is offered an appointment immediately regardless of reason.[97] For patients with LBP, duration of symptoms is commonly used in investigations of early interventions.[99-103]

Recommendations for when physical therapy treatment should be introduced for patients with acute LBP diverge.[30,60] Investigations of a comparison between a wait and see approach and early access to examination and physical therapy treatment for patients with acute LBP shows long-term positive effects on psychosocial factors, general health, quality of life[103] and days of work disability for the group with early access.[102] The subacute phase in LBP is described as critical for developing chronic pain and disability[1,2] Therefore, early

identification of risk factors[39,105] and intervention including clinical examination of the patient is suggested important for preventing chronic pain and disability in subacute LBP[62,99-101,104] but the right timing for interventions needs to be further explored.[4,62,63,66]

2.6. The problem

There is limited knowledge of the prevalence of WP among women with CLBP consulting PHC and differences in body function, activity, participation environmental factors, health-related quality of life and other health-related aspects in women with CLBP with or without simultaneous WP. New knowledge could provide ideas for better planning of the management of these patients. (Study I)

Various factors can impact disability in patients with CLBP such as body functions, functional demands and environmental factors. Despite several studies, their prognostic value for recovery or recovery delay of CLBP remains limited. Thus, there is a lack of longitudinal prospective studies for evaluating prognostic factors influencing activity and work status. (Study II)

There is a need to evaluate treatment programs in the occurrence of WP or FM. Physical exercise and education programs have been shown to be positive for overall health, physical functioning and symptoms. When planning treatment for patients with WP or FM in PHC it has been unclear which patients with WP or FM would benefit most from physical exercise. (Study III)

Early identification and intervention in patients at risk for developing CLBP has been shown to be essential for preventing disability due to LBP. The subacute phase of LBP has been described as the most critical phase for recovery. The clinical value of the optimal timing of intervention in this phase, however, remains to be proven. (Study IV)

There is extensive scientific literature on how bio-psycho-social factors influence the development of CLBP. However, better knowledge of the prevalence of WP in CLBP and long-term follow-ups is necessary to provide new knowledge on the course and factors of prognostic value. Moreover, evaluations of which patients with WP would benefit from physical exercise treatment are limited and the clinical value of early access to intervention in subacute LBP has not been conclusively shown.

2.7. Aims of the thesis

2.7.1. General aims

Identification of prognostic factors, intervention and early access to care seems important for influencing and preventing pain and disability in LBP and WP but further knowledge is warranted. The overall purpose of the present thesis was to obtain knowledge about a) prevalence and characteristics for WP in CLBP, b) prognostic factors for activity and work status, c) the effect of function-based interventions on health status and body functions in patients with WP or FM, and d) the effect of early access to physical therapy for patients with subacute LBP.

2.7.2. Specific aims

Study I
The aim of Study I was to estimate the prevalence of WP according to ACR's criteria in women with CLBP consulting primary health care. Furthermore, this study aimed to evaluate differences in body function, activity, participation, environmental factors, health-related quality of life and other health-related aspects between patients having CLBP with or without simultaneous WP.

Study II
The aim of Study II was to investigate changes in body function, activity, participation, environmental and other health-related factors in women with CLBP consulting primary health care and to identify prognostic factors for activity and work status at the two-year follow-up.

Study III
The aim of Study III was to investigate the effects of supervised physical exercise on health status and body functions in patients with WP or FM and to analyze whether pain level, distress, stress and activity limitations might influence the outcomes.

Study IV
The aim of Study IV was to evaluate the effects of early access (within two days of seeking care) to physical examination and individualized physical therapy treatment for patients with subacute LBP compared to standard access at four weeks.

3. Methods

3.1. Study designs, selection of participants and inclusion criteria (I, III, III, IV)

This thesis is based on the three samples described below. Patients with CLBP (I, II), FM or WP (III) and subacute LBP (IV). All three samples were recruited from PHC settings in southwestern Sweden. Patients who could be contacted, confirm participation and fulfill inclusion criteria were included.

3.1.1. Chronic low back pain: The cross-sectional study and the two-year follow-up (I, II)

A cross-sectional study (I) followed by a two-year prospective longitudinal cohort study (II). Studies I and II were based on the same sample (Figure 2). Female patients were identified by systematic journal search for LBP diagnoses "M545" (ICD-10) at eight PHC settings in 2004-2005. The inclusion criteria were: female patient, LBP (pain between costal margins and gluteal folds) with or without referred leg pain.[1] Further criteria were; greater than 12-week's duration of symptoms, not pregnant, no known spinal disorders, no other severe disorders, age between 18 and 60 years, and fluency in Swedish.

In Study I, one hundred and thirty women were assessed. Patients were invited to an assessment comprising a clinical examination conducted by a physical therapist and self-administrated questionnaires. After the assessment patients were categorized into either having CLBP with simultaneous WP (i.e. pain registered on both sides of the body, above and below the waist and in the axial skeleton)[3] or localized CLBP (i.e. WP criteria not fulfilled) to identify the prevalence of WP in CLBP patients. The differences between the CLBP group and CLBP+WP group were evaluated.

The clinical assessment included a standardized interview, tender point (TP) assessment, electronic pain pressure threshold (PPT) examination and physical performance tests (the six-minute walk test (6MWT) and hand grip strength). The patients were asked to fill in a package of self-administrated questionnaires (Table 1).

At the two-year follow-up (II), all patients included in the cross-sectional Study (I) who could be contacted and accept participation were assessed (n=123), containing the same study protocol as at the first assessment. Prognostic factors for later activity and work status were analyzed by multivariate regressions. Independent variables were selected based on known factors associated with disability in CLBP patients and were complemented with body functions, stress and private social support.[58,59] The measurements included were the number of pain localizations, pain intensity, fatigue, anxiety (Hospital Anxiety and Depression Scale (HADS-A)), depression (HADS-D), activity limitation (Roland Morris disability questionnaire (RMDQ)), work status, risk for long-term disability (Örebro musculoskeletal pain screening questionnaire (ÖMPSQ)), and health-related quality of life (SF-36 short form health survey (SF-36)). These measurements were complemented with measures of body functions using the six-minute walk test (6MWT), hand grip strength and PPT. A questionnaire of the clinical manifestation of stress (Stress and Crises Inventory (SCI-93)) and private social support (4-item version of Medical Outcome Study Social Support Survey (MOS-SSS)) were also included (Table 1).

By stepwise linear regression, the best predictor for activity limitation (RMDQ) two years later was established. Similarly, stepwise logistic regression was used to identify the best predictors for work ability two years later. A nomogram for predicting the probability of work ability two years later was constructed.

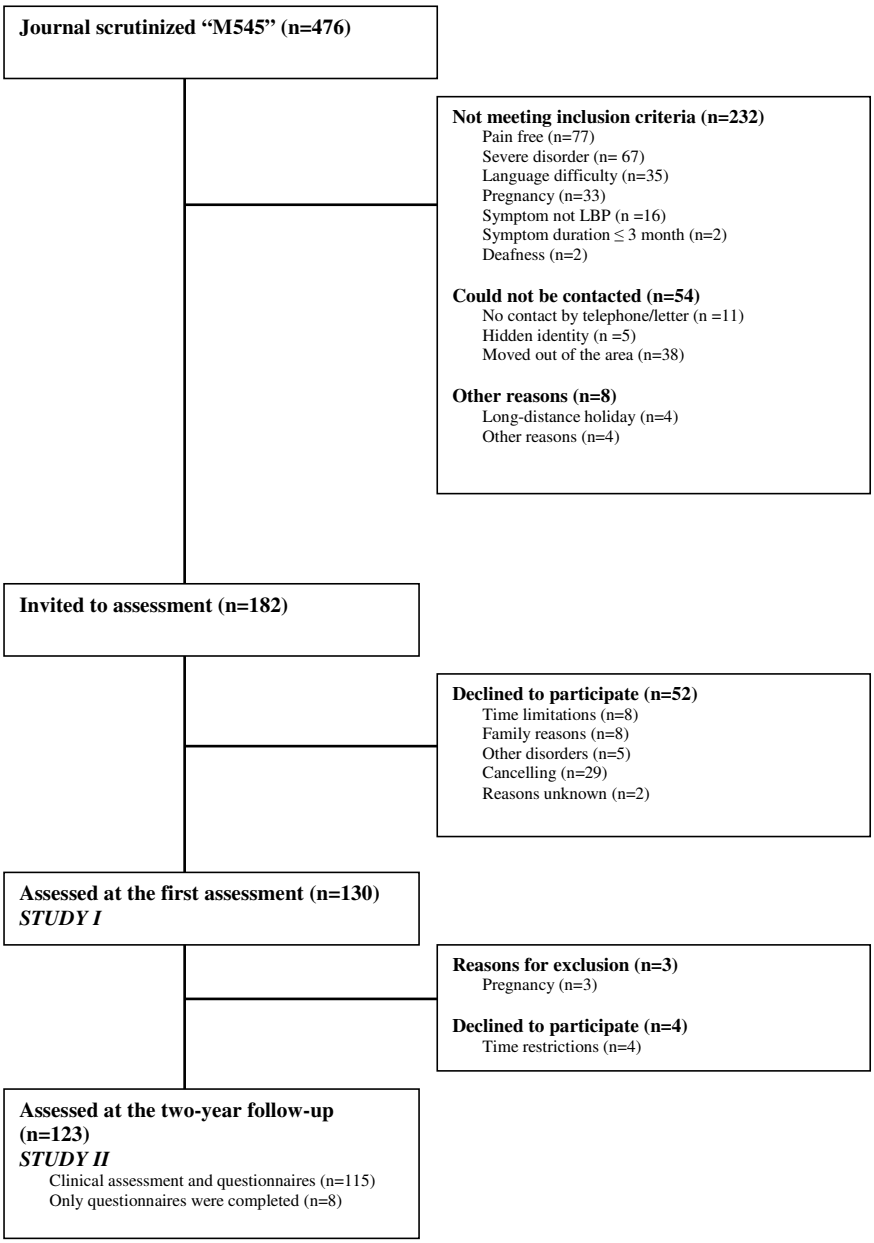


Figure 2. Participants flow Study I and II

3.1.2. Widespread pain or fibromyalgia: intervention study (III)

A randomized prospective clinical trial aiming to compare the effects of a 20-session pool exercise program combined with a 6-session education program with a control group undertaking the same education program. In this study, a total of 166 patients, 134 fulfilling the criteria for FM and 32 for WP, were included (Figure 3). Participants were recruited by systematic search of patient journals for the diagnoses of FM and WP (between 1995 and 2004) and by consecutive recruitment (in 2004 and 2005). The inclusion criteria were: female patients, FM (WP of at least 3 months and pain at manual palpation at 11 of a total of 18 TP[3]) or WP (WP for at least 3 months and not fulfilling the TP criteria) and age 18 to 60 years. Further criteria were no other severe somatic or psychiatric disorders, ability to understand Swedish, no allergy to chlorine and no ongoing or planned exercise therapy supervised by a physical therapist during the study period.

The primary outcomes were health status using the Fibromyalgia Impact Questionnaire total score (FIQ-Total) and body function (6MWT). The secondary outcomes included pain (FIQ-Pain), fatigue (FIQ-Fatigue), depression (HADS-D), health-related quality of life (SF-36), and amount of leisure time physical activity (the Leisure Time Physical Activity Instrument (LTPAI)). The exploratory outcomes included clinical manifestations of stress (SCI-93), multiple dimensions of fatigue (Multidimensional Fatigue Inventory (MFI-20)) and experience of physical activity.

Outcomes were evaluated using both an intention-to-treat and a per-protocol design, which was defined as attendance at least 60% of the sessions. The outcomes were assessed at baseline and after 20 weeks for comparison between groups. Follow-up was conducted 11-12 months after the baseline. The subgroups were created using rating scales assessing aspects of health that were hypothesized to influence the primary outcomes. The following variables were selected for subgroup analyses: pain (the FIQ-pain), distress (the HADS-D), stress (the SCI-93) and activity limitations (SF-36-Physical Function). To study clinical relevance of treatment effects, effect sizes were calculated.

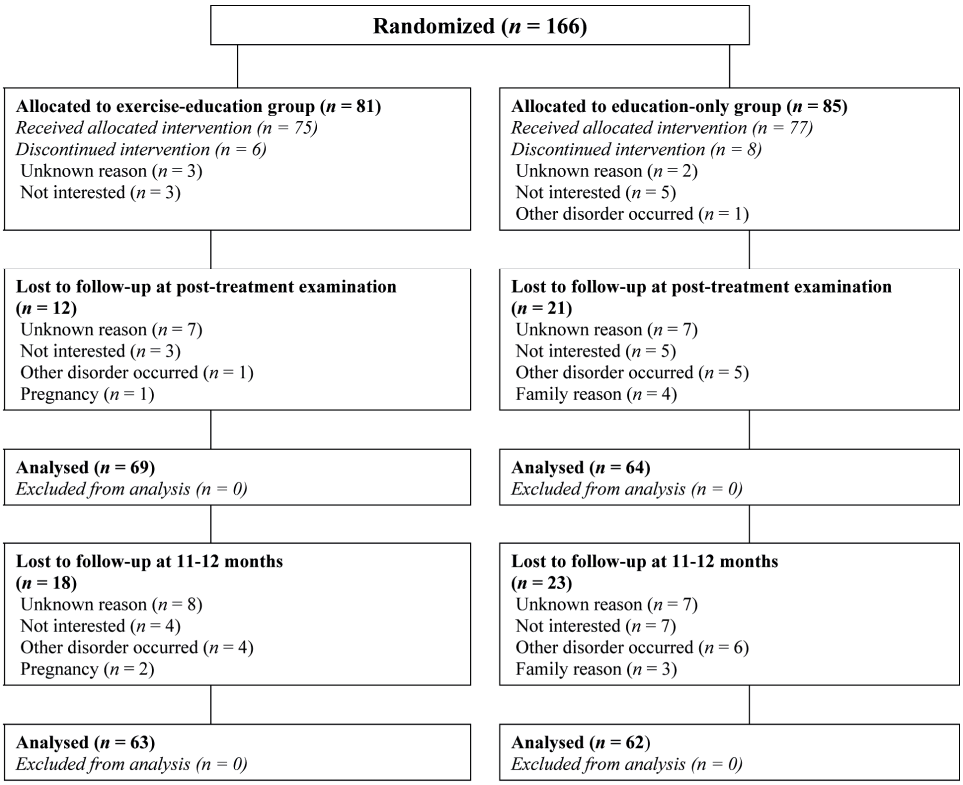


Figure 3. Participants flow Study III

3.1.3. Subacute low back pain: intervention study (IV)

A randomized prospective clinical trial aiming to compare the effect of early access (within two days) to examination and individualized treatment by a physical therapist with a control group undertaking the same procedure after 4 weeks' wait.

All consecutive patients who consulted two PHC physical therapy departments in Alingsås County from April 2002 until October 2003 were assessed for eligibility (Figure 4). Inclusion criteria were LBP (pain between costal margins and gluteal folds) with or without referred leg pain.[1] Further criteria were duration of symptoms 3 to 12 weeks from onset, LBP as the single cause for consultation, no pregnancy, no suspected or known spinal disorders, and age between 18 and 65 years.

The primary outcome measure was pain intensity (Borg category scale for rating of perceived pain (BRPP)). The secondary outcomes were activity limitation (RMDQ), risk for long-term pain and disability (ÖMPSQ). Other measures included were self-reported sick-leave and healthcare utilization. Frequency and type of treatment was documented by the physical therapist at discharge from treatment.

The outcome measures were assessed at baseline, discharge from treatment and 6 months after baseline for comparison between groups.

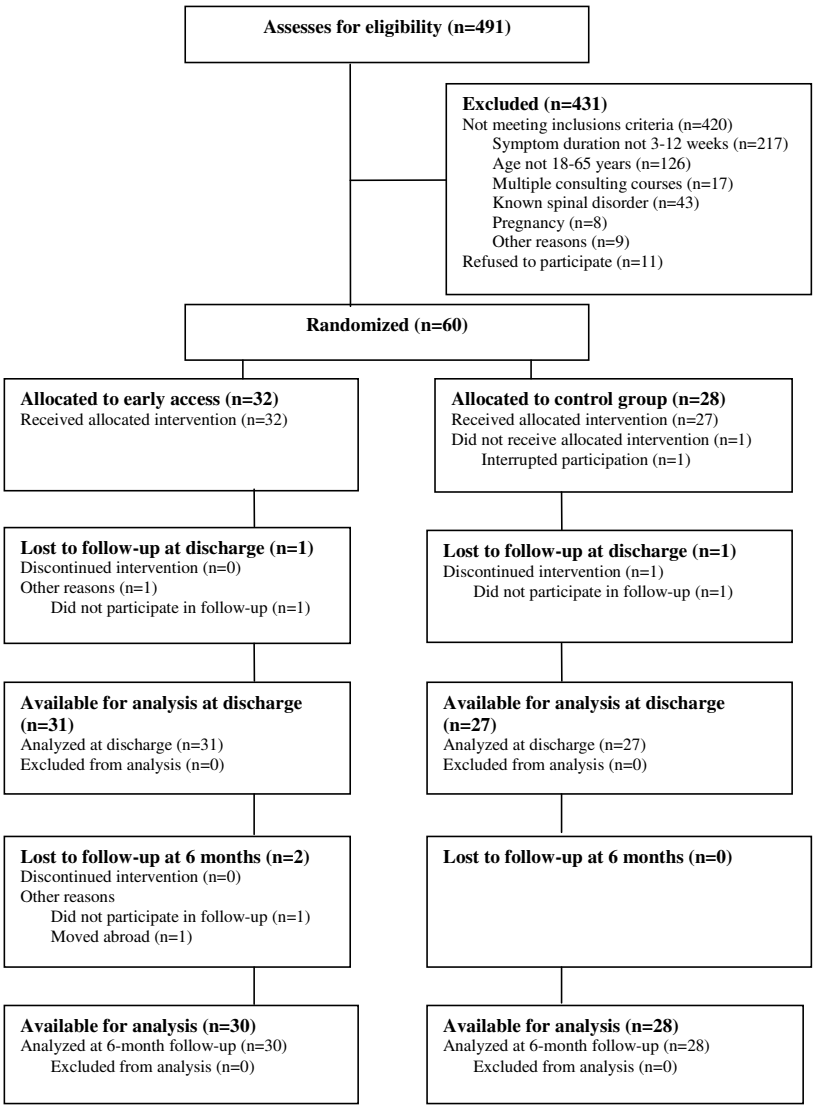


Figure 4. Participants flow Study IV

3.2. Data collection (I, II, III, IV)

The measurements included in this thesis are listed in Table 1 and below presented in detail.

Table 1. **Overview of outcome measurements. (Study I-IV)**

Measurements	Study I	Study II	Study III	Study IV
Body function				
Body mass index (BMI) [kg/m^2]	X	X		
Physical performance tests				
6-minute walk test (6MWT)	X	X	X	
Hand grip strength [Newton]	X	X	X	
Pain assessment				
Number of pain localizations [0-18]	X	X	X	
Tender points (TP) [0-18]	X	X	X	
Pain pressure threshold (PPT) [kPa/sec]	X	X	X	
Pain intensity [VAS, 0-100 mm]	X	X		
Fatigue [VAS, 0-100 mm]	X	X		
Multidimensional Fatigue Inventory (MFI-20)			X	
Borg category scale for rating of perceived pain (BRPP) [0-10]				X
Borg category scale for rating of perceived exertion (BRPE) [6-20]			X	
Distress				
The Hospital Anxiety and Depression scale-Anxiety (HADS-A) [0-21]	X	X	X	
The Hospital Anxiety and Depression scale-Depression (HADS-D) [0-21]	X	X	X	
Activity				
Leisure Time Physical Activity Instrument (LTPAI)			X	
Roland Morris Disability Questionnaire (RMDQ) [0-24]	X	X		X
Participation				
Work status	X	X	X	X
Environmental factors				
Private social support (4-item version of Medical Outcome Study Social Support Survey) (MOS-SSS) [4-20]	X	X		
Family status	X	X	X	
Educational status	X	X	X	
Health-related quality of life				
Short-form health survey SF-36 (SF-36) [0-100]	X	X	X	
Other health-related aspects				
Stress and Crises Inventory-93 (SCI-93) [0-140]	X	X	X	
Örebro musculoskeletal pain screening questionnaire (ÖMPSQ) [Sum score of < 90 estimate low risk, 90-105 medium risk, > 105 high risk]	X	X		X
Fibromyalgia Impact Questionnaire (FIQ) [0-100]			X	
Experience of physical activity			X	

3.2.1. Personal factors (I, II, III, IV)

In Studies I, II and III a standardized interview with questions on age, nationality, education, family and work status, back pain history (only in Studies I and II), co-morbidity and pharmacological treatment was performed by the physical therapist. In Study IV, the history was taken by the physical therapist followed by a physical examination and individualized treatment. Item "7" in the Örebro musculoskeletal pain screening questionnaire (ÖMPQ) was used to register duration of symptoms at baseline in Study IV.

3.2.2. Body function (I, II, III, IV)

BMI (I)

Body weight and height were assessed at the clinical examination, used for calculating the BMI (kg/m^2).

Physical performance tests (I, II, III)

The 6-minute walk test (6MWT) was used for performance capacity.[106,107] The distance (in meters) is measured while the patient walks up and down a 30-meter corridor for 6 minutes. The standardized instruction to the patient is to walk as rapidly as possible without running. Walk tests are considered reliable and valid for patients with chronic pain.[108]

Hand grip strength was measured with an electronic instrument, Grippit®.[73,109] The sustained voluntary force during 10 seconds was measured (Newton). The instruction to the patient was to grip as hard as they could for 10 seconds. One measurement was made for each hand.

Number of pain localization, TP, PPT, pain intensity, fatigue and exertion (I, II, III, IV)

For pain distribution, participants were asked to report pain location by checking boxes (0-18) with corresponding predefined regions in a body drawing.[28] After the standardized interview and before the physical performance tests, manual palpation of 18 tender point (TP) was performed.[3] The pain pressure threshold (PPT) was then assessed for 8 of 18 TPs with a Somedic® algometer using a flat rubber probe measuring 1.0 cm^2 (Range 0-2000 kPa and Slope 50 kPa).[110,111] Patients were told to say "stop" immediately upon feeling pain or discomfort as opposed to the sensation of pressure. The selected bilateral TP sites were: Trapezius, Supraspinatus, Gluteal and Knee. Participants were seated during the assessment and were asked to lie prone when assessing the gluteal points. Two assessments for each selected TP were performed and mean values for the two assessments were used to calculate the total mean value of PPT for each patient[112] (I, II, III).

Perceived pain intensity during the last week was recorded on a visual analogue scale 0-100 mm (VAS)[113] (I, II, III). In Study IV, the Borg category scale for ratings of perceived pain (BRPP) was used to register pain intensity.[114,115] BRPP consists of one question and the patient rates the pain on a numerical visual analogue scale ranging from 0-10 combined with descriptions of pain. Higher scores indicate more severe pain.[114,115]

Fatigue was recorded using VAS (I, II) or the Multidimensional Fatigue Inventory (MFI-20) comprising 20 statement building 5 subscales (4-20). Higher scores indicate greater fatigue[116,117] (III).

Borg category scale for ratings of perceived exertion (BRPE) was used in Study III to record exertion during the pool exercise[114] (III).

Distress (I, II, III)
The Hospital Anxiety and Depression scale (HADS) was used for assessment of anxiety (HADS-A) and depression (HADS-D).[118] HADS contains 14 items (7 items each for anxiety and depression scores), ranging from 0 to 3, where higher scores indicate more severe anxiety (0-21) or depression (0-21).[118,119]

3.2.3. Activity (I, II, III, IV)

For self-reported activity limitation related to LBP, the Roland Morris Disability Questionnaire (RMDQ) was used.[22] The RMDQ consists of 24 yes/no statements, where higher scores indicate greater activity limitation (I, II, IV).

The Leisure Time Physical Activity Instrument (LTPAI) was used for assessing the amount of physical activity during a typical week[120] (III).

3.2.4. Participation (I, II, III, IV)

Self-reported work status was registered by standardized questions. (I, II, III) Self-reported sick absenteeism has been shown to be reliable.[121]

In Study I and II work status was dichotomized into two categories, work ability or work disability. The category work ability required the patient to work or study full- or part-time, be applying for work, be on parental leave full- or part-time and part-time disability pension. Work disability required the patient to be on full-time sick-leave or disability pension.

In Study IV, work disability was registered with "item 6" on the Örebro musculoskeletal pain screening questionnaire (ÖMPQ). This item comprises 10 boxes for various intervals of sick-leave ranging from 0 to 365 days.[105]

3.2.5. Environmental factors (I, II)

The 4-item version of Medical Outcome Study Social Support Survey (MOS-SSS) was used to register private social support. MOS-SSS is a self-reported questionnaire reflecting emotional-informational, tangible, affectionate support and positive social interaction. The answers ranged from 1-5, where higher scores indicate more support (4-20).[122]

3.2.6. Health-related quality of life (I, II, III)

For health-related quality of life the Short-form health survey SF-36 (SF-36) was used. The SF-36 contains eight dimensions: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), social functioning (SF), role-emotional (RE), vitality (VT) and mental health (MH).[123-125] There are two summary scores representing an overall index of physical and mental health: the Physical component summary score (PCS) comprising PF, RP, BP, GH and the Mental component summary score (MCS) comprising VT, SF, RE, MH.

3.2.7. Other health-related aspects (I, II, III, IV)

The ÖMPSQ is a self-administrated measure.[39,105] The sum score of 21 items indicates the risk for future disability with the classification; low risk <90, medium risk 90-105 and high risk >105[105,126] (I, II, IV).

The Stress and Crises Inventory-93 (SCI-93) was used to quantify clinical manifestations of stress symptoms. The SCI-93 is a self-administrated questionnaire comprising 35 questions, ranging from 0 to 4, where higher scores indicate more severe clinical stress symptoms (0-140)[127] (I, II, III).

The Fibromyalgia Impact Questionnaire (FIQ) was used to measure symptoms, disability and health. The FIQ comprises 10 subscales ranging from 0 to 100 where higher scores indicate lower health status[128] (III). The subscales FIQ-Pain and FIQ-Fatigue were applied in Study III.

Experience of physical activity consists of 22 items, ranging from 0 to 7. Five aspects related to physical activity are measured: Activity-related physical relaxation, activity-related well being, activity beliefs, activity-related symptoms and activity habits[129] (III).

3.3. Interventions (III, IV)

3.3.1. Pool exercise and education (III)

The patients were allocated to one of the two treatment programs using stratified randomization for the disorder, FM or WP.[130] The two programs were either a 20-session pool exercise program combined with a 6-session education program or a control group undertaking the same education program. Sealed envelopes were prepared by the statistician, who created the allocation sequence. After baseline examination, the numbered envelope was opened by a person who was not involved in the examination, informing the patient to which group she had been randomized.

3.3.1.1. The pool exercise program

The exercise program (Appendix 9.1.) comprised 20-sessions of 45-min pool exercise once a week for 20 weeks in temperate (33°C) water, supervised by a physical therapist. The exercise was planned to permit individual progress, aiming to improve overall function and to motivate regular physical activity. The median value for exertion (6–20), measured by the BRPE[114] ranged from 9 ("very light") to 11 ("light") during flexibility, co-ordination and stretching exercises, while it was 13 ("somewhat hard") during aerobic exercise. Heart rate (HR) was monitored with a Polar S610i HR monitor (Kempele, Finland) and expressed in values for age-adjusted maximum HR, 220 minus age (HR_{max}). The mean value for HR during the program ranged from 48% to 65% HR_{max}, which corresponds with low to moderate intensity.[131]

3.3.1.2. The education program

The education program (Appendix 9.2.) was designed to introduce strategies to cope with the FM symptoms. It consisted of 6 one hour sessions, conducted once a week for 6 weeks. The program was led by a physical therapist. The pedagogical approach was based on the active participation of the patients through discussions and practical exercises. The topics were theories for chronic pain, pain alleviation, physical activity, stress, relaxation and modifications of lifestyle to enhance health. At each session, patients drew up a plan (a contract) for physical activity for the next week and performed a short relaxation exercise.

3.3.2. Early access to physical therapy treatment (IV)

The patients were allocated to either early access within two days for physical examination and individualized treatment by a physical therapist or a control group with a 4-week waiting list. The randomization was constructed by coin toss. The coin toss decided group assignment for the next two patients. This group assignment was transferred to notes placed in sealed, sequentially numbered, opaque envelopes. Initially and prior to baseline assessment, the respective coordinators provided the physical therapists with an envelope for each patient. A note inside the envelope allocated the patient to physical examination and individualized physical therapy treatment, initiated within two days or after four weeks.

3.3.2.1. The early access group

Early access (EA) consisted of history, physical examination and individualized treatment conducted by a physical therapist within two days of inclusion. Patients were given a same-day appointment to a physical therapist on the day of trial entry or were given an appointment within two days if they consulted the physical therapy department by telephone.[96] Treatment was individualized and based on history and physical examination.

3.3.2.2. The control group

The control group (CG) received the same procedure as the EA group but initiated after four weeks.

3.4. Statistical analysis (I, II, III, IV)

In all studies, (I, II, III, IV) the level of significance was $p < 0.05$. An overview of statistical test used is shown in Table 2. The SPSS Windows version 15.0 and 18.0 was used for statistical analyses in study I, II and III. The Epi-info version 3.1 was used in Study IV and the SAS system for Windows release 8.02 for parametric and nonparametric covariance analysis in Study IV. Analysis was by intention-to-treat in study III and IV. Analysis per-protocol was also done in Study III.

In study II, small units were transformed to larger ones for more meaningful clinical interpretation. In 6MWT one meter was transformed to 100 meters. In the PPT one kgPa/sek was transformed to 50 kgPa/sek. In the pain and fatigue scores, one mm was transformed to 10 mm (VAS).

In Study III several calculations were performed. To control possible Type I errors, the upper limit of expected number of false significances for the secondary and exploratory variables was calculated by the following formula: $\alpha/1-\alpha$ x number of tests – number of significant tests, where α is the significance level.

Table 2 Overview of statistical test.

Statistical test	Study I	Study II	Study III	Study IV
Descriptive statistics	X	X	X	X
Chi square with Yates' correction/ Fisher's exact test	X		X	X
Mantel-Haenszel chi square test			X	
t-test	X			X
Mann-Whitney test	X		X	X
Paired t-test		X		
Wilcoxon signed ranks test		X	X	
Sign test		X		
McNemar test			X	
Covariance analysis				X
Spearman correlation		X		
Multiple linear regression		X		
Logistic regression		X		
Multiple logistic regression		X		
Fisher's non-parametric permutation test			X	

3.4.1. Descriptive data (I, II, III, IV)

To present group characteristics, mean and standard deviations (SD), median and 25th and 75th percentile or the number and percentage was used.

3.4.2. Comparison within group (II, III)

P-values for change between first and second assessment were calculated. Both parametric paired t-test and the non-parametric Wilcoxon signed ranks test were used. For nominal scales the Sign test or McNemar test was used for dichotomous variables.

3.4.3. Prognostic factors (II)

Multivariate regressions were performed to identify predictors of self-reported activity limitation (RMDQ) and work ability (yes/no). The independent variables were age, 6MWT, hand grip strength, number of pain localizations, CLBP with or without WP, PPT, pain (VAS), fatigue (VAS), HADS-A, HADS-D, RMDQ, work status, MOS-SSS, ÖMPSQ, SCI-93, PCS and MCS.

Prior to the multiple linear regression, the variables were evaluated for assumptions of multivariate analysis. The critical values for Mahalanobis or Cook's distance values were not exceeded and the correlation matrix was checked. The RMDQ fulfilled the assumption of normal distribution when ranked using Blom's formula.[132]

To estimate predictors of activity limitation (RMDQ) at the two-year follow-up first, Spearman's correlation between RMDQ at two years and each of the independent variables was performed. For dichotomous variables, Mann-Whitney's test was used. Secondly, a stepwise multiple regression including the independent variables that had significant correlation to RMDQ was performed.

To estimate predictor for work ability first, a simple logistic regression was performed to assess the association between each of the independent variables and the dependent variable work ability. Secondly, a forward stepwise logistic regression including the independent variables with significant association to work ability was performed. The model including all the significant variables from the first logistic regression were statistically significant X^2 (df 3, n=114) = 43, $p< 0.0001$ indicating that this model was able to distinguish between patients with work ability or no work ability.

3.4.4. Nomogram (II)

A nomogram predicting the probability of work ability at two years was developed using the beta coefficients calculated in the forward stepwise logistic regression. To use the nomograms: First, identify if the patient has work ability (Figure 2a, Study II) or no work ability (Figure 2b, Study II). Then locate the patient's HADS-D score and follow the corresponding line. Finally, locate the patient's performance in 6MWT and draw a horizontal line straight to the probability of work ability axis and find the patient's probability of work ability at two years.

3.4.5. Differences between groups (III, IV)

Changes in total score were constructed by calculating raw differences between inclusion, post-treatment, and follow-up measurements. In Study IV, raw differences were transformed to the categories ''improvement'', ''worsening'' or ''unchanged'' and assigned the values +1, -1, and 0 respectively.

Chi square with Yates' correction was used for group comparison of nominal data. Fisher's exact test was used for small numbers. Mantel-Haenszel chi square test was used for trends in contingency tables for ordinal categorical variables. Because there is no international

consensus on how to compare changes in ordinal scales between groups, both the parametric t-test and the non-parametric Mann-Whitney test were used.

Covariance analysis was used to adjust for baseline differences between groups, gender, and whether referred by physician or not (IV).[133]

3.4.6. Effect size (III, IV)

Effect size was calculated for variables showing a significant difference between groups. Effect size for between-group analyses was calculated by dividing the mean difference between the post-test score (III) or 6-month follow-up (IV) and baseline score in the intervention group and in the control group by the pooled SD for change. To interpret the effect sizes, 0.20 to < 0.50 were regarded as small, while 0.50 to < 0.80 were regarded as moderate.[134]

3.4.7. Subgroup analysis (III)

Pre-specified subgroups were created by dichotomized values for the SCI-93, the FIQ-pain, the HADS-D and the SF-36-PF. The SCI-93, the FIQ-pain and the SF-36- PF were dichotomized by the median value, as there are no known cut-off points for these variables indicating more or less pathology in a pain population, while the HADS-D was dichotomized by a score of 8, which indicates possible depression.[119,135] The heterogeneity, an interaction between the independent variable, group membership and the change score for the FIQ-total and the 6MWT, was analyzed using a generalized linear model for subgroup analyses. A significant heterogeneity implies different effects of the intervention for two subgroups. Differences in the change scores were analyzed by Fisher's non-parametric permutation test, and mean differences with 95% confidence intervals within each subgroup are presented (Figure 5a and 5b).

3.5. Ethical considerations

The Ethics Committee, University of Gothenburg or the Regional Ethical Review Board in Gothenburg approved all studies (I, II, III, IV). Written informed consent was obtained from all patients.

4. Results

The present thesis will be available electronically. Therefore, the results of the submitted manuscript for Studies I and II are presented briefly here so as not to hinder later publication. The result tables are presented in detail in the attached manuscripts for Studies I and II within the printed thesis. Therefore, the table numberings are according to manuscript number and presented as seen below. Otherwise, only the table number is presented.

4.1. Prevalence and characteristics for widespread pain in female primary health care patients with chronic low back pain (I)

One hundred and thirty female patients with CLBP were assessed (Figure 2) and the total group characteristics are shown in Table 1, Study I. The mean values for age were 44 (SD 11) for the group with CLBP only and 47 (SD 9.7) for the CLBP+WP group (p=0.22).

4.1.1. Prevalence of WP in patients with CLBP

Thirty-seven (28%) women with CLBP fulfilled the ACR´s criteria for WP[3] and those remaining were considered having localized CLBP (n=93).

4.1.2. Difference between CLBP with or without WP

The CLBP+WP group showed significantly more severe impairments in body functions measured as physical performance (6MWT, hand grip strength), a higher number of TPs, more severe pain, fatigue and depression compared to the CLBP group ($p<0.05$). No differences between groups were found for the PPT and HADS-A (Table 2, Study I).

The CLBP+WP group showed more severe activity limitations and participation restrictions ($p<0.05$). The prevalence of work disability for the entire group was 21% (n=27/130). When comparing the CLBP and CLBP+WP groups the percentage of work disability was twice as high when WP was present, 35% (n=13/37) compared to 16% (n=15/93) in the CLBP group (p=0.032) (Table 2, Study I).

The CLBP+WP group reported significantly more negative environmental impact in terms of private social support. Both the CLBP and CLBP+WP group reported high private social support (MOS-SSS), but when comparing the two groups the CLBP+WP scores were significantly lower, reflecting lower private social support (Table 2, Study I).

The ÖMPSQ sum score was significantly lower for the CLBP group compared to the CLBP+WP group indicating a difference in risk for future disability[39] (Table 2, Study I).

The CLBP+WP group showed a higher sum score in the SCI-93 compared to the CLBP group implying more severe clinical stress symptoms when WP was present.

Three (PF, BP, VT) of eight subscales in the SF-36 showed lower median scores for the CLBP+WP group compared to the CLBP group ($p< 0.05$), indicating lower health-related quality of life in these dimensions while the median scores for the subscales RF, GH, SF, RE and MH did not differ between the groups (Table 2, Study I).

4.2. Prognostic factors for activity and work status in women with chronic low back pain consulting primary health care: a two year prospective longitudinal cohort study (II)

Ninety-five percent (123/130) were followed up at two years (Figure 2). The seven women, lost to follow-up were younger, with a mean value of 36 years (SD 12), (p=0.016), but no other first assessment measurements differed significantly. The characteristics at the first assessment are presented in Table 1, Study II.

4.2.1. Changes during two years

Thirty-four (28%) fulfilled the criteria of WP at first assessment and 29% (n=36) at the two-year follow-up. Three (2%) reported no pain at any site at the two-year follow-up. After two years, significant improvement was found for the walk test (6MWT), pain pressure threshold (PPT), pain intensity, activity limitation (RMDQ), risk for future disability (ÖMPSQ) and overall physical health (PCS) ($p<0.05$), while hand grip strength, number of pain localizations and private social support (MOS-SSS) worsened ($p<0.05$) (Table 2, Study II).

4.2.2. Predictors for self-reported activity limitation (RMDQ) at the two-year follow-up

The 6MWT, SCI-93 and ÖMPSQ showed the highest correlation with the RMDQ -0.41, 0.48, 0.53, respectively (Table 3, Study II). The stepwise multiple regression analysis showed that the 6MWT, SCI-93 and ÖMPSQ explained 43% of variance in the RMDQ at the two-year follow-up. Thus, these three variables were identified as the most important predictors.

4.2.3. Predictors for work ability at the two-year follow-up

The simple logistic regression analysis for each of the predictors showed that 12 variables were significantly associated with work ability (yes/no) (Table 4, Study II). The forward

stepwise regression model, 6MWT, HADS-D and earlier work ability were identified as predictors. This model accounted for 51% of the variance (Nagelkerke R-Square) of the dependent variable.

4.2.4. Nomograms of probability for work ability two years later

The 6MWT, HADS-D and earlier work ability, identified in the forward stepwise logistic regression (Table 4, Study II) were used to construct a nomogram predicting the probability of work ability two years later (Figure 2a + 2b, Study II).

4.3. Pool exercise for patients with fibromyalgia or chronic widespread pain: a randomized controlled trial and subgroups analyses (III)

One hundred and sixty-six patients were randomized to either the Exercise-Education group (n=81) or Education group (n=85) (Figure 3). No significant baseline differences were found (Table 3).

Table 3. Demographic data of the patients randomized to the Exercise-Education and Education programs (n = 166)

	Exercise-Education *n* = 81	Education *n* = 85	
	Mean (SD) [a]	Mean (SD)	*p*-value[b]
Age, years	44.6 (9.26)	46.5 (8.30)	0.235
Symptom duration, years	10.3 (6.85)	10.6 (7.46)	0.925
Tender points, *n*	13.4 (3.68)	13.6 (3.41)	0.796
Algometer, kPa/sec	180 (72.94)	187 (75.17)	0.702
Pain localization, 0–18	12.5 (3.42)	13.3 (3.42)	0.105
	n (%)	*n* (%)	
Living with an adult	59 (73)	64 (75)	0.854
Born outside Sweden	9 (11)	18 (21)	0.120
Education			0.819
≤ 9 years	18 (22)	20 (24)	
10–12 years	44 (54)	45 (53)	
> 12 years	19 (24)	19 (22)	
Employment			0.562
Not working	45 (55)	53 (62)	
Working part-time	28 (35)	23 (27)	
Working full-time	8 (10)	9 (11)	
Sick-leave			0.294
0%	61 (75)	68 (80)	
25–75%	7 (9)	9 (11)	
100%	13 (16)	8 (9)	
Sick-pension of limited duration			0.501
0%	61 (75)	61 (72)	
25-75%	10 (13)	9 (11)	
100%	10 (12)	15 (18)	
Disability pension			0.433
0%	51 (63)	49 (58)	
25-75%	14 (17)	15 (18)	
100%	16 (20)	21 (25)	
Pharmacological treatment			
Analgesics	57 (70)	61 (72)	0.978
Psychotropic drugs[c]	36 (44)	38 (45)	0.110

[a] SD: standard deviation.
[b] p-values for the differences between the two groups.
[c] Antidepressants, sedatives.

4.3.1. Differences between the groups after the 20-week treatment period

4.3.1.1. Intention-to-treat analysis

In primary outcomes, the FIQ-total showed greater improvement in the Exercise-Education group (-4.8, SD 13) compared to change in the Education group (-0.7, SD 12) 20-weeks after baseline (p = 0.040). The effect size for FIQ-total for the Exercise-Education group compared to the Education group was 0.32. For the 6MWT, no significant difference (p = 0.067) between groups was found at 20 weeks after baseline (Table 4).

In secondary outcomes, the FIQ-pain improved more in the Exercise-Education group (-7.8, SD 23) compared to change in the Education group (1.7, SD 20) after the 20-week treatment period (p = 0.018).The effect size for FIQ-pain was 0.45 (Table 4).

In explorative outcomes, the MFI-reduced motivation improved significantly in the Exercise-Education group (-0.8, SD 3.3) compared to change in the Education group (0.3, SD 3.2) 20 weeks after baseline (p=0.046). The effect size was 0.34. The Activity-related relaxation showed significant improvement in the Exercise-Education group (-0.4, SD 1.2) compared to change in the Education group (0.2, SD 1.4) 20 weeks after baseline (p = 0.017). The effect size was 0.45 (Table 4).

4.3.1.2. Per protocol analysis

Fifty-eight percent (47/81) in the Exercise-Education group and 66% (56/85) in the Education group were defined as active participants (≥ 60% participation).

In primary outcomes, the FIQ-total and 6MWT improved significantly in the intervention group (Exercise-Education) 20 weeks after baseline. The FIQ-total change in the Exercise-Education group was -6.3 (SD 14) compared to change in the Education group -0.6 (SD 12) 20 weeks after baseline (p = 0.013). The effect size was 0.44. The 6MWT improved significantly in the Exercise-Education group (14, SD 36) compared to the Education group (-6.4, SD 58) 20 weeks after baseline (p = 0.013). The effect size was 0.43 (Table 5).

In secondary outcomes, the FIQ-pain and LTPAI improved significantly in the Exercise-Education group compared to the Education group after 20-weeks of treatment. The FIQ-pain showed significantly reduced pain in the Exercise-Education group -10 (SD19) compared to the Education group 3.0 (SD 19) 20 weeks after baseline *(*p = 0.002). The effect size was 0.69. The LTPAI-total activity increased significantly in the Exercise-Education group (1.0, SD 3.7) compared to the Education group (-0.1, SD 5.1) 20 weeks after baseline (p = 0.026). The effect size was 0.25 (Table 5).

In explorative outcomes, the MFI-reduced motivation improved significantly (p = 0.005) in the Exercise-Education group (–1.1, SD 3.1) compared to the Education group (-0.7, SD 3.0), the effect size being 0.13. Significant improvement was found in the Activity-related physical relaxation (p = 0.002) as well for the Activity-related Well-being (p = 0.021) in the Exercise-Education group compare to the Education group. The effect size was 0.72 and 0.43 respectively (Table 5).

Table 4. Intention-to-treat analysis. Baseline values, change from baseline in outcome variables, within-group and between-group differences for the Exercise-Education group and the Education group.

	Exercise–Education group					**Education group**					**Ex–Edu vs Edu**
	Baseline *n* = 81 Mean (SD)	20 w *n* = 69 Mean (SD)	*p*	11–12 mo *n* = 63 Mean (SD)	*p*	Baseline *n* = 85 Mean (SD)	20 w *n* = 64 Mean (SD	*p*	11–12 mo *n* = 62 Mean (SD)	*p*	20 w *p*
Primary outcomes											
FIQ Total	61.6 (16.42)	-4.8 (13.19)	**0.006**	-3.9 (15.45)	0.077	66.6 (15.30)	-0.7 (12.22)	0.952	-4.5 (14.32)	**0.024**	**0.040**
6MWT	511 (79.7)	7.5 (53.51)	**0.047**	14.1 (57.59)	**0.013**	517 (77.2)	-2.0 (63.18)	0.591	3.9 (66.27)	0.800	0.067
Secondary outcomes											
FIQ Pain	67.7 (16.79)	-7.8 (22.57)	**0.007**	-6.5 (23.68)	0.119	70.4 (20.05)	1.7 (19.47)	0.674	-2.5 (19.85)	0.252	**0.018**
FIQ Fatigue	76.3 (22.49)	-5.0 (25.50)	0.103	-2.7 (24.35)	0.486	81.7 (17.64)	-3.8 (19.05)	0.035	-5.5 (21.88)	0.134	0.980
SF-36 PCS	30.8 (8.09)	3.1 (7.70)	**0.006**	2.86 (8.64)	**0.006**	29.4 (8.03)	0.6 (8.32)	0.776	1.3 (7.93)	0.234	0.129
SF-36 MCS	40.9 (13.77)	0.4 (10.64)	0.864	0.51 (13.93)	0.561	36.6 (12.29)	2.2 (12.02)	**0.040**	1.3 (11.26)	0.197	0.146
SF-36 PF	56.6 (19.00)	0.7 (11.98)	0.614	2.19 (14.46)	0.252	50.9 (18.30)	0.7 (16.79)	0.839	1.3 (16.93)	0.761	0.702
SF-36 RP	22.8 (32.16)	14.8 (44.26)	**0.008**	12.1 (40.68)	**0.035**	15.2 (26.04)	7.6 (33.34)	0.099	9.3 (43.62)	0.056	0.719
SF-36 BP	28.6 (14.32)	5.1 (16.72)	**0.014**	5.0 (21.13)	0.084	25.7 (16.09)	0.4 (17.07)	0.650	3.6 (18.22)	0.129	0.236
SF-36 VT	28.4 (21.09)	6.6 (20.67)	**0.009**	4.2 (23.03)	0.130	24.2 (16.72)	3.9 (21.57)	0.132	2.3 (21.02)	0.713	0.377
HADS-A	8.1 (5.53)	-0.7 (3.01)	0.117	-0.7 (3.30)	0.112	9.1 (4.82)	0.4 (3.39)	0.429	0.4 (3.79)	0.369	0.148
HADS-D	6.4 (4.01)	-0.2 (2.98)	0.508	-0.4 (3.26)	0.555	7.8 (3.64)	-0.1 (2.77)	0.748	0.0 (3.15)	0.673	0.993
LTPAI, total	5.4 (4.06)	1.0 (4.26)	**0.036**	-0.6 (4.09)	0.309	5.0 (4.23)	0.3 (4.64)	0.861	-0.4 (5.72)	0.811	0.117
LTPAI, mod	2.0 (2.14)	1.2 (2.91)	**0.000**	0.2 (2.85)	0.677	2.1 (2.72)	0.3 (2.69)	0.413	-0.5 (3.68)	0.530	0.068
Exploratory outcomes											
SCI-93	73.3 (23.43)	-2.8 (11.97)	0.094	-3.9 (13.23)	**0.011**	79.4 (26.09)	-0.8 (12.14)	0.650	-2.6 (12.36)	0.339	0.436
MFI GF	16.9 (2.65)	-0.4 (2.75)	0.394			17.8 (2.30)	-0.8 (3.07)	**0.037**			0.368
MFI PF	16.6 (3.06)	-0.6 (2.89)	0.083			17.6 (2.42)	-1.0 (3.80)	**0.010**			0.544
MFI RA	15.0 (3.38)	-0.6 (3.09)	0.075			16.0 (3.46)	-1.1 (3.25)	**0.008**			0.436
MFI RM	10.2 (3.89)	-0.8 (3.26)	**0.040**			10.8 (3.75)	0.3 (3.22)	0.451			**0.046**
MFI MF	14.4 (4.15)	-0.2 (3.34)	0.585			14.2 (3.86)	0.3 (2.79)	0.408			0.390
A-Relaxation	4.6 (1.50)	-0.4 (1.22)	**0.008**			4.6 (1.24)	0.2 (1.44)	0.439			**0.017**
A-Wellbeing	2.8 (1.46)	-0.4 (1.41)	**0.023**			2.9 (1.31)	-0.0 (1.41)	0.486			0.284
A-Beliefs	2.3 (1.35)	0.1 (1.39)	0.870			2.2 (1.25)	-0.2 (1.02)	0.838			0.983
A-Symptoms	3.4 (1.23)	-0.1 (1.42)	0.472			3.2 (1.23)	-0.1 (1.59)	0.518			0.993
A-Habits	3.4 (1.59)	0.2 (1.58)	0.500			4.0 (1.55)	-0.1 (1.85)	0.768			0.437

Significant values are shown in bold. A: activity; FIQ: Fibromyalgia Impact Questionnaire; HADS: Hospital Anxiety and Depression Scale; LTPAI: leisure time physical activity instrument; MCS: mental component score; MFI: multidimensional fatigue inventory; MFI GF: MFI general fatigue; MFI MF: MFI mental fatigue; MFI PF: MFI physical fatigue; MFI RA: MFI reduced activity; MFI RM: MFI reduced motivation; PCS: physical component score; SCI-93: stress and crisis inventory; SD: standard deviation; SF-36: 36-item short form health survey; SF-36 BP: SF-36 bodily pain; SF-36 PF: SF-36 physical functioning; SF-36 RP: SF-36 role-physical; SF-36 VT: SF-36 vitality; 6MWT: 6-minute walk-test.

Table 5. Per-protocol analysis. Baseline values, change from baseline in outcome variables, within-group and between-group differences for the active participants in the Exercise-Education group and the Education group

	Exercise-Education group					**Education group**					**Ex–Edu vs Edu**
	Baseline *n* = 47 Mean (SD)	20 w *n* = 46 Mean (SD)	*p*	11-12 mo *n* = 43 Mean (SD)	*p*	Baseline *n* = 56 Mean (SD)	20 w *n* = 50 Mean (SD)	*p*	11-12 mo *n* = 45 Mean (SD)	*p*	20 w *p*
Primary outcomes											
FIQ Total	61.2 (17.73)	-6.3 (14.41)	**0.003**	-4.7 (13.45)	0.063	65.9 (15.98)	-0.6 (12.47)	0.881	-4.4 (15.53)	0.121	**0.013**
6MWT	507 (75.05)	14.5 (35.79)	**0.024**	21.5 (48.18)	**0.007**	511 (71.07)	-6.4 (58.34)	0.287	3.7 (59.53)	0.856	**0.013**
Secondary outcomes											
FIQ Pain	68.8 (16.73)	-10.0 (18.83)	**0.002**	-9.1 (20.89)	**0.019**	68.3 (19.87)	3.0 (18.92)	0.512	-2.3 (19.69)	0.595	**0.002**
FIQ Fatigue	75.1 (23.74)	-7.6 (27.12)	0.063	-4.0 (25.31)	0.473	82.3 (17.76)	-4.7 (19.59)	**0.042**	-5.6 (21.33)	0.534	0.732
SF-36 PCS	30.4 (8.65)	2.9 (6.28)	**0.007**	3.0 (6.69)	**0.002**	29.3 (8.24)	-0.3 (8.73)	0.942	1.4 (8.44)	0.412	0.104
SF-36 MCS	41.9 (14.17)	0.1 (10.21)	0.562	0.0 (11.94)	0.856	36.2 (12.80)	3.8 (12.38)	**0.008**	1.8 (12.39)	0.162	0.085
SF-36 PF	53.6 (19.64)	1.5 (11.22)	0.346	4.2 (11.08)	**0.024**	50.6 (16.90)	0.2 (16.42)	0.856	1.3 (17.31)	0.724	0.583
SF-36 RP	26.2 (33.95)	11.4 (40.15)	0.074	8.3 (32.51)	0.134	15.2 (26.83)	9.9 (36.24)	0.079	10.2 (37.06)	0.067	0.697
SF-36 BP	27.9 (15.44)	6.1 (15.07)	**0.006**	6.7 (15.76)	**0.014**	25.1 (14.83)	0.7 (16.01)	0.782	4.1 (19.28)	0.207	0.183
SF-36 VT	30.3 (22.15)	6.1 (15.07)	**0.021**	2.6 (17.47)	0.192	23.0 (16.20)	4.9 (21.09)	0.154	3.3 (22.20)	0.659	0.329
HADS-A	8.16 (5.48)	-0.9 (2.74)	0.055	-0.8 (2.76)	0.071	9.15 (5.03)	0.4 (3.38)	0.471	-0.4 (3.87)	0.352	0.099
HADS-D	6.21 (4.18)	-0.2 (2.77)	0.327	-0.5 (2.56)	0.418	7.82 (3.41)	-0.3 (2.78)	0.472	-0.0 (3.18)	0.611	0.865
LTPAI, total	5.6 (4.43)	1.0 (3.68)	**0.017**	0.0 (3.37)	0.823	5.3 (4.15)	-0.1 (5.06)	0.678	-0.2 (4.99)	0.420	**0.026**
LTPAI, mod	1.9 (1.96)	1.3 (2.74)	**0.001**	0.8 (2.67)	**0.045**	2.1 (2.90)	0.2 (2.90)	0.654	-0.5 (3.93)	0.802	**0.048**
Exploratory outcomes											
SCI-93	72.3 (24.56)	-3.1 (9.53)	0.053	-4.5 (10.19)	**0.010**	81.4 (25.24)	-1.1 (9.83)	0.512	-3.2 (12.13)	0.168	0.382
MFI GF	17.0 (2.76)	-0.5 (2.68)	0.238			18.0 (2.73)	-0.6 (2.93)	0.217			0.819
MFI PF	16.7 (2.76)	-0.9 (2.71)	**0.036**			18.0 (2.11)	-0.7 (2.60)	0.074			0.738
MFI RA	15.3 (3.47)	-1.1 (2.78)	**0.010**			16.3 (3.02)	-1.0 (3.30)	**0.034**			0.868
MFI RM	10.0 (4.05)	-1.1 (3.13)	**0.031**			10.8 (3.68)	-0.7 (3.02)	0.089			**0.005**
MFI MF	14.6 (4.56)	0.1 (3.09)	0.978			14.3 (3.87)	0.5 (2.75)	0.101			0.379
A-Relaxation	4.8 (1.49)	-0.6 (1.21)	**0.001**			4.6 (1.31)	0.4 (1.54)	0.198			**0.002**
A-Wellbeing	3.0 (1.57)	-0.7 (1.36)	**0.001**			2.9 (1.35)	-0.1 (1.44)	0.943			**0.021**
A-Beliefs	2.5 (1.31)	-0.3 (1.14)	0.102			2.2 (1.36)	0.0 (1.00)	0.984			0.262
A-Symptoms	3.0 (1.08)	0.3 (1.16)	0.070			3.2 (1.27)	-0.0 (1.62)	0.723			0.294
A-Habits	3.4 (1.58)	-0.0 (1.66)	0.624			4.0 (1.63)	-0.2 (1.85)	0.603			0.960

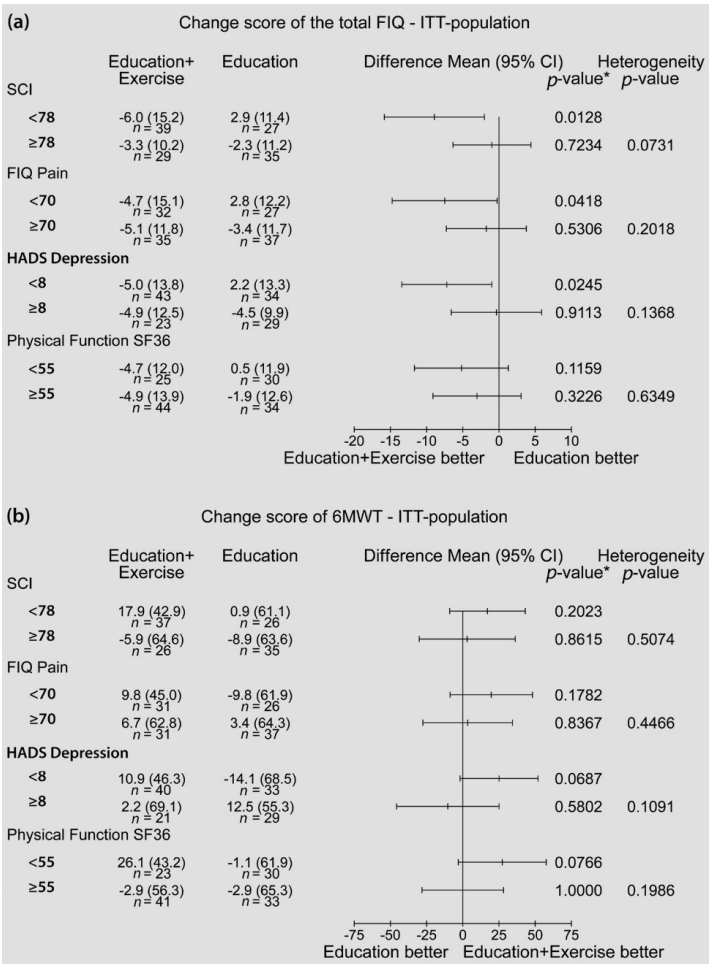
Significant values are shown in bold .A: activity; FIQ: Fibromyalgia Impact Questionnaire; HADS: Hospital Anxiety and Depression Scale; LTPAI: leisure time physical activity instrument; MCS: mental component score; MFI: multidimensional fatigue inventory; MFI GF: MFI general fatigue; MFI MF: MFI mental fatigue; MFI PF: MFI physical fatigue; MFI RA: MFI reduced activity; MFI RM: MFI reduced motivation; PCS: physical component score; SCI-93: stress and crisis inventory; SD: standard deviation; SF-36: 36-item short form health survey; SF-36 BP: SF-36 bodily pain; SF-36 PF: SF-36 physical functioning; SF-36 RP: SF-36 role-physical; SF-36 VT: SF-36 vitality; 6MWT: 6-minute walk-test.

4.3.2. Subgroup analysis

For change in the FIQ-total and 6MWT, no significant heterogeneity was found for the subgroups created by level of pain (FIQ-pain), distress (HADS-D), stress (SCI-93) and activity limitation (SF-36-PF) (Figur 5a and 5b).

Analyses within the subgroups characterized by lower scores in the FIQ-pain (< 70), HADS-D (<8), and SCI-93(<78) showed significant improvement in the FIQ-total in the Exercise-Education group compared to change in the Education group.
No significant change was found in the FIQ-total for patients reporting lower scores in the SF-36 PF (<55) (Figure 5a).

No significant change was found in the 6MWT for analyses within the subgroups characterized by lower scores in the FIQ-pain (< 70), HADS-D (<8), SCI-93(<78) and SF-36 PF (<55) (Figure 5b).



Figur 5a and 5b. Subgroup influences on change in primary outcomes.
(a) Fibromyalgia Impact Questionnaire (FIQ) total.
(b) Six-minute walk test (6MWT).
The subgroups were created by dichotomized values of the stress and crisis inventory (SCI-93), the FIQ-pain, the Hospital Anxiety and Depression Scale, depression (HADS-D), and the 36-item Short-Form Health Survey (SF-36)-Physical Function. Mean differences for the change score and 95% confidence intervals (CI) are presented in the graphs, followed by *p*-value, separately for each subgroup. *p*-value for heterogeneity (interaction between the randomized group and the change score of the primary outcome) is given in the right-hand column.
ITT: intention-to-treat.
*Fisher's non-parametric permutation test.

4.4. Early access to physical therapy treatment in primary health care for subacute low back pain: a prospective randomized clinical trial (IV)

Sixty patients with subacute LBP were randomized into either the EA group (n=32) or the CG (n=28) (Figure 4). There were no baseline differences except for waiting time ($p< 0.0001$) and durations of symptoms ($p=0.01$) (Table 6). The EA group showed shorter duration of symptoms but both groups fell well within the inclusion criteria (3 to 12 weeks).

Table 6. Baseline values for the early access (EA) and the control group (CG).

	EA (n=32)	CG (n=28)	P-values
Age-year [a]	39.0 (30.0, 49.5)	39.0 (33.0, 46.5)	0.69
	39.2 (12.1)	40.8 (11.1)	0.58
Sex (male/female)	12/20	14/14	0.23
Nationality Swedish (%)			
Yes	32 (100%)	28 (100%)	
Employment status (%)			0.33
Paid work	29 (90.6%)	25 (89.3%)	
Studying	2 (6.3%)	1 (3.6%)	
Unpaid work at home	1 (3.1%)	0 (0%)	
Other	0 (0%)	2 (7.1%)	
Unemployed	0 (0%)	0 (0%)	
Retired	0 (0%)	0 (0%)	
Waiting time [b]	0.0 (0.0, 3.0)	28.0 (23.5, 29.0)	**$<10^{-4}$**
Consult (%)			0.54
Referral	12 (37.5%)	11 (39.3%)	
Direct	20 (62.5%)	17 (60.7%)	
Sick leave during past 12 month [c]	3.0 (1.0, 5.0)	2.0 (1.0, 4.5)	0.78
	2.9 (1.9)	2.9 (2.4)	0.99
Duration [d]	3.0 (2.0, 5.5)	5.0 (3.0, 7.0)	**0.01**
	3.7 (2.2)	5.0 (2.2)	**0.02**
Pain intensity [e]	5.0 (3.5, 7.0)	5.0 (3.5, 6.5)	0.78
	5.0 (1.9)	4.9 (2.0)	0.75
Risk for long-term disability [f]			
Sum score	100.0 (79.0, 115.0)	94.0 (80.5, 110.5)	0.67
	98.5 (23.7)	96.4 (23.6)	0.73
Risk group (%):			0.64
high risk	12 (39%)	8 (29%)	
medium risk	8 (26%)	7 (25%)	
low risk	11 (35%)	13 (46%)	
Disability [g]	11.5 (6.0, 15.5)	11.5 (7.0, 14.0)	0.72
	10.9 (5.5)	10.6 (4.9)	0.84

[a] Age. First line median values (25th and 75th percentile). Second line mean values (SD).
[b] Days before initiating treatment. Median values (25th and 75th percentile).
[c] Örebro musculoskeletal pain screening questionnaire (ÖMPSQ) item number six was used. Ten boxes with different intervals of sick leave scores 1 to 10 points. Higher values indicate more days at sick leave. First line is median values (25th and 75th percentile). Second line is mean values (SD).
[d] Duration of symptoms. ÖMPSQ item number seven was used. Ten boxes with different intervals of duration scores 1 to 10 points. Higher values indicate longer duration. First line is median values (25th and 75th percentile). Second line is mean values (SD).
[e] Borg categorical scale for perceived pain (BRPP) rates pain on a scale (0-10). Higher values indicate higher pain intensity. First line is median values (25th and 75th percentile). Second line is mean values (SD).
[f] ÖMPSQ. Total sum score indicates risk for future pain and disability. Sum score >105 estimates high level of risk, 90-105 medium risk and < 90 low risk. First line is median values (25th and 75th percentile). Second line is mean values (SD).
[g] Roland Morris disability questionnaire (RMDQ) indicates disability related to LBP. Higher scores indicate more severe disability. First line is median values (25th and 75th percentile). Second line is mean values (SD).

4.4.1. Post-treatment differences between groups

The type and number of treatments did not differ between the groups (Table 7). No significant difference in primary or secondary outcomes was found between the EA and CG after treatment (Table 7).

Table 7. Physical therapy treatments used and number of treatment sessions for early access (EA) and control group (CG).

	EA (n=32)	CG (n=27)	P-values
Manual therapy (%)[a]	40.6	44.4	0.48 [b]
Active exercise (%)[a]	37.5	48.1	0.28
Group education (%)[a]	0	0	
Advice, self-care instruction (%)[a]	87.5	81.5	0.38
Number of treatments[c]	3 (2, 4.5)	3 (2, 6)	0.56[d]
	4.06 (3.06)	5.11 (5.06)	0.33[e]

[a] Patients may receive more than one type of treatment.
[b] Fisher's exact test.
[c] Number of treatment sessions. First line median values (25th and 75th percentile). Second line mean values (SD).
[d] Mann-Whitney test.
[e] T-test, ANOVA.

4.4.2. Six-month follow-up differences between groups

Six month after baseline the EA group showed significantly greater reduction in perceived pain compared to the CG (Table 8). The effect size for perceived pain (BRPP) at the 6-month follow-up for the EA group compared to CG group was 0.51 (95% CI -0.02- 1.0).

For group comparison of pain reduction at 6-months, the covariance analysis showed that when adjusting for baseline differences in symptom duration, sex, and physician referral, the *P* values increased (0.06 to 0.079, 0.025 to 0.049, and 0.003 to 0.015). The greater reduction in perceived pain in the EA group compared to CG group remains statistically significant in the two non-parametric tests (Table 8).

In secondary outcomes, no significant difference was found between the groups (Table 8).

The number of visits to a physician between baseline and 6 months was 1.0 (0.0-1.0) and 0.0 (0.0-0.5) for the EA and CG group respectively, (median, 25th and 75th percentile). No significant difference between the two groups was found (p=0.11). The median value was zero for consulting other health care providers for both groups (25th and 75th percentile 0.0-0.0), (p=0.63).

Table 8. Changes in scores from baseline to discharge and 6-month follow-up for the early access (EA) and control group (CG).

	Discharge		p-values[a]			6-month follow-up		p-values[a]		
	EA (n=31)	CG (n=27)	T-test	M&W	MWT	EA (n=30)	CG (n=28)	T-test	M&W	MWT
Pain[b] (0-10)	-3.1 (2.0) -3.0 (-2.0, -4.0)	-3.0 (2.3) -3.0 (-1.0,-5.0)	0.88	0.75	0.18	-3.0 (1.7) -3.0 (-2.0, -4.0)	-2.0 (2.2) -1.5 (0.0,-3.0)	0.06	**0.025**	**0.003**
Disability[c] (0-24)	-4.8 (5.0) -3.0 (-2.0,-9.0)	-5.7 (4.5) -6.0 (-2.0,-10.0)	0.47	0.52	0.28	-6.3 (5.3) -7.0 (-2.0,-10.0)	-5.3 (5.6) -3.5 (0.5,-9.0)	0.48	0.40	0.31
ÖMPSQ[d] (EA n= 28, CG n=25)	---	---	---	---	---	-26.5 (31.1) -25.0 (-1.0, -46.0)	-20.2 (23.4) -21.0 (-5.0, -39.0)	0.41	0.55	0.42
Work disability[e] (EA n =29, CG n=25)	---	---	---	---	---	+0.7 (1.8) ±0.0 (+2.0, 0.0)	±0.0 (2.2) ±0.0 (0.0,0.0)	0.13	0.20	0.25

[a] P-values for comparison of groups. T-test =Students t-test, M&W= Mann-Whitney's test, MWT= Mann-Whitney's test using transformed data where improvement is coded as +1, worsening -1 and unchanged 0.
[b] Primary outcome: change in pain intensity in Borg category scale for ratings of perceived pain (BRPP). Negative values indicate a decrease in pain level.
[c] Secondary outcome: change in disability level related to LBP in Roland Morris disability questionnaire. Negative values indicate a decrease in disability level.
[d] Secondary outcome: change in sum score for estimated risk developing long- term pain and disability in Örebro musculoskeletal pain screening questionnaire (ÖMPSQ). Negative values indicate a decrease in level of risk.
[e] Secondary outcome: change in sick-leave during past 12 month in item number six, ÖMPSQ. Positive values indicate an increase in level of sick-leave.

5. Discussion

Twenty-eight percent of women with CLBP consulting PHC fulfilled the ACR's 1990 criteria for WP comparable to findings of 32% and 38% in studies conducted in secondary care.[68,69] (I) At the two-year follow-up the figure for WP was 29% (II). When WP was present, significantly more severe impairments in body functions, more severe activity limitation and participation restrictions, more negative environmental impact in terms of private social support, lower health-related quality of life and other health-related aspects were found compared to the women with CLBP without WP (I).

One hundred and twenty-three (95%) female patients with CLBP were followed up at two years. At this two-year follow-up, all measurements except hand grip strength, number of pain localizations and private social support (MOS-SSS) were unchanged or improved (II). The 6MWT was best for predicting variation in activity limitation (RMDQ) and work ability after two years. Other variables with predictive ability were higher risk scores for future disability (ÖMPSQ), clinical stress symptoms (SCI-93), depression (HADS-D) and work ability at the first assessment (II).

For patients with FM or WP, a 20-session supervised pool exercise program combined with a 6-session education program significantly improved overall health (FIQ-total) compared to the control group undertaking the same education program (III), confirming previous recommendations for treatment of patients with FM.[75]

When it comes to early intervention for patients with subacute LBP, early access within two days to examination and individualized treatment by a physical therapist the reduction in perceived pain at 6 months was greater compared to the group with access after a 4-week wait (IV).

5.1. Methodological aspects

5.1.1. Study design and study population (I, II, III, IV)

The present thesis was based on studies with different designs. A cross-sectional study was conducted to estimate prevalence and characteristics for WP in women with CLBP consulting PHC. A cross-sectional design is appropriate when the purpose is to estimate prevalence and characteristics of the subject of interest. All patients from Study I were invited to a two-year follow-up and those who could be contacted and confirmed participation were included in the longitudinal prospective cohort study (II). The selection of participants for these studies aimed to reflect clinical practice and the results can be generalized to women consulting PHC which need to be considered when interpreting results. It can be expect that the findings are representative for women in countries belonging to the western civilization. Some of the findings might be valid for women living in other countries.

Two RCT studies (III, IV) were performed to compare differences between groups and were reported according to the CONSORT statement.[136] In Study III, the examiner was blinded for the group the patient was allocated to, but to blind patients was impossible since they actively participated in treatment. In the study of early access to treatment compared to a four-week waiting list the possibility to blind the treating physical therapist for group status was small. (IV) Although treatment was individualized and based on history and clinical assessment in both groups, knowledge of group assignment might have influenced the physical therapist's attitude toward treatment. However, the number or type of treatment did not differ between groups.

The present thesis used definitions of LBP for localization and duration described as useful when planning the included studies (I, II, IV).[1,2] However, there are methodological problems in defining LBP making it difficult to compare results.[137] The subacute phase is described as critical but some clinical guidelines do not distinguish subacute from acute LBP for management and treatment recommendations.[7,30] Moreover, a review of interventions for subacute LBP presumed that duration of symptoms and sick-leave are equivalent[138] making it difficult to compare result and compile results to evidence. To enable more homogeneous groups of patients with LBP, a recent standardization of a back pain definition for use in epidemiological studies of LBP was developed and agreed on by an international panel of LBP experts.[137] They suggest using standardized questions on localization, frequency, duration and severity.[137] However, this new questionnaire needs further validation. Moreover, sub grouping patients within the non-specific LBP category by various classification systems is also available but has been suggested as requiring further evaluation.[34-37,139] Thus, future studies may have definitions of non-specific LBP that will not completely match the definitions used in this thesis.

In this thesis women with WP and FM were identified by using the ACR's 1990 criteria (I, II, III) previously recommended.[3] How to distinguish between WP and FM is under discussion, since both disorders are associated with alterations in the central pain processes. The criterion of tenderness on 11 of 18 TPs is the one which separate these conditions according to ACR 1990[3] where a higher number of TPs has been associated with more severe symptoms.[70,72] Recently a new preliminary set of criteria for the diagnosis of FM was presented and designed to complement the ACR's 1990 criteria and suggested suitable in health care. These criteria comprises the ACR criterion of WP, a symptoms severity-scale built on characteristic features of FM but do not require TP examination.[140] However, this new set of criteria has not yet been validated and ACR's 1990 criteria for WP and FM is still recommended for clinical research.[3]

There were patients who were lost to follow-up (II, III, IV). Seven patients with CLBP could not be assessed at the two-year follow-up, mainly due to pregnancy an exclusion criteria (II). The follow-up frequency was also considered high when following patients with subacute LBP over a period of 6 months (97%) (IV). Another follow-up pattern was found for the study including patients with WP or FM. Twenty percent of the patients in Study III did not complete the post-treatment test. The reasons for dropping out were time limitation associated with change in work schedules, family commitments or concomitant disorders. Other reasons were experience of exacerbation with accompanying signs and symptoms or unknown reasons. Dropout rates of approximately 20% are not rare in exercise treatment studies enrolling patients with WP.[141]

5.1.2. Gender (I, II, III)

Including only women may be considered a limitation but the purpose of the studies included in this thesis was not to explore gender differences. Previous studies have shown that CLBP and WP are more common in women than in men[28,55,67-69] and women are shown to be more severely affected by LBP with a poorer prognosis.[142] Thus only women were included in Studies I, II, and III.

5.1.3. Measurements (I, II, III, IV)

A comprehensive set of measurements was used in Studies I, II and III to evaluate different aspects of health representing all the components of the ICF.[19] Self-administrated questionnaires are commonly used for assessment of activity limitation and are recommended for monitoring disability in LBP.[143] However, self-reporting may suffer from the fact that some patients may under- or overestimate their limitations[144] and physical performance tests

are suggested to complement self-reporting.[144] Thus, semi-objective measures of body function were used in this thesis (I, II, III).

In Study III, including patients with FM and WP, overall health (FIQ-total) and physical capacity (6MWT) were primary outcomes and pain intensity (FIQ-pain) was regarded as the most important secondary outcome.

High pain intensity and disability ratings due to LBP have been shown to be reasons for consulting care.[145] Thus, in Study IV, outcome measurements for the severity of symptoms were used in accordance with previous recommendations.[18] Pain intensity (BRPP) was the primary outcome and activity limitation related to LBP (RMDQ) and risk for future disability (ÖMPSQ) was secondary outcomes.

5.1.4. Interventions (III, IV)

Two RTC studies were included in this thesis. In Study III, the absence of a control group with inactive patients, i.e. no treatment at all, might have been a disadvantage. A better design might have been a two-factor design to evaluate the effect of the pool exercise factor and the education factor. However, offering no treatment at all to the patients included in the study might result in a large dropout rate. In this study, the control group undertook the same education program as the exercise group. Since the control group also was an intervention it may be difficult to demonstrate the magnitude of the effect of the Exercise-Education program.

In Study IV, both groups received individualized treatment based on history and clinical examination. The experimental factor was time. The type or number of treatments did not differ between the two groups and the treatment consisted of advice with self-care instruction, and/or active exercise and/or manual therapy. In this study, 82% to 88% of patients received advice and self-care instruction (Table 7) which is similar to the results reported from a survey of physical therapists treating LBP where advice was given to 89% of patients.[146] When asking patients consulting PHC for their LBP, 81% sought advice and self-care instructions to manage LBP and resume normal activities.[147] Thus, the present study is in accordance with patient requests and clinical praxis.

5.1.5. Statistical analysis (I, II, III, IV)

In Study II, a cohort of patients with CLBP was followed over a period of two years. Within-group analysis was performed for changes between first assessment and the two-year follow-up. Results from within-group analysis were also presented for the Exercise-Education group and Education group which provide valuable information about changes in the groups (III). However, Study III was primarily designed to compare the effect of two different interventions. Therefore, the between-group analysis should be in focus when comparing the effect of the two different treatments (III, IV).

In Study IV, duration of symptoms at baseline was shown to be shorter in the EA compared to CG (Table 6). This could theoretically influence results, whereby the time factor is important in the process of developing chronic pain and disability. However, duration of symptoms was well within the inclusion criteria of 3 to 12 weeks for both groups. Furthermore, covariance analysis adjusting for differences in symptom duration showed that the results remained statistically significant.

To assess predictors for activity and participation at the two-year follow-up multiple linear and logistic regression were used. (II) Predictors evaluated in previous publications were used together with new variables not previously assessed in this context. Thus, a large number of variables were included in the analysis. There were different possible strategies to evaluate which variables should remain in the final statistical model. The two major strategies were either to put in all variables in a multiple forward stepwise regression or to select some

variables to be entered in the multiple forward stepwise regression. The choice, in Study II, was to first assess how each variable correlated to the two dependent variables. Those independent variables that were statistically correlated to the dependent variable were entered into a multiple forward stepwise regression where the computer calculated the variables that should remain in the final model.

The nomograms (Figure 2a and 2b, Study II) present a mathematical model derived from data where the range for 6MWT was 310-741 meters. Thus, the lines below 300 meters should be interpreted with caution.

Changes within the CLBP group over two years were statistically significant but clinically small (II). The RMDQ decreased by two points in this study ($p<0.0001$) (Table 2, Study II). Minimal clinical detectable change in the RMDQ is considered to be 2 to 3 points.[18] Others have suggested a change of 4 to 5 points to be of clinical value.[148] Thus, the statistically significant change in RMDQ during a two-year period is probably not a clinically significant change, which should be considered when interpreting results.

5.2. The prevalence and characteristics for widespread pain in patients with chronic low back pain (I)

5.2.1. WP in patients with CLBP

In accordance with the results of two studies from secondary care,[68,69] 28% of women consulting PHC for CLBP fulfilled the ACR's 1990 criteria for WP at the first assessment. At the two-year follow-up 29% of the women fulfilled the WP criteria.

The distribution of pain was a criterion for the patients with CLBP to be categorised into either localized CLBP or CLBP with simultaneous WP. CLBP is suggested to reflect nociception because of structural abnormalities in the lumbar spine due to injuries and degenerative changes or a dysmodulation of central pain processes or both.[149] WP is suggested to be primarily of a central pain process origin and associated with impaired physical and mental body functions, activity limitations and participation restrictions.[71-73] CLBP and WP are suggested to be overlapping conditions where presence of WP in patients with CLBP might reflect a more complex process involving nervous system processing of sensory information merely representing the upper end of a continuum. Increased pain sensitivity is associated with WP and FM.[3] The group with CLBP+WP showed mean and median values ≥11 TP, which indicates that several participants might fulfil the ACR's criteria for FM, associated with even more severe signs and symptoms.[3] The mean and median values for the number of TPs in the CLBP group was 7.5, 7.0, respectively (Table 2, Study I). This is a higher number of TPs compared to the general population indicating that women with CLBP may be more sensitive to pain than people in general.[70]

5.2.2. Impairment and disability when WP is present in patients with CLBP

Women with CLBP with simultaneous WP showed significantly more severe impairments in body functions compared to the women with localized CLBP. The mean difference for the performance in the walk test (6MWT) between these groups was 63 meters ($p<0.0001$). The mean distance for women with CLBP +WP is concordant with studies of similarly aged female patients with FM.[71,150] Sustained hand grip strength was negatively influenced by WP which is concordant with a previous study.[71]

Chronic pain is reported to be associated with distress in some individuals but it is argued that this is not the rule.[15] Scores of 8 or more in the HADS-A and HADS-D are described as associated with clinical anxiety or depression.[118,119] Women with CLBP only or CLBP with

simultaneous WP did not fulfill these criteria indicating no signs of clinical anxiety or depression at group level (Table 2, Study I).

More severe activity limitations were shown when WP was present. The CLBP+WP group reported more severe activity limitation related to their LBP (RMDQ) compared to the CLBP group and the difference of three points in the sum score could be clinically important as previously suggested.[18,148] The RMDQ median score values for the CLBP and CLBP+WP group was 7 and 10, respectively (Table 2, Study I) A cut-off point of 14 of a maximum of 24 has previously been reported as associated with poor outcome.[148] Twelve (32%) women reported a sum score of 14 or more in the CLBP+WP group. This is twice as high compared to the CLBP group (16%).

More severe participation restrictions were found in the CLBP+WP group. Work ability was dichotomized into work ability or not. (I, II) While there is no definition of work ability the category work disability required the patients to be on 100% sick-leave or disability pension leaving patients with only some ability to work in the work ability group. Work ability was significantly lower in the group with CLBP with simultaneous WP compared to group with CLBP only (p=0.032). However, 65% of the patients with simultaneous WP were available for work.

Environmental factors were registered in terms of private social support. Women with CLBP with simultaneous WP reported significantly more negative impact on private social support (MOS-SSS). The MOS-SSS 4-item scale comprises four questions dealing with emotional support, material aid or assistance, expressions of love and someone to do enjoyable things with[122] Emotional support has a positive impact for elderly patients with CLBP[151] but the knowledge about how CLBP or WP influence private social support or vice versa is limited.[151]

Physical dimensions of self-reported health-related quality of life appear to be negatively influenced by WP in women with CLBP (Table 2, Study I). This is supported by the fact that women with WP showed constantly lower scores in body functions such as more severe pain, lower performance in physical capacity test and more severe activity limitation (Table 2, Study I). No difference was found for mental health dimensions between women with CLBP with or without simultaneous WP.

More severe clinical stress symptoms (SCI-93) were found in the CLBP+WP group compared to CLBP only (Table 2, Study I). On a group level mean and median values for both groups were within the range according to mild stress (26-50p)[152] but the mean and median values were lower than previously reported for women with FM.[153]

The above findings illuminate the difficulties in daily life that patients with CLBP with simultaneous WP may describe. Therefore it should be important to evaluate the prevalence of WP in patients with CLBP.

5.3. Prognostic factors for activity and work status in patients with CLBP (II)

5.3.1. Self-reported activity limitation

The performance in a walk test (6MWT) was shown to be of good prognostic value for activity limitation (RMDQ) after two years (Table 3, Study II). Body function is usually assessed by physical measures such as spinal motion, muscle strength, and palpation. In patients with LBP, physical measures assessed at the initial visit to health care is of limited prognostic value for long-term pain and disability but the prognostic value are improved when assessed 4 weeks after initial assessment.[54,59] However, clinical guidelines for patients with CLBP summarize that physical measures have poor prognostic value for later disability.[6] The

6MWT was seen to provide valuable information for later activity limitation (RMDQ) and should complement the clinical assessment of patients with CLBP.

In patients with CLBP, decreased pain sensitivity (PPT) correlates with disability.[68] However, PPT was not identified as having prognostic value for self-reported activity limitation (RMDQ) at the two-year follow-up.

Higher scores of the ÖMPSQ, indicating higher risk for future disability, independently predicted more severe activity limitation (RMDQ) two years later. The ÖMPSQ has been developed for acute and subacute LBP and previously shown to predict future disability.[39,105] This study showed that the ÖMPSQ also can predict activity limitation (RMDQ) in patients with CLBP.

More severe clinical stress symptoms, i.e. higher scores of the SCI-93, could independently predict more severe activity limitation (RMDQ) two years later. Signs and symptoms in patients with chronic pain might be associated with prolonged stress but measurement of clinical stress symptoms is not standard in the clinical assessment of patients with CLBP. Therefore, the SCI-93 could provide valuable information for predicting later activity limitation for these patients.

In Study II, the final model including the 6MWT, ÖMPSQ and SCI-93 explained 43% of the variance in activity limitation (RMDQ) at the two-year follow-up. (Table 3, Study II) This result is concordant with a literature review of different predictive models found to explain 28-51% of variance in persisting disability in LBP.[154]

5.3.2. Work ability

The 6MWT predicted work ability after two years. This is a new finding in patients with CLBP not described previously. The forward stepwise logistic regression analysis showed that for every 100 meters the patient walks at the first assessment the OR for work ability increases by 3.3 (95% CI 1.5-7.4) (Table 4, Study II). Walking capacity is reported to predict work disability in patients with subacute LBP, showing that perceived reduced long-distance walking ability predicted no return to work at the one-year follow-up (OR 2.6, 95% CI 1.3-5.4).[155] The performance in the 6MWT can involve several components such as pain, fear of pain, musculoskeletal dysfunctions and aerobic capacity. It is difficult to say which contributed most to the performance in patients with CLBP, but more knowledge is warranted, as the 6MWT appears to provide useful information on future work ability.

It has been suggested that prospective studies are necessary to determine whether pain sensitivity (PPT) can predict future disability in CLBP.[68] However, PPT was not identified as having prognostic value for work ability in the study of patients with CLBP. (Table 4, Study II).

Lower scores for depression (HADS-D) were identified as significant predictors for work ability at the two-year follow-up (Table 4, Study II), which is concordant to a previous study.[58]

Work ability was dichotomized into work ability or not (I, II). The category work disability required the patients to be on 100% sick-leave or disability pension leaving patients with some ability to work in the work ability group as described above. Earlier work ability predicted future work ability which is concordant with a previous report.[58]

Probabilities of work ability after two years could be assessed by calculations based on the 6MWT, HADS-D and earlier work ability by constructing a nomogram. (Figure 2a+2b, Study II) The nomogram may provide useful information when assessing an individual's probability of future work ability and treatment planning.

5.4. Education and physical treatment for patients with fibromyalgia or widespread pain (III)

5.4.1. Benefits from physical exercise

The 20-week supervised pool exercise program combined with education improved health status (FIQ-total) compared to education in patients with WP and FM, which is concordant with a literature review.[75] The effect size for the improvement assessed by FIQ-total was considered small (0.32) for the Exercise-Education group compared to the control group when analyzed by intention-to-treat. However, the effect size increased to 0.45 in the per-protocol analysis, where only patients with at least 60% attendance were included. These effect sizes for improvement are comparable to those found in pharmacological and non-pharmacological treatment studies conducted in PHC.[156]

The improvement in FIQ-total for the Exercise-Education group was supported by improvement in other health-related aspects compared to the education only group. The intention-to-treat analysis showed greater reduction of perceived pain (FIQ-pain) in the Exercise-Education group compared to the Education group (p=0.018). In explorative outcomes, the MFI-20-reduced motivation improved more in the Exercise-Education group compared to the controls and the significantly enhanced activity-related relaxation among exercisers might also contribute to improved health status.

The 6MWT, primary outcome at body function level, did not significantly improve in the Exercise-Education group compared to the education group in the intention-to-treat analysis. One reason for this poor improvement might be the good baseline walking capacity of the patients (> 500 m, SD > 70 m), which possibly resulted in ceiling effects for several patients. It is probable that patients today are more physically active than in previous years, as the mean baseline walking distance in the present study appears to be higher than in a previous study (467 m) published in 2000.[80] An increased public awareness of the benefits of exercise may have contributed to a higher activity level. However, in the per protocol analysis the difference between the groups was significant (0.013), indicating that some attendance in the exercise program was needed to obtain improvements in physical capacity.

The pool exercise program lasted for 20-weeks, which is a common training period when studying effects of physical exercise for patients with WP and FM.[75] The pool exercises were planned to permit individual adjustments to pain and fatigue and to enable individual progress. The perceived exertion (BRPE) ranged from “very light” to “light” during flexibility, co-ordination and stretching exercises, while it was “somewhat hard” during aerobic exercise,[114] considering the program to be of low-to moderate-intensity. The patients exercised in the pool once a week and additional sessions per week might have improved the effects of exercise.

Supervised aerobic exercise recommended for patients with WP and FM should be of low or moderate intensity with a gradual progression avoiding worsening of symptoms.[75] However, physical exercise induces exacerbation in signs and symptoms for some patients while other appears to manage it. A high level of stress or distress have been previously shown to impact the ability to perform physical exercise.[157] Therefore, the second purpose of Study III was to investigate the influence of clinical stress symptoms, pain, distress and activity limitation on changes in the primary outcomes. There was no significant heterogeneity found for change in the FIQ-total or 6MWT. The non-significant finding for change in the 6MWT might be related to the small improvements.

In the separate analysis about change within the subgroups characterized by lower ratings of stress, pain and distress performed, it was found that the patients with milder distress (HADS-D, < 8), lower level of pain (FIQ-Pain, < 70) and less clinical stress symptoms (SCI-93, < 78) improved more by the Exercise-Education program than education only (Figure 5a

and 5b). These findings are in line with a previous study showing that distress was associated with poor physical activity.[157]

5.4.2. Why education?

The Exercise-Education group improved more in health status compared to the group undertaking the same education program (III). For patients with chronic pain, knowledge of contributors and consequences of chronic pain is reported to be essential for self-management.[141] The 6-session education program was based on active participation including self-management strategies with the purpose of enhancing self-efficacy for the management of signs and symptoms (Appendix 9.2). There are different techniques to enhance self-efficacy one of which is to provide strategies for influencing behavior through dialogue between the patient and the therapist.[158] Another is to perform a desired activity e.g. to experience an improved ability to perform a specific physical activity or movement.[158] Supervised physical exercise provides the patient with an opportunity to practice movements and to understand how to adjust the exercises to individual capacity or limitations and how to increase them progressively when possible. If the aim is to improve health and body functions, group education alone might not be sufficient. The combination of education and exercise might result in a greater improvement than the individual treatments, which was implicated in Study III. However, to confirm this, a new intervention study based on a two factor design is needed.

5.5. Early access to physical therapy treatment in primary health care (IV)

5.5.1. Self-referral to a physical therapist

Study IV was conducted three years after self-referral to a physical therapist was introduced to the study area. About 60% of the participants included consulted a physical therapist without a physician's referral (Table 6). This is more than in previous studies.[82,159,160] However, most studies investigating the prevalence of self-referral (direct access) to a physical therapist are observational [82,159,160] making it difficult to compare results with the present study (IV). In the Netherlands, an investigation of self-referral utilization one year after introduction showed that 28% of the patients consulted a physical therapist directly.[82] Another study reported that 40% of the patients were self-referred, where 22% referred themselves and 18% were self-referred by their physician's suggestion.[160]

Investigations of demographics and clinical profiles for patients using self-referral, have shown that they are younger and more highly educated compared to patients who are first seen by a physician.[82] Moreover, patients with acute non-specific musculoskeletal conditions,[82,160] recurrent conditions or previous physical therapy are more likely to refer themselves.[82] Other have suggested that patients who refer themselves are more compliant to attendance and have greater beliefs in the ability to improve their condition[159] but this could not be confirmed in another study.[160]

In Study IV, it was hypothesized that patients who referred themselves may have had less severe symptoms. Since study participants were a mixture of self-referred and referred patients this might be a confounding factor. However, when adjusting for baseline differences of gender, duration of symptoms and self-referral or not, the results of clinical improvement at the 6-month follow-up remained statistically significant.

5.5.2. Advanced access models

In Study IV, a same-day appointment scheduling model to a physical therapist was applied to investigate the effect of early examination and individualized treatment compared to a waiting list of four weeks for patients with subacute LBP.

Waits and delays to a physical therapist within PHC are not rare. To achieve accessibility to healthcare, theories, detailed strategies and models are provided by Murray et al.[96] There are three common models briefly described here; first the traditional model where the care-provider's schedule is filled in advance which keeps the waiting list constant. Patients with urgent conditions are squeezed in to an already saturated schedule. The second model aims to improve accessibility for urgent cases by keeping some appointment slots open daily ("Carved-out model"). The third type of access model is the so-called advanced access model i.e. a same-day appointment model. This model does not distinguish between appointments for patients considered having urgent or non-urgent conditions. By knowledge of the predicted demand to the care-provider or department, enough appointments are available each day to offer patients an appointment the same day of request irrespective of reason. However, this model requires that the supply and demand of care within the department are in balance. Further, maintaining the balance between supply and demand requires the care-provider to " do all of today's work today." [96] Another powerful strategy to maintain a balance between supply and demand is to optimize the care team and offer appointments to the most appropriate care provider within the team.[98] A self-referral system to a physical therapist is compatible with this model. Moreover, a same-day appointment model corresponds to recommendations for patients with LBP by offering an early clinical examination, identification of risk factors and early intervention if needed as was available to the EA group (IV).[7] In Study IV, the early access model could be introduced by reorganization without additional resources.

5.5.3. Early intervention and the importance of timing

The EA group, showed significantly greater reduction of perceived pain (BRPP) at the 6-month follow-up compared to the control group (Table 8). At baseline, the median value for BRPP was 5 for both groups corresponding to "strong" pain (Table 6). At discharge from treatment, the median value for BRPP decreased by approximately 3 points indicating "weak" pain in both groups, and no significant difference was found between groups. The pain intensity remained "weak" in the EA group while pain increased to "moderate" in the CG group at the 6-month follow-up, indicating that early access to physical therapy treatment appears to improve symptoms for patients with subacute LBP. This is in line with previous studies of patients with acute LBP, showing that early active intervention by a physical therapist compared with a watchful waiting approach improves long-term overall health and psychosocial factors.[103] In an occupational setting, early intervention by a physical therapist showed positive effects on work disability and less health care utilization.[102]

There were no differences found between the two groups in primary (BRPP) or secondary outcomes (RMDQ) at discharge from treatment (Table 8). The short-term effect may be dependent on the intervention, thus both groups received the same individualized intervention, and experienced the same short-term results (Table 7). However, a more positive long-term effect on perceived pain was found in the EA group compared to the CG.

High pain intensity and disability are associated with patients seeking care because of LBP.[145] It seems that when consulting PHC, patients with LBP seek a clinical examination, advice and self-care instructions for the management of LBP to resume normal daily activities.[147] Therefore, one theory could be that patients seek medical care when motivation reaches a threshold level. By providing early access to a clinical examination and reassurance of no serious pathology, initiating intervention when motivation is high may make patients

more receptive to advice on self-care, preventing fear-avoidance behaviour. If a motivated patient applies self-care instructions persistently, it might lead to better long-term results compared to initiating intervention later when motivation might be lower.

6. Summary and conclusions

Important factors for influencing functioning and health in patients with LBP and WP are early assessment of prognosis and efficient management of these patients within PHC.

This thesis showed that early access to a physical therapist in PHC for patients with subacute LBP indicated greater improvement in perceived pain at the 6-month follow-up compared to later access. Other studies of patients with acute LBP have shown that early active intervention by a physical therapist compared with a watchful waiting approach improves long-term overall health and psychosocial factors.[103] In an occupational setting, early intervention by a physical therapist has shown positive effects on work disability and health care utilization.[102] Despite a high probability that patients with acute/subacute LBP will recover spontaneously,[1,25,41] improvements in perceived pain, psychosocial factors, work status and overall health appears to be positively impacted by the timing to examination and active intervention. Thus, these findings support an early active intervention and challenge a watchful waiting approach for patients with acute/subacute LBP. Therefore, an early physical therapist access model should be considered for the management of patients with LBP in PHC. To determine whether an early access, physical therapist model can influence other health-related aspects or maintain work ability further studies are needed.

Another important finding was that WP was present in almost one third of the women with CLBP consulting primary health care. CLBP with or without WP are suggested to be overlapping conditions where the difference in symptoms is caused by central pain processes modulating symptom experience. Having CLBP with or without WP might reflect different ends of a continuum where the presence of WP might indicate a more severe dysmodulation in central pain processes.[15] WP was found to negatively impact body function, activity, participation, environmental factors in terms of private social support, health-related quality of life and other health-related aspects. It might be possible to prevent worsening in signs and symptoms for patients with CLBP by offering early access to clinical examination and treatment. At this early examination, self-reported pain distribution is a simple method for identifying patients with CLBP with simultaneous WP in need of a more individualized intervention.

For patients with WP or FM, supervised aerobic exercise[75] and educational programs including self-management strategies are recommended.[76] Study III provides evidence that a supervised pool exercise program combined with an educational program improved health status and other health-related aspects in patients with WP or FM. The effect on physical capacity and leisure time physical activity appears to be dependent on at least 60% active attendance of the 20-week pool exercise program. Therefore, a supervised pool exercise program combined with education for the self-management of symptoms should be considered as a treatment alternative for these patient groups.

In this thesis one aim was to identify prognostic factors for future activity and work status in women with CLBP. A walk test (6MWT), a measure of body function, predicted both activity limitation and work ability at the two-year follow-up and should be considered as a complement to the clinical examination of patients with CLBP. Lower performance in a walk test (6MWT), higher risk scores for future disability (ÖMPSQ) and more severe clinical stress symptoms (SCI-93) predicted activity limitation (RMDQ) two years later. The model including these three predictors explained 43% of the variance in self-reported activity limitation (RMDQ) after two years which is comparable to a previous review of predicting models for activity limitations in patients with LBP.[154]

For future work ability, higher performance in a walk test (6MWT), lower level of distress (HADS-D) and earlier work ability were identified as predictors. Probability of work ability

two years later could be assessed by calculations based on these three predictors. This nomogram might be useful for health care providers, which have the responsibility of managing and estimating an individual's work ability.

Concluding remarks:

- Widespread pain was present in 28% of women with chronic low back pain consulting primary health care. At the two-year follow-up 29% of the women fulfilled the widespread pain criteria.
- Women with chronic low back pain with simultaneous widespread pain showed more severe impairments in body functions, more severe activity limitations and participation restrictions. Environmental factors, health-related quality of life and other health related aspects were also negatively impacted compared to women with localized chronic low back pain.
- The six-minute walk test (6MWT) predicted both future activity limitation and work ability and should be considered as a complement to the clinical assessment of women with chronic low back pain.
- The six-minute walk test (6MWT), risk scores for future disability (ÖMPSQ) and stress symptoms (SCI-93) predicted activity limitation at the two-year follow-up.
- Higher performance in a walk test (6MWT), lower level of distress (HADS-D) and earlier work ability predicted future work ability.
- A supervised pool exercise program combined with an education program was found to improve health status in women with widespread pain or fibromyalgia and should be considered as a treatment alternative for these patient groups.
- Early access to examination and individualized treatment by a physical therapist in primary health care resulted in greater improvement in perceived pain at the 6-month follow-up compared to later access for patients with subacute low back pain.

7. Summary in Swedish

Ländryggssmärta och generaliserad smärta är vanligt förekommande och innebär stora samhällskostnader som till största del beror på sjukskrivning och produktionsbortfall. God tillgänglighet till sjukvård för undersökning, behandling samt tidig identifiering av prognostiska faktorer anses ha betydelse för påverkan på förlopp av smärta och funktionsnedsättning hos patienter med ländryggssmärta och generaliserad smärta men mer kunskap efterfrågas. Syftet med avhandlingen var att få mer kunskap om: a) prevalens och vad som karaktäriserar generaliserad smärta hos patienter med långvarig ländryggssmärta, b) prognostiska faktorer för aktivitet och arbetsförmåga, c) effekten av funktionsinriktad behandling på hälsostatus och kroppsfunktioner för patienter med generaliserad smärta eller fibromyalgi, samt d) effekten av tidig tillgänglighet till klinisk undersökning och individuell behandling av sjukgymnast inom primärvård för patienter med subakut ländryggssmärta.

Studie I

Syftet med studien var att undersöka prevalens av generaliserad smärta enligt American College of Rheumatologys (ACR, 1990) kriterier hos kvinnor som sökt primärvård för långvarig ländryggssmärta, samt jämföra gruppen kvinnor med lokal långvarig ländryggssmärta med gruppen som samtidigt uppfyller kriterier för generaliserad smärta utifrån kroppsfunktion, aktivitet, delaktighet, omgivningsfaktorer i form av privat socialt stöd, självskattad hälsorelaterad livskvalitet och andra hälsorelaterade aspekter.

I en tvärsnittsstudie inkluderades 130 kvinnor med långvarig ländryggssmärta. Tjugoåtta procent av kvinnorna med långvarig ländryggssmärta uppfyllde ACRs kriterier för generaliserad smärta. Patienter med långvarig ländryggsmärta som samtidigt uppfyllde kriterier för generaliserad smärta visade signifikant mer nedsatt kroppsfunktion, större aktivitet- och delaktighetsnedsättning ($p<0.05$). Dessutom visade gruppen med samtidig generaliserad smärta mindre privat socialt stöd, lägre hälsorelaterad livskvalitet samt negativ påverkan på andra hälsorelaterade aspekter jämfört med gruppen patienter med lokal långvarig ländryggssmärta ($p<0.05$).

Studie II

I en prospektiv longitudinell studie följdes under två år en kohort kvinnliga patienter med långvarig ländryggssmärta som sökt primärvård. Syftet var att undersöka förändring av kroppsfunktion, aktivitet, delaktighet, omgivningsfaktorer i form av privat socialt stöd, hälsorelaterad livskvalitet samt andra hälsorelaterade aspekter. Prognostiska faktorer identifierades för aktivitetsnedsättning och arbetsförmåga vid en uppföljning efter två år. Nittiofem procent (123/130) av patienterna som inkluderades i tvärsnittsstudien (Studie I) kunde följas upp efter två år. Prognostiska faktorer för en senare aktivitetsnedsättning (Roland Morris Disability Questionnaire (RMDQ)) och arbetsförmåga (ja/nej) analyserades med multivariat regressions analys. Tjugoåtta procent (n=34) av patienterna uppfyllde ACRs kriterier för generaliserad smärta vid första undersökningstillfället och 29 % (n=36) vid uppföljning efter två år. Sex-minuters gångtest (6MWT) predicerade både aktivitetsnedsättning och arbetsförmåga efter två år. Andra faktorer som predicerade aktivitetsnedsättning vid två års uppföljning var, Örebro musculoskeletal pain screening questionnaire (ÖMPSQ), ett screeningsformulär som indikerar risk för långvarig funktionsnedsättning, samt kliniska stress symtom (Stress and Crisis Inventory-93). Prognostiska faktorer för arbetsförmåga två år senare var: högre kapacitet i ett gångtest (6MWT), lägre grad av depression (Hospital Anxiety and Depression Scale (HADS-D)) samt arbetsförmåga vid första undersökningstillfället. Dessa tre prediktorer användes för att

konstruera ett nomogram som kan användas för att uppskatta sannolikheten för patientens arbetsförmåga två år senare.

Studie III
Syftet med studien var att undersöka effekten av fysisk träning i varmt vatten för kvinnor med långvarig generaliserad smärta eller fibromyalgi samt undersöka vilka faktorer som kan påverka effekten av fysisk träning. Etthundratrettiofyra kvinnor med fibromyalgi och 32 med generaliserad smärta randomiserades till 1) fysisk träning i varmt vatten vid 20 träningstillfällen i kombination med ett undervisningsprogram som gavs vid 6 tillfällen, eller till 2) en kontrollgrupp som fick samma undervisningsprogram. Primärt utfallsmått var Fibromyalgia Impact Questionnaire (FIQ) totalsumma och 6-minuters gångtest (6MWT). FIQ förbättrades i interventionsgruppen ($p=0.04$) med effektstorlek 0.32. Patienter som hade deltagit minst 60 % i interventionsgruppen förbättrades i FIQ (effektstorlek 0.44), 6MWT (effektstorlek 0.43) och FIQ-smärtintensitet (effektstorlek 0.69) jämfört med kontrollgruppen ($p<0.05$). Fysisk träning i varmt vatten i kombination med ett undervisningsprogram visade signifikant förbättring av hälsostatus för patienter med generaliserad smärta eller fibromyalgi jämfört med kontrollgruppen som enbart fick undervisningsprogrammet. Patienter med lindrigare symtom förbättrades i större utsträckning av denna behandling.

Studie IV
Syftet med studien var att undersöka effekten av tidig tillgänglighet till klinisk undersökning och individuell behandling av sjukgymnast i primärvård jämfört med samma åtgärd initierad efter 4 veckors väntan. Sextio patienter med subakut ländryggssmärta randomiserades till 1) tidig tillgänglighet, inom två dagar, till undersökning och individuell behandling av sjukgymnast (n=32), eller 2) till en kontrollgrupp (n=28) som fick vänta 4 veckor för samma åtgärd. Primärt utfallsmått var smärtintensitet (Borg category scale for ratings of perceived pain). Sekundära utfallsmått var ÖMPSQ, ett screeningsformulär som indikerar risk för långvarig funktionsnedsättning, självskattad funktionsnedsättning på grund av ländryggsmärta (RMDQ), sjukskrivning, antal besök i sjukvården, samt vilken vårdåtgärd patienten fick. Det fanns ingen skillnad mellan grupperna efter avslutad behandlingsperiod. Vid uppföljning efter 6 månader visade gruppen som fått tidigt insatt behandling signifikant minskad smärta jämfört med kontrollgruppen ($p=0.025$), vilket indikerar att tidig tillgänglighet till undersökning och individuell behandling av sjukgymnast ger större förbättring av upplevd smärtintensitet efter 6 månader jämför med om patienten får vänta.

Konklusion:
Förekomst av samtidig generaliserad smärta hos kvinnor med långvarig ländryggssmärta har negativ påverkan på kroppsfunktion, aktivitet och delaktighet, omgivningsfaktorer, i form av mindre privat social stöd, hälsorelaterad livskvalitet och andra hälsorelaterade aspekter. Därför bör förekomst av generaliserad smärta undersökas hos patienter med långvarig ländryggssmärta.

Lägre kapacitet i ett gångtest (6MWT), högre riskpoäng för långvarig funktionsnedsättning (ÖMPSQ), samt högre grad av kliniska stressymtom (SCI-93) predicerade aktivitetsnedsättning två år senare hos kvinnor med långvarig ländryggssmärta.

Större kapacitet i ett gångtest (6MWT), tidigare arbetsförmåga och mindre grad av depression predicerade arbetsförmåga efter två år. Sannolikheten för arbetsförmåga efter två år kunde undersökas genom beräkning av dessa tre variabler (Ett nomogram).

Ett undervisningsprogram i kombination med fysisk träning i varmt vatten visade förbättring av hälsostatus hos kvinnor med generaliserad smärta eller fibromyalgi och bör erbjudas som behandlingsalternativ för dessa grupper av patienter.

Tidig tillgänglighet till undersökning och individuell behandling av sjukgymnast i primärvård för patienter med subakut ländryggssmärta visade kliniska förbättringar efter 6 månader. Patienter med ländryggssmärta som söker primärvård bör därför erbjudas en tidig tillgänglighet till sjukgymnast.

8. Acknowledgements

I wish to express my warm and sincere gratitude to everyone who in various ways have contributed to making this thesis possible. I would like to thank:

Ronny Gunnarsson, my chief advisor, for inspiring me to begin my research and for providing invaluable support throughout my research education. His skills in explaining the world of statistics and scientific methodology and your positive attitude, for example, when saying, “I have a suggestion”, were always constructive in improving the study methodology, which has provided me with both challenges and new knowledge. Without his belief in me, this thesis would not have been possible.

Kaisa Mannerkorpi, my co-advisor for generously sharing her wide range of knowledge of widespread pain, fibromyalgia and research with me. Her enthusiasm toward research to increase knowledge of these patient groups has been invaluable to me. I am so grateful that you involved me in the “GAU” studies, which have become a part of this thesis.

Margareta Möller, my co-advisor for encouragement, generous support and excellent suggestions.

The Department of Public Health and Community Medicine, Primary Health Care Unit, for accepting me as a PhD student and for professional support during my training.

Helen Andersson, my colleague and former boss, for her encouragement, positive attitude toward my research and continuous support.

Lena Thorselius, my friend, colleague and ”open access” partner, for inspiring professional and philosophical discussions and visions.

Anneli Henriksson, for entering data and for invaluable help during the entire study period.

My colleagues at the physiotherapy unit, Ängabo health care center, for help with data collection and for maintaining and developing the “open access” model.

Anna Ericsson, my fellow research student, for valuable discussions on scientific research.

Elisabeth Enhörning, for helping me examine patients and for stimulating talks.

Rebecca Kantola, in Uddevalla, for all her invaluable help.

Rosenhäll physiotherapy unit, primary health care, Uddevalla, for interest in my research and a positive attitude even when I occupied your examination room for assessing patients.

Grethe Jonasson, for generously taking time to read my manuscripts and for constructive criticism, excellent advice and feedback.

Gun Rembeck, for joyful and creative discussions about research.

Annika Billhult, my colleague, “in the next room”, for patience in answering my questions at all times and for an exciting exchange of ideas.

Mark Rosenfeld, for his greatly appreciated help with English language editing. His accessibility during the revision process was of utmost importance.

Ermin Catic and Nihad Keserovic, my computer saviours …for expert and sure IT support whenever needed and for always reassuring me that everything would be fine.

Nils-Gunnar Pehrsson, for his statistical guidance.

Göran Jutengren, for his skilful and kind support in help with methodological problems.

Aris Seferiadis, for valuable statistical discussions concerning multiple regression analysis and for inspiring scientific chats.

Ängabo primary health care center, for support and a positive attitude in achieving an advanced access model by optimizing the team.

Everyone at the research and development unit of Södra Älvsborg for their help and support.

Björn Nilsson, co-author, for helping and advising me in the early stage of my work.

Maudh Arndorw, co-author, for valuable discussions.

The GAU-study group, Mona Lind, Eva Melin, Anne Fredrikson, Marianne Hjerpe, Åsa Holmestrand, Mattias Hjelm, Elisabeth Enhörning and Anne-Kristine Neuman.

All patients, for their time and participation in the studies.

All my friends, for always giving me new energy by listening and laughing. Thank you for putting up with me during these years!

My wonderful parents Gun and Ebbe for always believing in me. Thanks for being there whenever I needed you. Without your generous involvement with the family, I would not have been able to write this thesis. There are no words for how much you mean to me!

Last but most of all my beloved family. Anders, my husband, thank you for your endless patience, support and love throughout the years of my PhD studies and research. Thank you Sara for just being you and your ”Don’t worry be happy” approach. Nils, thank you for taking so much responsibility during these years and Per, thank you for your patience when I was busy doing other things and my thoughts were elsewhere.

Financial support for this thesis was obtained from the research and development council of Södra Älvsborg, Västra Götaland Region, Sweden. The Health & Medical Care Committee of the Regional Executive Board, Region Västra Götaland, Sweden.

9. Appendix

The following appendix describes the intervention, in Study III.

9.1. Pool exercise (III)

The pool exercise program

The pool exercise program was designed for patients with WP or FM. Each session lasted for 45 minutes in temperate (33°C) water. The aim was to enable the participants (*i*) to perform movements with awareness and to find their own rhythm and harmony when exercising and to learn the limits and potential of their bodies, (*ii*) to understand how to modify the exercises individually, (*iii*) to be confident about their ability to choose optimal resistance and control pain while exercising, (*iv*) to increase their motivation for physical activity, and (*v*) to improve function. At the start of each pool group, the physiotherapist demonstrated all the movements at a slow and smooth pace, emphasizing that everyone should adjust the exercise individually with respect to their threshold of pain and fatigue. When the participants had learned the movements and performed them correctly, the pace was increased for those who were able to accept it. Individual instructions were given whenever needed. A floating device that provides stability, assistance and/or progression when exercising was used in different parts of the program.

Warming up

Walking or jogging forwards, backwards and to the side with increasing speed either paddling with the arms in order to achieve resistance, or smoothly stroking the arms in the water.

Two program sets of co-ordination and flexibility exercises

The participants were instructed to select the pace and resistance by positioning their hand during the movement with respect to their current threshold of pain.

- Arm movements combined with transferring weight from side to side while standing.
- Reciprocal shoulder flexion and extension with paddles combined with knee bending while standing.
- Bilateral elbow extension and flexion with the upper arms held towards the thorax.
- Bilateral shoulder internal and external rotation with the upper arms held towards the thorax.
- Swimming strokes with arms.
- Arm movements with bilateral elbow flexion and extension holding the floating device at the surface in front of the body with progression, for those who were able to manage this, pushing the floating device in the direction of the bottom and close to the body.
- Arm movements holding the floating device at the surface in front of the body while rotating from side to side.
- When standing, unilateral hip extension and flexion.
- Reciprocal diagonal movement with the hand touching the knee.

Two program sets of aerobic exercises

- Jogging and walking while sitting on a floating device, combined with arm movements.

Two program sets of body awareness and breathing exercise

- Performed when standing, combined with pelvic movements.

Stretching

- Stretching exercises for arm and leg muscles.

Relaxation

- Performed either standing and leaning against a wall or in a supine position. Floating devices such as tire tubes or neck collars were provided.

9.2. Education (III)

The education program

The education program consisted of 6 one-hour sessions, once a week, based on self-efficacy principles requiring active participation of the patients. The aim was to introduce strategies to cope with fibromyalgia symptoms and to encourage regular physical activity.

The topics were:

1. Symptoms and explanatory theories for long-lasting pain. The session started by listing the patients' symptoms on a flip chart, followed by a discussion of these symptoms. A short presentation of theories for long-lasting pain was given, followed by a discussion of the participants' own theories and beliefs. A short relaxation exercise was performed while seated.
2. Pain and pain alleviation. Physical activity and exercise. A short presentation of the local (gate theory) and central (central nervous system) levels of pain modulation and strategies for pain alleviation was given, followed by a discussion of the participants' experience. The participants were encouraged to use different techniques, including physical activity and relaxation. A contract for physical activity for the forthcoming week was written. A short relaxation exercise was performed while seated.
3. Stress, pain and depression. Feedback for physical activity during the past week was given and a new contract for activity for the forthcoming week was written. A short presentation of theories about stress was given, followed by the participants' own experience of what makes them stressed and how they prevent and alleviate stress. A short relaxation exercise was performed while seated.
4. Physical relaxation and body awareness. Feedback for physical activity during the past week was given and a new contract for activity for the forthcoming week was written. Continuation of discussion about stress. Methods for active and passive relaxation and body awareness were presented and practiced.
5. Lifestyle. Feedback for physical activity during the past week was given and a new contract for activity for the forthcoming week was written. Identification of possible causes of increases in pain and stress and opportunities to do something about them were discussed. The participants were asked to write down their own plans for changes, according to a model that was presented.
6. Lifestyle. Feedback for physical activity during the past week was given and a new contract for activity for the forthcoming week was written. Continuation of the topic introduced at session 5.

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11. Original publications

I. Nordeman Lena, Gunnarsson Ronny, Mannerkorpi Kaisa. Prevalence and characteristics of widespread pain in female primary health care patients with chronic low back pain. Submitted

II. Nordeman Lena, Gunnarsson Ronny, Mannerkorpi Kaisa. Prognostic factors for activity and work status in women with chronic low back pain consulting primary health care: a two-year prospective longitudinal cohort study. Submitted

III. Mannerkorpi Kaisa, Nordeman Lena, Ericsson Anna, Arndorw Maudh, and the GAU Study Group. Pool exercise for patients with fibromyalgia or chronic widespread pain: A randomized controlled trial and subgroup analyses. J Rehabil Med 2009;41:751-760

IV. Nordeman Lena, Nilsson Björn, Möller Margareta, Gunnarsson Ronny. Early access to physical therapy treatment for subacute low back pain in primary health care. A prospective randomized clinical trial. Clin J Pain 2006;22:505-511

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