

Biopsychosocial analyses of acute and chronic pain, especially in the spine

The effect of distress on pain intensity and disability

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-The effect of distress on pain intensity and disability-

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“Man is the measure of all things”

Protagoras

*To everybody who deals with pain relief in daily practice and deals carefully with patients’
experiences of pain*

ABSTRACT

The overall purpose was to assess factors that influence the experience of pain and disability due to acute low back pain (LBP) and chronic musculoskeletal pain (CMP). A further purpose was to outline the conceptual framework behind pain—with emphasis on the spine—and its management in primary healthcare.

Methods: In Studies **I-III**—cross-sectional design—174 patients on long-term sick leave due to CMP were referred by the Social Insurance Office for orthopaedic assessment and evaluation of their ability to work. Additional psychiatric evaluation was required for 83/174 patients. Study **I** investigated the association between excessive illness behaviour—measured by Waddell signs (WS)—and clinical findings, pain intensity, depressed mood, disability, and duration of sick leave. In Study **II**, the occurrence of somatic and mental health comorbidity was studied, and the assessment of ability to work was compared between patients who only underwent an orthopaedic evaluation and patients who underwent both orthopaedic and psychiatric evaluations. In Study **III** (71/83), scores for mood in the Beck Depression Inventory (BDI) were compared with diagnosis of depression made by a psychiatrist. Study **IV**, a cross-cultural validation study of 288 patients with CMP and 161 controls, tested different psychometric characteristics of the Swedish version of the DAPOS (Depression, Anxiety, and Positive Outlook Scale) through confirmatory factor analysis. Study **V**, a randomised clinical trial involving 109 patients with acute-onset LBP, was performed to evaluate compliance with the treatment advice “Stay active” or “Adjust activity”, and to assess the influence of distress on pain-related disability and physical activity during a 7-day follow-up.

Results: Study **I**: 27% of patients exhibited WS. Such patients exhibited distress and greater pain and longer sick leave than WS-negative patients. **II**: Neck pain was the main cause of disability, and patients with neck pain often suffered pain in more than two sites, and greater pain. 84% of all patients were able to return to work to different degrees. However, unrecognised psychiatric disorders (vs. somatic) were the main cause of inability to work in 69% of patients who underwent team evaluation. **III**: There was good agreement between the BDI scores and diagnosis of depression made by a psychiatrist. **IV**: The Swedish version of the DAPOS demonstrated good validity, and the three DAPOS constructs were equivalent with respect to sex. **V**: Pain-related disability decreased in all patients by the end of the follow-up. Patients with depressed mood who had been advised to “Adjust pain” exhibited worse pain-related disability over time. A tendency toward compliance with treatment advice was confirmed and patients advised to “Stay active” were more physically active (greater step count), with the exception of those with fear of movement.

Conclusions: Distress is associated with increased pain intensity and disability/inability to work in acute LBP and CMP. Undiagnosed psychiatric disorders are common in patients on longterm sick leave due to CMP. The early identification of distress, and giving the advice to “Stay active” early during care, may prevent pain-related disability in patients with acute severe LBP.

Keywords: pain analyses, chronic musculoskeletal pain, pain intensity, disability, acute low back pain, psychological distress, fear of movement, ability to work, mental health comorbidity, patient’s compliance

LIST OF PAPERS

- I. Illness behaviour in patients on long-term sick leave due to chronic musculoskeletal pain. Olaya-Contreras P and Styf J. *Acta Orthop*. 2009 Jun;80(3):380-5.
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- III. Comparison between the Beck Depression Inventory and psychiatric evaluation of distress in patients on long-term sick leave due to chronic musculoskeletal pain. Olaya-Contreras P, Persson T, and Styf J. *J Multidiscip Healthc*. 2010 Sep 1;3:161-7.
- IV. Cross-validation of the Depression, Anxiety, and Positive Outlook Scale (DAPOS) for clinical use. Olaya-Contreras P, Styf J, Lundberg M, and Jansson B. In press: *Clin J Pain*, 2011 May;27(4):330-7.
- V. Compliance and the effect on pain-related disability of two treatment advices in patients with acute severe low back pain: a randomised controlled trial. Olaya-Contreras P, Styf J, Kaigle Holm A, Olsson M, Hansson T. (submitted).

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ABBREVIATIONS

| | |
|-------|-----------------------------------------------|
| BDI | Beck Depression Inventory |
| CFA | Confirmatory Factor Analysis |
| CMP | Chronic musculoskeletal pain |
| DAPOS | Depression Anxiety and Positive Outlook Scale |
| DRI | Disability Rating Index |
| LBP | Low back pain |
| NRS | Numerical Graphic Rating Scale |
| RCT | Randomised controlled trial |
| TSK | Tampa Scale of Kinesiophobia |
| VRS | Verbal Rating Scale |
| VAS | Visual Analogue Scale |
| WS | Waddell signs |

DEFINITIONS IN SHORT

| | |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Construct | A hypothetical concept/domain, not directly observable and which can thus only be measured indirectly through observed scores ¹ |
| External validity | The degree to which the results of a study can be generalised to persons or settings outside the experimental situation ² |
| Internal validity | The degree to which the relationship between the independent and dependent variables is free from the effects of systematic errors or bias ² |
| Invariance | The equivalence of a construct from a single measuring instrument across particular groups ¹ |
| Nociception | The neural processes of encoding and processing noxious stimuli ³ |
| Pain | An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage ³ |
| Precision | The exactness of a measure. The degree of precision in a measurement is a function of the sensitivity of the measurement instrument ⁴ |
| Predictive factor | A condition or finding that can be used to help predict whether a person will respond to a specific treatment. 'Predictive factor' may also describe something that increases a person's risk of developing a condition or disease ² |
| Prognostic factor | A condition or a characteristic of a patient that can be used to estimate the probability of recovery from a disease or the chance of the disease recurring ² |
| Reliability | The degree to which the scores in a particular sample are free from random error. It means that an instrument produces the same result when repeatedly applied to the same person under the same circumstances ² |
| Relative risk | The ratio of the probability of an outcome such as disease occurring in the exposed group versus a non-exposed group. RR assesses the risk of an outcome in one group relative to the other in prospective studies ² |
| Type I error | Rejection of the null hypothesis when it is true, that is: the conclusion that the observed difference was not due to chance, when in fact it was (α) ⁴ |
| Type II error | Failure to reject the null hypothesis when it is false, that is: the conclusion that the difference could be due to chance, when in fact it was not (β) ⁴ |

1 INTRODUCTION

1.1 Background

Pain as an unpleasant sensory and emotional experience clearly impacts health and the quality of life. Enjoyment of life and work are severely affected in patients experiencing chronic musculoskeletal pain (CMP).⁵⁻⁷ Research has shown that patients with CMP report greater levels of physical and emotional distress and suffering, and are more likely to discontinue or avoid activities that may be associated with pain.⁸⁻¹⁰

When accompanied by social and economic inactivity, and in the absence of a specific diagnosis, CMP may cause persistent psychological distress and a loss of self-esteem that itself is linked to a low self-estimate of the capacity to work.¹¹ It has been stated that what distinguishes persons with and without pain is not just how they feel but how they behave.^{12,13} High rates of utilisation of healthcare services due to nonspecific CMP have been reported.¹⁴

Chronic spinal pain is one of the more costly health problems facing industry today. Estimates suggest that post-initial episodes account for more than two thirds of compensated medical and lost-time costs.¹⁵⁻¹⁷ It has been shown that 90% of patients in primary care stop going to their doctor after three months, but that most still experience LBP and related disability one year after the first consultation.¹⁸⁻²¹

At least in the scientific literature, the patient's active role in his/her recovery is an issue that is almost ignored when pain is assessed. Today, as before, pharmaceuticals play a central role in the treatment of CMP.²²

According to evidence-based medicine, the presence of CMP is associated with significantly poorer self-rated health, lower functional status, somatic and psychological distress, and with physicians' views of how CMP ought to be treated.^{23,24} Interestingly, the named associated factors for CMP, especially in the spine, have also been found among patients with other diagnoses such as osteoporosis, knee osteoarthritis, and complex chronic health disorders.²⁵⁻²⁷ Psychological factors can influence the experience of CMP. Thus, psychological treatments can be useful in helping patients to better adjust to pain and prevent chronicity and disability.^{9,28,29} In contrast, there has been relatively little research into positive personal emotional resources, which are considered to be protective factors for CMP and the disability it produces.³⁰

1.2 Epidemiological spectrum of chronic musculoskeletal pain

Chronic musculoskeletal pain (of duration longer than 3 months) has been proposed to be endemic, with a point prevalence of 35-50% in the general population.^{19, 31-34} Nonspecific LBP is experienced at least once in about two-thirds of the population during their lifetime and about half of the adult population will suffer from LBP at some time during a 12-month period.³⁵ Recently, it was found in a 10-year follow-up study conducted in Sweden that CMP predicts hospitalisation due to other serious medical conditions.³⁶ Moreover, a prevalence of 11% has been documented for chronic widespread pain in Sweden.³⁷ However, in general, only a small minority of patients develop chronic LBP after an acute episode.³⁸ Conversely, it was recently found that as many as 30% of people with an episode of nonspecific LBP do not recover within 1 year.^{21, 39} The cumulative incidence of LBP during a 1-year follow-up is around 4% for subjects with a previous history of LBP, older age, or receiving workers' compensation.^{21,40} Moreover, there are regional geographical differences in the prevalence of CMP. In developed countries, the experience of CMP and resultant disability are widespread.⁴¹ The Scandinavian countries have the highest rates of sick leave and disability due to CMP in an international comparison.⁴² In Sweden, the high prevalence of spine problems is a major source of disability. In addition, its treatment necessitates high levels of health care expenditure.¹⁵ Additionally, important differences regarding the experience of pain by sex and ethnic background, and for some psychological characteristics of subjects, have been found (Table 1).⁴³

Table 1. Risk and prognostic factors for chronic spinal pain, sorted by pain location and type of study.

| Location | Identified risk/prognostic factors | Author and type of study |
|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Neck and shoulders | Women aged 45-64 years, low grade of education, healthcare users. Psychosocial factors, including psychological health, coping patterns, and need to socialise | Dutch survey; Bionka M et al., 2008 Task force on neck pain and its associated disorders, 2000-2010; Carroll LJ et al., 2008 |
| Low back | Consultation behaviour, self-reported disability and pain intensity. Number of painful sites, history of previous LBP Emotional distress, previous LBP, high physical job stress, low grade of education. Emotional distress and somatisation | Prospective, population-based, UK; Croft P et al., 1998 Prospective study, UK; Papageorgiou et al., 1996 Prospective population-based study; Brage S et al., 2007 Multi-practice survey, Denmark; Jorgensen et al., 2000 |
| Spine | Major depression (19.8%) and pain severity | Community health survey, Canada; Currie SR and Wang J, 2003 |

1.3 Gender differences in chronic musculoskeletal pain

It has been stated that women are more likely to report pain and have an increased risk for somatic diagnoses.⁴⁴⁻⁴⁶ Greater pain intensity, a greater number of pain sites, and higher rates of seeking care have been reported for women compared to men.^{5, 27, 47-49} In line with this, higher incidences of neck pain, fibromyalgia, widespread pain, and pain after an osteoporotic fracture have been documented for women.^{37, 46, 50-51} In contrast, incidence of LBP has been found to be higher in men compared to women.^{11, 52} Women with CMP have also reported more negative experiences during medical encounters.⁵³⁻⁵⁴

1.4 Ethnic background and chronic musculoskeletal pain

A higher proportion of people with a non-Swedish ethnic background have been shown to suffer from CMP and long-term illness, and to be on sick leave due to CMP.^{37, 55-56} A substantial proportion of them are refugees who have fled famine and natural disasters, among other things. In a recent study, patients born in a country other than Sweden had an increased risk of suffering from a combination of both a psychiatric diagnosis and CMP.⁵⁷ Widespread musculoskeletal pain originating from the spine or the neck-shoulder region was described as the most common cause of long-term sick leave in a Swedish study in which 40% of patients were of foreign origin.⁵⁸

1.5 Conceptualisation of pain over time

Historically, pain has been viewed as a symptom secondary to the presence of tissue pathology, with the amount of pain experienced and reported being directly proportional to the amount of tissue pathology. Once the physical pathology has been resolved, the pain should subside.⁵⁹ Later, the “gate control theory” focused on the multidimensional and variable relationship between pain and tissue damage.⁶⁰ Nowadays, the so-called “neuromatrix theory of pain” has recognised the potential involvement of psychological factors in pain processes.⁶¹ This theory proposes that the output patterns of the neuromatrix engage perceptual, behavioural, and homeostatic systems in response to injury and chronic stress.^{62,63} Several medical disciplines such as neuroscience, genetics, and orthopaedics have been involved in the search for CMP mechanisms.^{64,65} Physicians assume that underlying pathology is both a necessary and sufficient cause of pain. Consequently, medical assessments/physical examinations/diagnostic imaging procedures are used to identify or confirm the presence of an underlying pathology. In the absence of organic pathology, the physician may assume that the report of pain stems from other factors.⁶⁴

1.6 Use of the biopsychosocial model to study CMP

The biopsychosocial model posits that the pain experience and its impact on the individual are a result of interacting combinations of somatic inputs, psychological processes, and environmental conditions.^{66,67} Further components—cognitive behavioural, affective, and social factors—have been sequentially integrated

into the medical approaches dealing with pain analysis. Affective factors (depression and anxiety) and cognitive behavioural factors (such as pain catastrophising and fear-avoidance beliefs) have been reported to be predictive factors for CMP.^{28, 68-73} There is a tendency to refer to psychosocial factors without explaining them or the level at which these factors operate in relation to CMP.^{68-70, 72-74} Consequently, among patients with CMP, most interventions have targeted psychosocial factors without regarding the appropriate level at which the intervention should occur. Additionally, while some interventions show positive outcomes and may contribute to the development of specific pain interventions, they are not always effectively disseminated or accepted.⁷⁵⁻⁷⁷ In this context, it is possible that patient deconditioning may directly decrease with physical inactivity in patients with CMP.^{68, 78-79}

1.6.1 Biomedical aspects of CMP

Denomination and classifications of pain

Nociceptive pain: A mode of pain that is generated by an injury activating nociceptors in peripheral tissues, for instance, inflammatory pain, where pain itself is the subjective experience that does not necessarily represent tissue damage.^{3, 80} Musculoskeletal pain is best understood when pain is thought of as a perception and not only as a sensation in the nervous system. In CMP, the brain changes in response to nociceptive and non-nociceptive stimulation, and forms memory traces in the central nervous system. These learning processes may, according to recent research, be affected by both genetic and environmental factors.⁸¹ At the neuronal level, imbalances in a variety of neurotransmitters may result in increased membrane excitability, as well as neuroendocrine-immune dysfunction.^{3, 82, 83}

Neuropathic pain: Pain that arises as a direct consequence of a lesion or disease affecting the somatosensory system.³ This revised definition fits into the nosology of neurological disorders.³

Other definitions of pain: Pain can vary in duration, intensity, quality, and referral. In terms of duration, pain is classified as chronic, sub-acute, and acute.³ Those definitions are based on pain history, with a focus on pain persistence and the number of days with pain.⁸⁴ With respect to intensity, two approaches defining chronic pain can be contrasted: 1) measurement of pain intensity and its interference with activities;⁸⁵ and 2) definition according to a prognostic approach, using the current pain status to predict future pain severity.⁸⁶⁻⁸⁸ Based on this perspective, chronic spinal pain should be defined by its prognosis rather than its duration.⁸⁹

Origin/nature of pain: Specific CMP is directly related to changes in morphological structures, such as inflammatory process, radicular syndrome, ankylosing spondylitis, fracture, and cauda equine syndrome. Nonspecific CMP is defined as CMP not attributed to recognisable, known specific pathology or physiological changes.^{90, 91} Thus, it is difficult to specify the cause of the pain, and to accurately perceive its severity. The cause of nonspecific CMP and its physiological or anatomical substrate remain unclear. Nonspecific LBP can last for hours to months and recurrence is frequent, especially within the first year.⁹² Nonspecific CMP is the cause of LBP in approximately 90% of all cases and the prognosis for a return to

work within six weeks is excellent.⁹³ However, the cost of treating patients suffering from nonspecific CMP are strikingly high in Sweden, and in other countries.^{15, 90, 94}

1.6.3 Oral opioid treatment and CMP

In the last decade, rapid increases in the use of opioids to treat CMP have been reported in several countries.⁹⁵ Oral opioids have not been regarded as the first-line treatment for persistent non-cancer pain in primary care, and their efficacy is uncertain.⁹⁶⁻⁹⁹ Concerns regarding opioid treatment of CMP have primarily been based on the fear of addiction. However, the outcome of long-term opioid treatment in CMP is often unsatisfactory owing to side effects such as fatigue, sweating, and mood changes.¹⁰⁰ Additionally, opioids influence hormonal release at the hypothalamic-pituitary level and reduce levels of pituitary hormones.¹⁰¹ Altered menstrual flow, probable reduced fertility, opioid-associated depression, osteoporosis, and hyperalgesia have been described in women who have taken opioids for long periods of time.¹⁰² People treated with opioids probably report severe pain from the beginning, and their pain may therefore have been moderated with comparatively high doses of strong opioids.¹⁰³ Finally, whether physicians prescribe opioids for CMP is mainly determined by their personal beliefs about the appropriateness of opioids for this problem.¹⁰⁴ After a biophysiological overview regarding the cause of CMP, the following question arises:

- Can the presence of physical symptoms/organic signs alone explain the duration of sick leave in CMP, and pain-related disability in acute musculoskeletal pain?
- How strong is the association between physical symptoms/organic signs and the prolongation of pain and disability, in patients on long-term sick leave due to CMP?
- How strong is the association between physical symptoms/organic signs and disability in acute musculoskeletal pain?

1.7 Psychosocial approaches for explaining CMP: a literature review

Several theoretical models describe the development and prolongation, otherwise known as the ‘chronification’, of CMP from a psychological point of view. These models are important because obtaining better knowledge of risk factors for the onset of CMP and prognostic factors for its chronicity may provide better-tailored interventions for clinicians. What is the association between CMP and these psychological factors? To be able to answer this question, different approaches are considered below.

1.7.1 The cognitive behavioural and affective models

These models focus on the sensory dimensions of the pain system, integrating behaviour as a central feature of the system.^{13, 105-107} Previously, behaviour has not been integrated into the development of conceptual pain models, and maybe impeding the development of effective treatment approaches for CMP.¹⁰⁸⁻¹⁰⁹

1.7.2 Pain behaviours

Pain behaviours, verbal and non-verbal, are overt communications of pain, distress, and suffering, and refer to the ways in which people display that they are experiencing pain.¹¹⁰⁻¹¹³ Such behaviours provide information on pain experience and intensity, and the causes of pain. Maladaptive overt illness-related behaviour that is out of proportion to the underlying physical disease has been given the name 'excessive illness behaviour'.¹¹⁴⁻¹¹⁵ Pain behaviours that are excessive for the degree of known physical disease, are common in patients with chronic LBP.^{38, 116-118} In orthopaedics, for example, clinical usefulness when assessing illness behaviour is with regard to choice of treatment.³⁸

1.7.3 The fear-avoidance model of musculoskeletal pain

Building upon the knowledge derived from general fear and anxiety theories, Vlaeyen and Linton proposed a cognitive behavioural model of chronic LBP.¹¹⁹ According to the fear-avoidance model, patients are likely to maintain engagement in daily activities when acute pain is perceived as non-threatening, which promotes functional recovery. In contrast, a vicious circle may be initiated when the pain is catastrophically misinterpreted, leading to avoidance/escape and hypervigilance behaviours.¹¹⁹⁻¹²⁰

1.7.4 The cognitive affective and trauma factor model

This model explains the transition from acute pain (of less than 6 weeks' duration) to chronic pain and the associated disability. Associations between negative pain beliefs, depression, learned helplessness, cognitive distortions, and pessimism about the future and pain chronicity have been described.¹²¹⁻¹²² Baseline depressive symptoms in acute pain and disability predict persistent pain in individuals with musculoskeletal problems.^{22, 123-124}

1.7.5 The stress process model: disability related to low back pain

This model considers that LBP episodes and related events can trigger stress adaptation processes at biological and psychological levels.¹²⁵ It attempts to explain how individuals react to life events that are generally associated with substantial adaptations, and their coping resources.^{66,106} The ultimate goal of the model is to support the development of clinical interventions, focusing on functional status in the presence of disability due to chronic LBP.¹⁰⁶

All these theories have their own paradigms that explain how, for patients with CMP, cognitive, behavioural, environmental, and affective factors, as well as pain intensity, can operate as distinct constructs. In this sense, a relevant question arises: Are these psychological factors determining or predicting pain chronicity, or is pain chronicity the cause of psychological problems in patients with CMP? Furthermore, it is a big leap for the scientific community to try to elucidate the primary role of factors that may aggravate the experience of acute LBP and its consequences.¹²⁶

1.8 Disability perspective

Disability because of CMP has a multifactorial origin that comes not only from physical impairment, but also from psychosocial and environmental factors. For this reason, it warrants interdisciplinary research. According to Truchon et al., the relationship between pain experience and cause of disability is not simple, and they are not at all the same entity.¹²⁷ As a consequence, failure to distinguish between pain and disability has a major impact on the management of CMP.¹²⁸ In this context, it has been stipulated that individuals with CMP are more often occupationally disabled than individuals with other complaints.^{119, 129} A survey in the UK showed that 1 in 4 patients with LBP experience disability.^{130, 38} Frequently shared predictors for disability and long-term sick leave because of CMP include low educational level, high levels of pain, fear of movement, psychological distress, somatisation, and employment in a job that requires lifting.^{93, 131-132} In Sweden, the main diagnostic groups leading to absence from work and the claiming of disability pension in the working population are musculoskeletal and psychiatric disorders.¹³³ Many efforts have been made to rehabilitate patients with CMP, but they have not been successful.^{70, 134} CMP is considered to be a widespread public health problem in Sweden, causing more sick leave than in other Scandinavian countries.¹³⁵

1.9 Healthcare giver's role and patient's compliance

Even though European clinical guidelines for managing acute spinal pain have been established, the choice of treatment and the prognosis for recovery remain uncertain today.¹³⁶ While most patients with acute LBP improve rapidly, the risk of recurrence and development of chronic LBP is between 2% and 56%.^{92, 137, 138} Pain avoidance beliefs in general practitioners is associated with prescribing sick leave during painful periods for acute LBP, and a physician is less prone to advising patients to maintain the maximum bearable physical activities for chronic LBP.¹³⁹ Management of first time acute LBP varies, reflecting uncertainty about the optimal approach.^{32, 140} There is evidence that the type of advice given to a patient can alter the course of an episode of acute LBP.^{141, 142} Many physicians hold the belief that LBP necessitates some avoidance of activities and work.¹⁴³ In regard to pain, the treatment advice given by health care givers to patients is still focused on the pain itself, rather than on the patient's functioning or physical activity.^{144, 145} The attitudes and beliefs of general practitioners may influence patients' ability to overcome CMP, influence treatment decisions, and the duration of sick leave in patients with CMP.^{146, 147} The belief that LBP necessitates some avoidance of activities and work has not yet been changed to any significant extent, as reported in several studies.^{146, 148} On the other hand, patients' compliance with treatment advice has not yet been studied in acute severe LBP.

1.10 Summary of problem areas presented in the Introduction

1.10.1 General problem area

Despite a variety of diagnostic methods in general practice, a specific diagnosis can only be reached in around 10-20% of all patients with LBP. In the remaining 80-90% of patients, the diagnosis is nonspecific pain, which commonly causes long-term sick leave and disability. In addition to somatic parameters, psychological and social factors are thought to influence the duration of nonspecific CMP. Measurement of these factors is therefore essential not only for research, but also for optimising clinical practice.

Pain is considered in this thesis to be a complex condition in which the pain experience runs parallel with distress and physical inactivity, with both personal and social consequences. These factors act as a chain and depend on each other. Psychosocial factors play a central role in initiating this complex. One of these factors may cause the next step, worsening the pain experience, and leading in this way to long-term sick leave and/or mental health comorbidity. It is, therefore, very important to highlight the role of health care givers in clinical settings in the prevention, management, and treatment of CMP. Health care givers need to transform the perspective for treating nonspecific CMP. What is needed is the demedicalisation of CMP in which the patient's engagement acts as his/her own monitor in the rehabilitation process.

1.10.2 Specific problem areas

While a significant number of patients with CMP experience psychological distress and mental health comorbidity, physicians sometimes misdiagnose, fail to detect, or do not treat this type of comorbidity among patients suffering from CMP.

Diagnoses and the level of ability to work have been difficult to establish for patients on long-term sick leave due to CMP. Frequently, psychiatric disorders among these patients have been unrecognised due to the lack of a multidisciplinary team assessment.

Validated questionnaires are necessary to assess pain-associated symptoms. Notably, distress is associated with poor outcomes in nonspecific CMP. For these reasons, these factors were analysed in this thesis. Even through the "Stay active" advice seems to be the most appropriate treatment recommendation in acute LBP, several clinicians still recommend that patients adapt work and activities to their pain intensity. When a patient is advised to stay active, little is known about his/her compliance and physical activity after the onset of acute severe LBP. Questions remain regarding the patient's understanding and interpretation of the advice to stay 'as active as possible without risking further spinal injury'.

2 AIMS OF THE THESIS

The overall aim of this thesis was to assess factors that influence the experience of chronic and acute pain and the duration of the associated disability. A further aim was to outline the conceptual framework behind chronic and acute pain and their operationalisation and management in orthopaedic and healthcare settings. The investigation was performed through five separate studies with the following aims:

Study I

To study the association between illness behaviour (Waddell signs) and clinical findings, pain intensity, depressed mood, self-reported disability, sex, origin, and degree of sick leave at the time of orthopaedic consultation.

Study II

To investigate the occurrence of somatic and mental health comorbidity among patients referred from the Social Insurance Office who had been on long-term sick leave due to chronic musculoskeletal pain. An additional aim was to compare the assessment of ability to work before and after a team assessment by an orthopaedic surgeon and a psychiatrist.

Study III

To compare the score for depressed mood obtained on the Beck Depression Inventory (BDI) with the diagnosis of depression made by a psychiatrist, and to study the prevalence of undiagnosed psychiatric disorders in patients on long-term sick leave due to CMP.

Study IV

To investigate different psychometric characteristics of the Swedish version of the DAPOS (Depression, Anxiety, and Positive Outlook Scale) and its clinical use in patients with pain in the locomotion system.

Study V

To evaluate patients' compliance and to compare the effect on pain-related disability of the treatment advice "Stay active" and "Adjust activity" in patients with acute severe LBP. A further aim was to assess how distress and traits of fear of movement affect disability and physical activity over time.

3 PATIENTS, PARTICIPANTS AND METHODS

Table 2. Summary of the main characteristics of the subjects included in the studies.

| Characteristics of the participants | Studies I-II patients | Study III patients | Study IV patients/participants | | | Study V patients |
|-------------------------------------|-----------------------|--------------------|--------------------------------|------------------|------------------|------------------------|
| n | | | | | | |
| Total | 174 | 83 | 144 ¹ | 144 ¹ | 161 ² | 109 |
| Men | 84 | 36 | 68 | 76 | 76 | 78 |
| Women | 90 | 47 | 76 | 68 | 85 | 31 |
| n | | | | | | |
| Swedish ³ | 94 | 40 | 118 | 129 | 142 | 98 |
| Non-Swedish | 80 | 43 | 26 | 15 | 19 | 11 |
| Age (years) | | | | | | |
| Mean (SD) | 45 (9) | 45 (9) | 51 (12) | 37 (15) | 34 (13) | 42 (42) |
| Range (min- max) | (23-63) | (23-61) | (23-86) | (18-87) | (18-80) | (20-63) |
| n | | | | | | |
| Pain location ⁴ | | | | | | |
| Neck -shoulders | 103 | | 17 | - | 16 | - |
| Upper extremity | 5 | | - | 13 | 9 | - |
| Low back | 47 | | 127 | - | 17 | 109 |
| Lower extremity | 19 | | - | 131 | 19 | - |
| Duration of pain | | | | | | |
| Mean (SD) | 62 (54) | 63 (54) | 63 (92) | 64 (67) | 48 (62) | 2.4 (1.1) ⁵ |
| (min- max) | (6 – 240) | (6 – 240) | (3-725) | (3-360) | (0-240) | (1- 5) |
| | (months) | (months) | (months) | (months) | (months) | (days) |
| n ⁶ | 157/157 | 75/83 | 62/125 | 35/99 | - | 99 ⁷ |
| Sick leave duration | | | | | | |
| Mean (SD) | 21 (16) | 21 (17) | 17 (43) | 6 (19) | - | 1.4 (3.5) |
| (min- max) | (3 – 96) | (3 – 96) | (0 - 348) | (0-108) | - | (0-29) |
| | (months) | (months) | (months) | (months) | | (days) |

¹ Patients from the orthopaedic clinic “Spine and Extremities sample”, ²The reference group, n=61 referring pain,

³ Ethnic background of the participants, ⁴ Pain location is defined by the PPD as the main location of pain;

⁵ Information available in days, only patients who answered the diary (n=99), ⁶ Patients on sick leave/Total available information on sick leave, ⁷ Information on sick leave available for patients who completed the diary (n=99)

3.1 Patients

3.1.1 Patients in Studies I-II

In studies I-II, 174 consecutive patients with pain in the locomotion system for more than 3 months were referred by the Social Insurance Office for evaluation of physical function and assessment of the ability to work. The patients had been on sick leave for a mean of 21 (range 3-96) months due to a somatic (orthopaedic) diagnosis (ICD-10). 52% were women and 46 % were patients with a non-Swedish background. The mean age was 45 (SD 9.4) years for the women and 45 (SD 9.0) years for the men. The main characteristics of the study population are described in Table 2.

Inclusion and exclusion criteria for studies I-II

Consecutive patients, aged 18 to 65 years who were able to understand and write in Swedish and who consented to participate in the study, were eligible. Excluded were those who could not understand the Swedish language, and those for whom the main reason of the sick leave was any other somatic diagnosis than musculoskeletal pain.

Patient participation in studies I-II

Of 175 consecutive patients invited to participate in the Study, only one was excluded because another somatic diagnosis was the main reason for sick leave.

Non-responders in Studies I-II

The BDI questionnaire was not answered by 25 of 174 patients, the DRI questionnaire was not answered by 11, and the Verbal Rating Scale was not answered by 19 of 174 patients. There were no statistically significant differences between the responders and the non-responders regarding age, origin, sex or pain intensity.

3.1.2 Patients in Study III

A subsample of 83 patients of the 174 who had undergone an orthopaedic examination underwent a psychiatric evaluation. The mean age of the patients was 45 (SD 9) (23-61) years, 57% were women and 52% were patients with a non-Swedish background. The sample in Study III was 71 patients with a team evaluation and who had completed the BDI questionnaire.

3.1.3 Patients and participants in Study IV

A total of 449 participants constituted the sample in Study IV. 288 were patients recruited from the Department of Orthopedics (occupational orthopedic and spine team), Sahlgrenska University Hospital, in Gothenburg, Sweden. All the patients had had musculoskeletal pain for at least 3 months. They were divided into two groups based on their pain location: Patients with problems in the spine and patients with pain in the extremities. The reference group comprised 161 subjects recruited from two gyms located in the city (89%) and recruited as a convenience sample (Non-probability sampling) from neighbourhoods around Gothenburg (11%). Of 144 patients with pain in the spine, 53% were women, for whom the mean age was 51.6 (SD 12.0) years, while it was 51.4 (SD 11.6) years for the men. Of 144 patients with pain in the extremities, “the extremities sample”, 47% were women, for whom the mean age was 34.7 (SD 15.0) years, while it was 38.6 (SD 14.0) for the men. In the reference group, 53% were women. The mean age was 35.4 (SD 14.5) years for the women and it was 33.0 (SD 11.5) years for the men.

Inclusion and exclusion criteria for Study IV

Participants older than 18 years, with pain in the locomotion system of nonmalignant origin lasting for at least 3 months who consented to participate in the study. In the reference group, participants with or without CMP, not on sick leave due to CMP, were included in the study. Excluded were those not able to read and write the Swedish language, and those with a psychiatric diagnosis.

Patient participation in Study IV

Four hundred and ten patients were invited to participate in the study. Of these, 145 patients from the Occupational Orthopaedics team and 143 patients from the Spine team accepted. Of 161 participants who were invited to participate in the reference group for the study, all accepted and were included.

Non-responders in Study IV

From the spine sample, 44% (114) of patients refrained from participation. The mean age was 47.2 (SD 11.6) years, which was not significantly so than the mean age of the patients who consented to participate in the study ($p > 0.05$). 56% (64/114) of patients were women and 32% (36) were patients with a non-Swedish background. The main reason in the last group for refraining from participation in the study was difficulty in understanding the questionnaires in the Swedish language. For the Swedish participants, the main reason was the length of the questionnaires, while some felt uncomfortable about answering the questionnaires. In the “extremities sample,” eight patients did not participate. One was a patient with a non-Swedish background, and six were women. The mean/median age was 29.5/18.5 (SD 18) years. Additionally, 49% (70/144) did not answer the Beck Depression Inventory (BDI), and 49% (70/144) the State-Trait Anxiety Inventory (STAI). There were no statistically significant differences between the responders and non-responders to BDI and STAI regarding age, origin, sex, pain intensity, scores on DAPOS-D, or on DAPOS-A ($p < 0.05$).

3.1.4 Patients in Study V

One hundred and nine subjects were recruited consecutively from different automobile factories in Gothenburg with acute severe LBP. 72% were men, and 10% had a non-Swedish background. 57% were white-collar workers and 43% blue-collar workers. The mean age of all participants was 42 (SD 10) years, 42 (SD 10) for the men 41 (SD 11) for the women.

Inclusion and exclusion criteria for Study V

Eligible participants were all subjects with acute severe LBP, with duration from onset less than or equal to 48 hours, with or without radiating leg pain, with or without neurological signs, scores on VAS > 5 and between 18 and 65 years of age. Patients were requested to fill out and return a seven-day diary and those

who did so were included. Excluded were those who had been on sick leave because of LBP in the last month or because of pain in the spine.

Patient participation in Study V

One hundred and nine consecutive patients who satisfied the inclusion criteria were enrolled into the project. Of them, 99 completed and returned the seven-day diary.

Non-responders in Study V

Ten patients did not return the diary. Their average age was 37 years (SD=10), which was lower than the average age for those completing the ($p>0.05$). There were no statistically significant differences between responders and non-responders for sex or origin ($p>0.05$).

3.2 Methods

3.2.1 Musculoskeletal function

Musculoskeletal function was estimated by examining the ranges of motion of the cervical and lumbar spine, and all major joints of the upper and lower extremities. The muscle strength was assessed manually in the lower extremities, elbow, shoulder, and wrist joints, as was motor and sensory function. Reflexes, motor function, and sensory function were measured by clinical means. Strength of hand grip was measured with a vigorimeter (Martin GmbH & Co KG, Gebrüder). The results of the imaging methods were also considered. Musculoskeletal function was evaluated by several orthopaedic surgeons participating in the different studies.

3.2.2 Waddell signs (WS)

The Waddell signs (WS) used in this thesis were complaints of pain on 1) simulated axial loading of the spine, 2) simulated rotation test of the spine, 3) limited straight leg raising, 4) overreaction to the clinical examination, 5) verbal and/or nonverbal behaviour to communicate the experience of pain, 6) sensory loss or weakness that was inconsistent or could not be accounted for by recognized physiological processes or actual measurement. Three or more WS were considered as excessive illness behaviour.^{116, 149-150} The number of positive WS was assessed during the physical examination carried out by an orthopaedic surgeon.

3.2.3 Psychosocial function

Psychosocial function was assessed by means of the scores on distress, i.e. depression and anxiety, and self-perceived disability. Mental health comorbidity was assessed by a psychiatrist. Additional information on civil status, number of children, education, employment, occupation, ethnic background, and degree of sick leave was included in the social function.

3.2.4 The insurance medicine evaluation (Försäkringsmedicinsk utredning)

When a person receives sick-leave allowance for longer than 3 months, the Social Insurance Office requires an evaluation of the person’s ability to work. The main purpose of this procedure is to determine the cause of the sick leave, the level of physical function, the degree of disability, and the goals for rehabilitation.¹⁵¹

3.2.5 Ability to work

Ability to work was estimated by the Swedish index of work ability (scale) used by the Social Insurance Office and the healthcare system in Sweden (www.socialstyrelsen.se). This evaluation was carried out by the physician for all the patients, to validate the somatic diagnosis, measure physical function and estimate the person’s ability to perform his/her regular work as employed or to perform other regulatory work tasks on the labour market if the patient was unemployed (Study II).

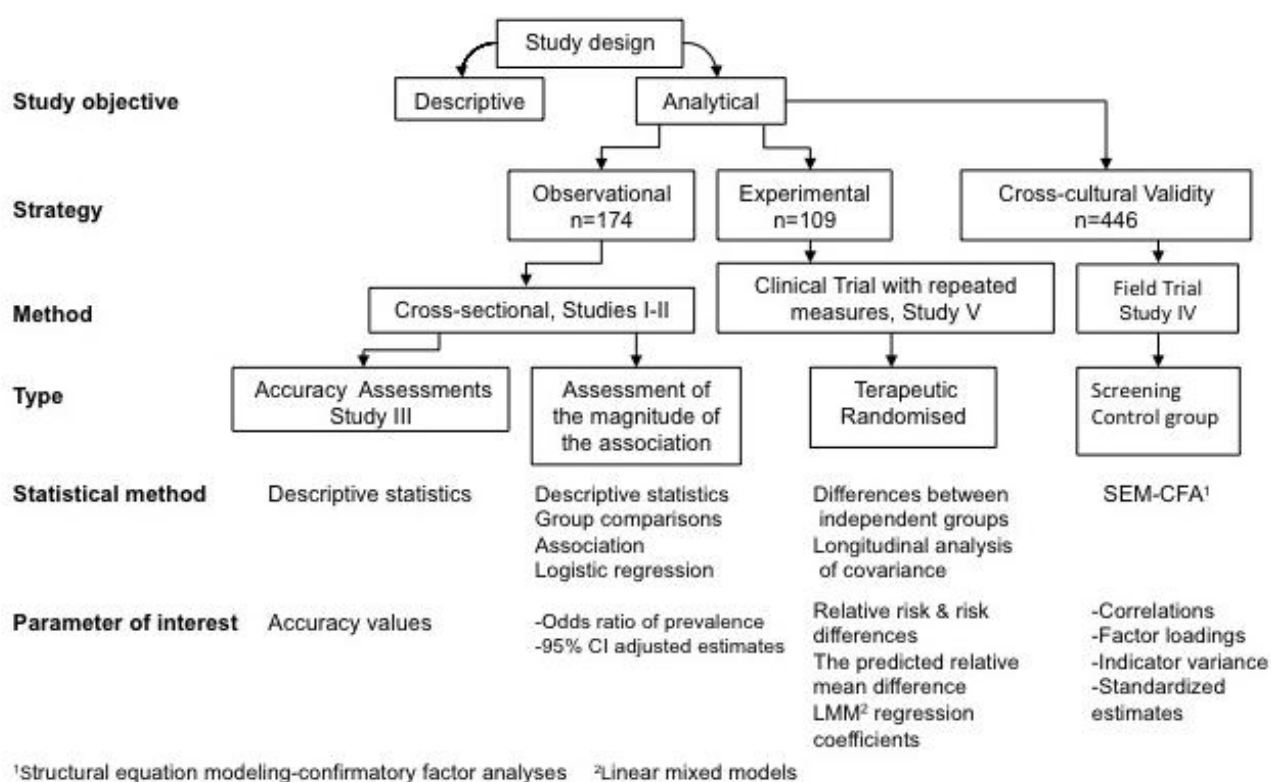


Figure 1. Overview of epidemiological and statistical methods used in Studies I-V.

3.2.6 Epidemiological methods

The designs used in this thesis and their main features are described below and summarised in Figure 1.

Studies I-II

An observational cross sectional study was performed to investigate the association between clinical status, pain intensity, depressed mood, self related disability, sex, origin, duration of sick leave and excessive illness behaviour (Waddell signs; Study I). The association between psychosocial factors and the main pain

location (neck/non-neck) was investigated in study II. Furthermore, the prevalence of mental health comorbidity was calculated in this group of patients.

Study III

An agreement study (concordance) was carried out between scores obtained on the BDI questionnaire and the diagnosis of depression made by a psychiatrist. The Structured Clinical Interview for DSM-IV-TR Disorders (SCID), the Swedish version, was employed as the gold standard.

Study IV

A population based cross cultural, observational validity study was performed to investigate different psychometric characteristics of the Swedish version of the DAPOS (Depression, Anxiety, and Positive Outlook Scale).

Study V

A blinded randomised controlled trial (RCT) with repeated measures, using a longitudinal follow up (7 days), was performed to evaluate compliance to two different treatment strategies that were advised: “Stay active” and “Adjust activity” (Se pag 21). Psychometric measures outcomes, disability and physical activity over time were compared between the two groups given two different types of advice in patients with acute LBP.

3.3 Questionnaires

3.3.1 Disability Rating Index (DRI)

The subjective grade of disability, indicating the difficulty experienced due to pain in carrying out usual/ daily living activities, was assessed by means of the DRI questionnaire. This instrument ranges from 0 “No pain” to 100 “Worst possible pain”. It has been validated and widely used in studies of pain in Sweden.¹⁵²

Table 3. A summary of the questionnaires used in the studies.

| Variables | Measures | Study | | | | |
|---------------------------|------------------------------------------------------------------------------|-------|----|-----|----|---|
| | | I | II | III | IV | V |
| Pain intensity | Visual Analogue Scale Verbal Rating Scale Numeric Graphic Rating Scale | ● | ● | ● | ● | ● |
| Pain location | Pain drawing | ● | ● | ● | ● | ● |
| Physical exercise | Step count (pedometer) | | | | | ● |
| Disability | Disability Rating Index | ● | ● | ● | ● | ● |
| Depressed mood | Beck Depression Inventory | ● | ● | ● | ● | |
| Psychological distress | Depression Anxiety and Positive Outlook Scale (DAPOS) | | | | ● | ● |
| Anxiety | State and Trait Anxiety Inventory | | | | ● | |
| Mental health comorbidity | Psychiatric assessment | | ● | ● | | |

3.3.2 The Depression Anxiety and Positive Outlook Scale (DAPOS)

DAPOS was constructed by selecting questions from existing instruments, the Beck Depression Inventory, the Hospital Anxiety and Depression Scale and the SF-36 scale.^{153,154} DAPOS is divided into three subscales with separate scores. The subscale for depression (DAPOS-D) ranges from 5-25 points, indicating normal mood to severely depressed mood. The range for the anxiety subscale (DAPOS-A) is 3-15 points (no anxiety to maximal anxiety) and the range for the positive outlook subscale (DAPOS-PO) runs from 3-15 points, where 15 indicates maximal wellbeing. The scale is able to measure distress and positive affect in populations with CMP. The Swedish version of DAPOS is presented in the Appendix.

3.3.3 Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI-IA) was used to assess depressed mood. It ranges from 0-63 points, and a score below 9 points is considered to be none or minimal depression.¹⁵³ The first versions of BDI have been criticized with regard to the overrepresentation of somatic symptoms reported by patients with CMP.¹⁵⁵

3.3.4 The State-Trait Anxiety Inventory (STAI)

The State and Trait Anxiety Inventory is a self-evaluation questionnaire (STAI-S, and STAI-T) of anxiety. The STAI-S form assesses temporary or emotional state anxiety, whereas the STAI-T form assesses the long-standing personality trait ‘anxiety’ in adults. Each questionnaire comprises 20 questions and they range from 20-80 points.¹⁵⁶

3.3.5 The Tampa Scale for kinesiophobia (TSK)

Kinesiophobia or fear of movement was measured using the Swedish version of the TSK.¹⁵⁷ The TSK questionnaire comprises 17 items assessing the subjective rating of fear of movement. The total score ranges between 17 and 68, where 68 indicate maximal fear of movement.

3.3.6 Pain severity assessment

Measures of pain intensity, interference with activities, and pain-related role disability define the general concept of pain severity.¹⁵⁸ Pain severity was assessed in the work presented in this thesis using multiple measures of pain intensity, interference with activities, and role disability. The number or the adjective that the patient indicated on the scale expressed the subjective experience of pain during the previous three months or at the present. The pain intensity scales used in this thesis are described below.

Visual Analogue Scale (VAS)

The Visual Analogue Scale assesses the pain intensity, and its ends are labelled as the extremes of pain, “No pain” and “Worst possible pain”. VAS is easy to administer and has many response categories. Its scores can

be treated as ratio data and there is good evidence for its construct validity. The paper-and-pencil-method of scoring can take more time and add an additional source of error.¹⁵⁸

Verbal Rating Scale (VRS)

The Verbal Rating Scale is scored by listing adjectives in order of the severity of aches and pains: None (0), Mild (2.0), Moderate (3.0), Severe (4.0) and Very Severe (5.0).¹⁵⁸ The VRS is easy to administer and there is good evidence for its construct validity. The main limitation with this scale is that the score given to a word by one patient differs from that given by other patients. This indicates that standardized scores for VRS adjectives may be less reliable than originally proposed.¹⁵⁹

Numerical Graphic Rating Scale (NRS)

The Numerical Graphic Rating Scale is a box scale consisting of 11 numbers, 0 to 10, indicating no pain to pain as bad as it could be. The patients were asked to place an “X” at the number that represents their pain. The validity and main advantages of NRS in pain research have been well documented. It is easy to administer and has many response categories. The scale has demonstrated sensitivity to treatments that are expected to have an impact on pain intensity.¹⁵⁸ In Study V, the full day score for pain intensity (NRS) was used in the follow up.

3.3.7 Pain location

Pain location was defined as the perceived location(s) of pain sensation that patients experience on or in their bodies.¹⁵⁸ It was marked by the patient in a pain drawing (PPD).¹⁵⁸ The pain location indicated by the patient in the PPD was a part of the clinical evaluation.

3.4 Step count

Daily step count was measured as an indicator of physical activity by means of pedometers in Study V. A digital pedometer (Yamax SW 200/LS 2000; Keep Walking Scandinavia AB, Kalmar) was issued to the patients with the instruction to wear it during all waking hours. This type of pedometer has been tested and validated in earlier studies for estimating the total daily number of steps.¹⁶⁰

3.5 7-day diary

Each patient received a diary to report pain intensity (NRS), disability (DRI) and daily step count (pedometer), together with any other physical activity performed during the seven days' follow up. The pain intensity was rated separately in the morning and evening, and was estimated also for the whole day, using the Numerical Graphic Rating Scale (NRS).

3.6 Measurement of patient's compliance

Compliance to the two pieces of treatment advice, “Stay active” and “Adjust activity”, was measured by means of daily step count and by the daily activity level reported in the diary. This information indicated whether the recommended treatment advice was followed by the patient.

3.7 Statistical analyses

The level of significance was set at 5%, and 2-tailed statistics were calculated in all studies (p -value). A result was considered as “statistically significant” if the p -value was less than 0.05. The confidence intervals (CI) were established at the 95% level.

3.7.1 Hypothesis testing

To compare proportions in the different groups, the Chi-squared test, as a two-tailed test ($n > 30$), and Fisher's exact test (for cell counts less than 5) were employed for two independent samples in studies I-II. Student's t -test was used in the comparison of two groups for unpaired data with normal distributions (studies I-II, and IV-V), and the Mann Whitney U test for unpaired data that were not normally distributed. The test of hypothesis on relative risk (RR) in Study V, and the odds ratios (OR) in studies I-II, were carried out using the Chi-squared parameter for two independent samples² (Figure 1). Odds ratios (OR) were calculated to test the association between the outcome variables i.e. dependent variable, as binary categories (yes/no), or as binary categories defined by the median value of the outcomes ($</>$) if the variable was a continuous variable. In Study V, risk ratios (RR) were calculated to compare the proportions in the two groups. The 90th percentile values of the scores on DAPOS-D, and the median values of the scores on DRI and on NIRS at Day 4 of the follow up, were used for comparisons across the two pieces of treatment advice.

3.7.2 Agreement

In Study III, the agreement between the scores on the BDI and the diagnosis of depression made by a psychiatrist were assessed by the degree of agreement. A BDI cut-off of 13 was employed. Inter-rater agreement was determined by comparing the psychiatric diagnosis and the BDI scores, calculating Cohen's kappa (k) for categorical judgments.¹⁶¹

3.7.3 Bivariate correlations

In Study I, Spearman correlation coefficients were calculated between the scores and WS. These scores were handled as ordinal data in a conservative way. The Pearson correlation coefficient (r) was calculated in Study IV. These scores were handled as continuous variables, and were classified according to interval scales.¹⁵⁸

3.7.4 Multivariate methods

a) A logistic regression was performed in Study I-II to test associations between the presence of an outcome and the associated factors, and to find the joint or net effect on the dependent variable of each of the independent factors in the model (Figure 1).

b) Cross cultural validity of the DAPOS (Study IV): Conceptual levels of precision and accuracy employed are described below.

Reliability: The Wilcoxon matched-pair signed-rank test was performed to measure test retest reliability.

Cronbach's alpha was calculated to estimate the internal consistency reliability of the DAPOS subscales for the whole group and for each subsample. Values of Cronbach's alpha between 0.7 and 0.8 were considered to be 'good'¹ However, for constructs with relatively few items, alpha values with pairwise item intercorrelations within a range of 0.20 to 0.40 were judged to be 'acceptable'.¹⁶²

Convergent validity: Convergent validity was tested by a series of Pearson correlations between the DAPOS sub-scale scores and the total scores on the BDI, STAI-S, and STAI-T in the clinical group (n=288). The BDI affective items were correlated with DAPOS-D. Selected items of the STAI-S and STAI-T were correlated with the DAPOS-A. Further, the positive items of the State were correlated with the DAPOS-PO.

Construct Validity: To test the multidimensionality of the theoretical construct of the DAPOS, confirmatory factor analysis (CFA) was performed. Further, multigroup confirmatory factor analysis was performed to test measurement invariance of the theoretical constructs of DAPOS across sex and diagnostic groups ("the spine sample" and "the extremities sample"). The differences in the structure of the instrument were tested for equality to determine whether it meant the same thing for everyone. The indices for approximate fit reported were the root mean square error approximation (RMSEA) for which values of 0.60 or lower indicates good fit. The respective 95% confidence intervals (CI), and the comparative fit index (CFI) were also used, for which values above 0.95 indicate good fit of the model. AMOS 7 and Mplus version 5 were used for statistical analysis.

c) Predictions from repeated measures, linear mixed models (LMM): In Study V, the outcome variables were followed for seven days. These observations and their corresponding errors were correlated. When one follow-up measurement is analysed, longitudinal analysis of covariance is the most appropriate statistical method because it handles random effects, thereby dealing with the problem of correlated error terms.^{163,164} All statistical analyses in Study V were performed using SAS (version 9.2) and SPSS (version 17).

3.7.5 Internal Missing Data

Missing data, questions missed or not responded to within the questionnaires, was treated according to the rules given by each scale respectively. Missing observations of DAPOS were imputed by use of expectation-maximization method.

3.8 Procedures

3.8.1 Procedure for Studies I-III

All patients, consecutively recruited from the Capio Lundby Hospital during the period 2003-2004, underwent an orthopaedic evaluation and an assessment of their ability to work. They completed the questionnaires before the clinical examination. In studies II-III, an additional psychiatric evaluation was performed for 83 patients, and both physicians carried out a common assessment of the ability to work.

3.8.2 Procedure for Study IV

The DAPOS, BDI, STAI questionnaires, a general questionnaire to collect socio-demographic data, pain-related questions, and the written consent were sent to the patient's home before they met the physician. A healthy reference group was asked about their participation and after they had given consent, completed the questionnaire on DAPOS, and on additional information directly at the place of the interview.

3.8.3 The cross cultural validation of DAPOS, Study IV

The international guidelines for the process of cross cultural adaptation of self-report measures were followed.^{154,165} The validation procedure was performed in several steps, face validity, convergent and construct validity. The reliability of the DAPOS was tested using the test-retest method (n=60). Test invariance across groups was carried out as a further assessment of construct validity for all participants.

3.8.4 Procedure for Study V

Patients who satisfied the inclusion criteria and who gave informed consent to participate were enrolled into the study. They were examined radiographically after recruitment, and completed the questionnaires before they met an orthopedic surgeon. The physician made the randomisation. The patients in the "Stay active" group received the advice to continue with as normal activities as possible in spite of the pain, whereas the patients in the "Adjust activity" group received the advice to avoid motion or activities that worsened or caused pain. All patients received the 7-day diary. The coordinating nurse gave the patients standardized instructions regarding the diary, and acted as a study monitor throughout the entire study, accompanying each patient throughout the study.

3.9 Ethical approval

Studies I-III were part of a more extensive study that was approved by the Swedish Regional Committee of Medical Ethics at the University of Göteborg (Reference No. 7-94). Study IV was approved by the Regional Ethics Review Board at the University of Gothenburg, 2006 (Reference No. 249-06), as was Study V (Reference No. 366-08).

4 RESULTS

The results have been divided into two sections. The first presents the main results of each paper individually, while the second consists of a topic presentation based on further analyses of pain and disability measurements. This section includes supplementary analyses not presented in the papers. This information is likely to contribute to a more complete framework for this thesis.

4.1 Diagnoses of respondents' symptoms and signs in this thesis

In studies I-II, cervicalgia and shoulder myalgia were the most frequent nonspecific diagnosis (45%). In Study IV, disc herniation and spinal stenosis were the most frequent specific diagnoses in the “spine sample” (66%), and more commonly seen among women than in men (prevalence 64% vs. 36%).

Table 4. Summary of types and frequencies of diagnoses in the different studies.

| Type of diagnosis Specific/nonspecific main diagnoses (ICD-10) | Study I-III ¹ n=174 | Study IV ^{2/3} n=143 [@] n=144 | | Study V ³ n=109 |
|---------------------------------------------------------------------|-----------------------------------|-----------------------------------------------------|----------|-------------------------------|
| Specific | | | | |
| Spondylosis/arthrosis epycondylitis (M43.0, M16, M77, M47.8-9, M19) | 12 | 6 | 14 | - |
| Disc herniation, spinal stenosis (M51.1, M48.0, M50.1) | 4 | 95 | - | 13 |
| Other specific diagnoses (M62.8, M17, M76.8, M75) | 19 | 11 | 69 | - |
| Specific diagnoses (% of the total) | 35 (20%) | 112 (78%) | 83 (58%) | 13 (12%) |
| Nonspecific | | | | |
| Cervicalgia/shoulder myalgia (M54.2, M79.1)* | 79 | 3 | - | - |
| Lumbago (M54.5) | 34 | 8 | - | 96 |
| Lumbago sciatica/sciatica (M54.4, M 54.3) | 7 | 8 | - | - |
| Generalized pain (R52.9) | 16 | - | - | - |
| Fibromyalgia (M79.7) | 2 | 3 | 2 | - |
| Other nonspecific pain (M79.6C-H, M25.5, M17.9) | 1 | 9 | 59 | - |
| Nonspecific diagnoses (% of the total) | 139 (80%) | 31 (22%) | 61 (42%) | 96 (88%) |

ICD-10: International Classification of Diseases and Related Health Problems; ¹ Patients with CMP referred by the Social Insurance Office; ² Patients from the Orthopaedic Spine Team (Study IV); ³ Patients from the Occupational Orthopaedic Clinic, the Extremities sample (Study IV) at Sahlgrenska University Hospital; *only four patients had a S13.4 diagnosis; [@] Information for one patient was not available.

Other specific pain in the extremities was the most frequent specific diagnosis (48%) in the “extremities sample”. In studies I-IV, the prevalence of fibromyalgia, widespread pain, and nonspecific pain in the knee was higher in women than in men. In studies I-III, widespread pain was seen in 16 patients, of whom 81% were women. In Study IV, in the “extremities sample”, nonspecific pain in the knee was more frequent in

women (prevalence 63%). Additionally, women with widespread pain and fibromyalgia reported more somatic comorbidities than men did (studies I-IV).

Types of Diagnoses: In studies I and V, the most common diagnoses were nonspecific (prevalence 80% and 73% respectively; Table 4). In Study IV, nonspecific diagnoses were seen in 22% of individuals in the “spine sample” and 42% of individuals in the “extremities sample” (Table 4). Type of diagnosis (specific/nonspecific) was not related to ethnic background, sex, duration of pain, sick leave, distress, or pain intensity in studies I-IV. There were no differences related to the type of diagnosis for psychiatric disorders (studies II-III). In Study V, type of diagnosis (specific/nonspecific) was not associated with pain intensity or any of the other variables.

4.2 Summary of results of the papers

4.2.1 Study I

Waddell signs (WS) were observed in 27% (47/174) of patients, 16% of whom manifested excessive illness behaviour. In general, more patients with WS were depressed (OR=4.4; 95% CI: 1.8-11) and experienced greater pain intensity (OR=2.9; CI: 1.1-7.7). Normal physical function was observed in two-thirds of the patients. Other predictive factors for WS at the clinical examinations were longer sick leave and previous full-time sick leave episode(s) ($p<0.05$). More patients (39%) with a non-Swedish background manifested WS than did Swedish patients (17%) ($p=0.002$). The mean BDI score for patients with a non-Swedish background was 26 (SD 13), as compared to 17 (SD 11) for Swedish patients ($p<0.001$). Moreover, patients with a non-Swedish background rated their own pain intensity to be greater than Swedish-born patients did (median values 7.5 and 5.0, respectively; $p=0.001$). There were no associations between WS and sex or age. These results show that excessive illness behaviour is related to psychological distress in patients on long-term sick leave due to CMP.

4.2.2 Study II

Out of 174 patients, 79% were blue-collar workers, 58% employed, 64% married. The educational level was low in 59% of patients, and 46% had a non-Swedish background. No loss of musculoskeletal function was found in 67%, and the neck was the most frequent main pain location. Patients with neck pain were more often women (prevalence 59% vs. 40% for men), exhibited greater pain intensity, and 99% of them reported two or more sites of pain ($p<0.05$). Among the patients with only orthopaedic assessment (91/174), 56.5% exhibited signs of depressed mood (BDI \geq 13 points).

Psychiatric assessment: Of 83/174 patients evaluated by orthopaedic surgeon and psychiatrist, 84% (70/83) suffered from mental health comorbidity. Depression was the most common comorbidity, especially among women (69%) and immigrants (62%). Greater pain intensity and inability to work were commonly seen

among patients with depression ($p < 0.05$). The prevalence of mental health comorbidity was higher in patients whose main pain location was the neck.

Assessment of the ability to work: Of 91/174 patients who underwent only the orthopaedic assessment, 48% were able to return to work, 51% had partial ability to work ranging from 25-75%, and 1% had no ability to work. After orthopaedic and psychiatric assessment, 32.5% (27/83) of patients were unable to return to work, and 67.5% (56/83) had a reduced ability to work because of mental health comorbidity. After team assessment, the main cause of sick leave changed from a somatic diagnosis to a psychiatric diagnosis in 69% of these patients.

161 of the 174 patients reported the use of analgesics, and 55 patients (34%) were using prescribed opioids. Of them, 45 (82%) had nonspecific diagnoses. A greater percentage of Swedish patients used opioids than patients with a non-Swedish background used them (56% vs. 44%). There were no differences related to the use of opioids for age, sex or psychiatric diagnosis.

4.2.3 Study III

Good agreement (80%) between BDI score and diagnosis of depression made by a psychiatrist was found in 71/83 patients with common assessment. The sensitivity of the BDI to detect depression was 87.5%. Psychiatric illness was diagnosed in 83% (59/71) of patients. 56% of patients were diagnosed with depression, and 31% with other psychiatric illnesses. 13% of patients were mentally healthy. Almost 10% of all patients had a previous psychiatric diagnosis. According to the positive likelihood ratio, a higher score on the BDI (≥ 13) was 1.6 times more likely to occur in patients with depression. The median BDI score was 26 in depressed patients and 23 in patients with other psychiatric diagnoses. Undiagnosed psychiatric disorders were seen in over 80% of the patients with CMP.

4.2.4 Study IV

Study IV, examined the psychometric properties of the DAPOS, and showed that its reliability, validity, and internal consistency are good, both in patients with CMP and in the control group.

Reliability: Test-retest reliability was acceptable. High correlations between the items for pretest and retest ($p < 0.01$) were found, confirming that the scores on the DAPOS are reliable. Furthermore, the 11-item DAPOS demonstrated good internal consistency with highly acceptable alpha scores on all three subscales in all samples. However, internal consistency was much better in the patient sample ($n=288$).

Convergent validity: Statistically significant correlations were found between DAPOS-D and the BDI affective items ($p < 0.001$), and between the DAPOS-A and the selected STAI items ($p < 0.001$).

Construct validity: All items loaded to their respective factor (construct) in all groups (standardised regression weight estimates p -value < 0.001 ; Figure 2), supporting both the internal consistency and the

internal structure of the questionnaire. The correlations among the constructs—depression, anxiety, and positive outlook—were positive and highly significant, corroborating the construct validity of the questionnaire (Figure 2). Moreover, the positive outlook subscale of the DAPOS was independent of both the anxiety and depression subscales, and was negatively correlated with scores for depression and anxiety, as well as pain intensity. The CFA analyses for the whole population (nongrouped) indicated that the DAPOS model met the fit criteria ($\chi^2(41, n=444)=53.37; p=0.093; CFI=0.993; RMSEA=0.026$). The three DAPOS constructs were measurement-invariant with respect to sex ($\chi^2(97, n=444)=103.13; p=0.316; CFI=0.997; RMSEA=0.017$; Figure 2). Across diagnostic groups, the anxiety and positive outlook scales were almost measurement-invariant ($\chi^2(123, n=444)=165.00; p=0.007; CFI=0.976, RMSEA=0.048$).

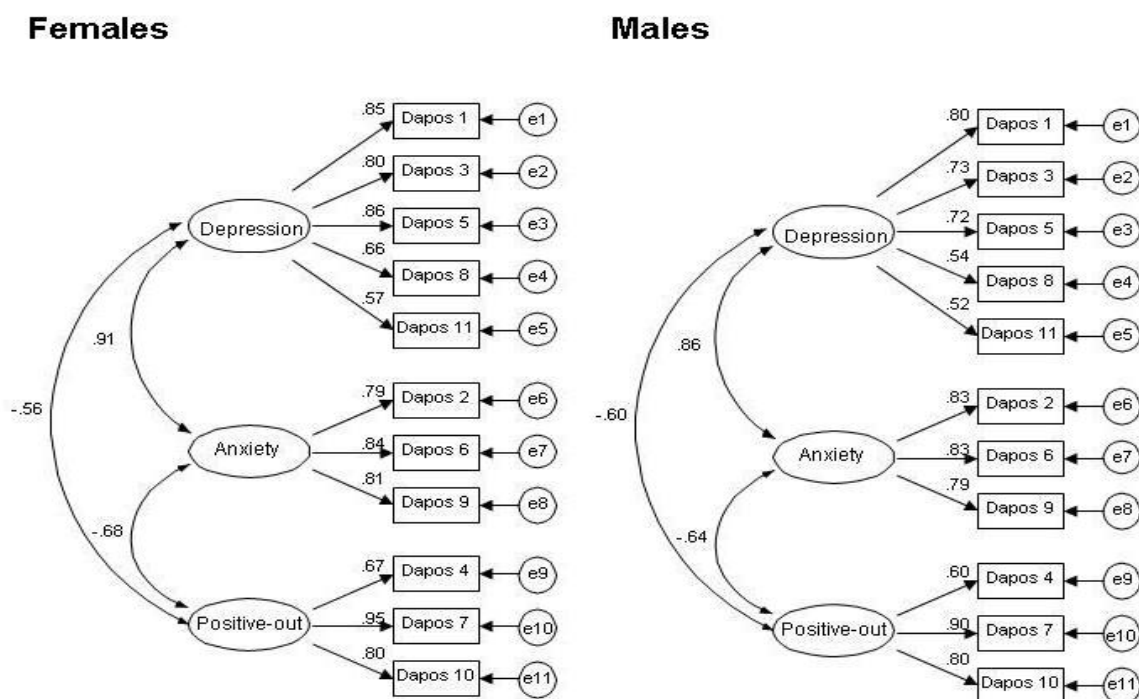


Figure 2. Model of the DAPOS for invariance across sex.

4.2.5 Study V

In many patients, back pain began to improve within hours after the onset of the pain episode, and an improvement occurred at an almost exponential rate during the first 2-3 days. 35% of patients claimed that their LBP started while they worked. The majority of patients (76%) returned to work directly after their clinical examinations, and all returned to work within 8 days. At baseline, there were no differences between the “Stay active” and the “Adjust activity” groups with regard to the reported cause of LBP, occupation, pain intensity (VAS), disability, or fear of movement ($p>0.05$). However, there were differences between the groups with regard to DAPOS-D and DAPOS-A scores, which were higher for patients in the “Stay active” group.

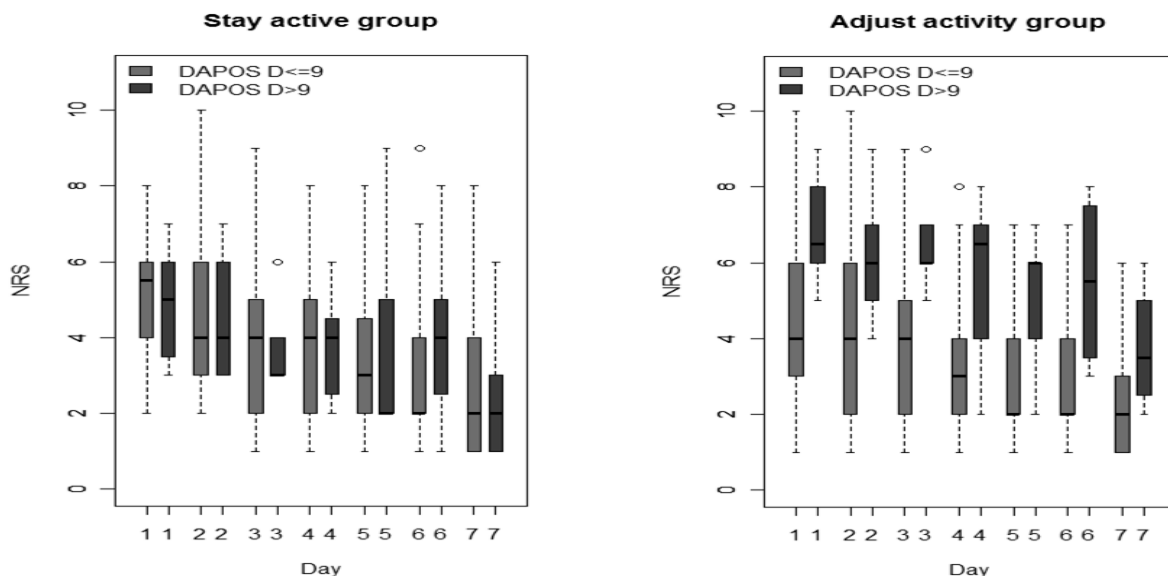


Figure 3. The effect of treatment advice (“Stay active” vs. “Adjust activity”) in interaction with depressed mood (DAPOS-D>9) on pain intensity (NRS) over time. NRS: Nonverbal Rating Scale (0-10). The figure shows the median of the scores of NRS (25th-75th percentiles) per day.

Follow up: Pain and its related disability disappeared in almost all patients with acute LBP during the 7-day follow up period ($p < 0.001$; Figure 3, Table 5). For all patients, step count increased over time ($p < 0.001$; Table 7, Figure 5). According to the LMM, pain-related disability over time was associated with the type of treatment advice ($p < 0.01$; Table 5-6). Patients in the “Stay active” group reported higher scores for pain-related disability and pain intensity than patients in the “Adjust activity” group, especially in the first three days of follow-up (Figure 3, Table 5-6).

Table 5. Model for pain-related disability across time according to the linear mixed models (LMM).

| Effect on DRI (0-100) | Estimate, β | Standard error | p |
|------------------------------------------|-------------------|----------------|----------|
| Intercept | 10.89 | 10.64 | 0.31 |
| Sex [†] | 5.77 | 4.09 | 0.16 |
| Intervention group ^{&} | 32.11 | 11.15 | 0.005* |
| Age | 0.37 | 0.17 | 0.04* |
| DAPOS-D | 3.27 | 0.10 | 0.004* |
| Days | -5.08 | 0.46 | <0.0001* |
| DAPOS-D* intervention group [†] | -3.96 | 1.47 | 0.008* |

[†]Women as the reference group; [&]“Adjust activity” advice as the reference group
 *Significant at $p < 0.05$

Table 6. Differences in least squares means in the scores on the DRI for Days 1 and 4, for DAPOS-D scores, and between the intervention groups in patients with acute severe LBP.

| Mean DAPOS-D score by percentile, Day 1 | Effect on DRI score, “Stay active” group | Effect on DRI score, “Adjust activity” group |
|-----------------------------------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------------|
| DAPOS-D (5 points 25th percentile) | Mean difference in DRI Estimate, β (SE) [@] 53.39 (4.7)** | Mean difference in DRI Estimate, β (SE) [@] 40.43 (3.76)** |
| DAPOS-D (6 points 50th percentile) | 52.53 (4.18)** | 43.77 (3.33)** |
| DAPOS-D (9 points 90th percentile) | 49.93 (3.89)** | 53.76 (3.99)** |
| Mean DAPOS-D score by percentile, Day 4 | Mean difference in DRI Estimate, β (SE) [@] | Mean difference in DRI Estimate, β (SE) [@] |
| DAPOS-D (5 points 25th percentile) | 38.51 (4.32)** | 24.91 (3.29)** |
| DAPOS-D (6 points 50th percentile) | 37.64 (3.71)** | 28.24 (2.78)** |
| DAPOS-D (9 points 90th percentile) | 35.04 (3.38)** | 38.24 (3.54)** |

**Significant at $p < 0.0001$; [@] Estimates were calculated based on a mean age of 42.4 years for Day 4, and adjusted for sex, days and for DAPOS-D. Intervention group: The “Adjust activity” group was used as the reference category.

The influence of distress: Adjusting for all variables, depressed mood (DAPOS-D) was found to be associated with pain-related disability over time ($p=0.004$). However, this effect interacted with the treatment advice ($p=0.008$) (Table 5). Although pain-related disability decreased in all patients over time, average pain-related disability was significantly higher for patients in the “Adjust activity” group than those in the “Stay active” group on Days 1 and 4, but only in patients with higher scores for depressed mood (DAPOS score >9) ($p < 0.02$; Table 6, Figure 3). The interaction between treatment advice and depressed mood in the scores on the pain-related disability (DRI) is illustrated in Table 6.

Table 7. Mixed models calculation (repeated measures, LMM) for daily step count: solution for fixed effects of intervention group, time (days), and interaction effects.

| Effect on daily number of steps ^{&} | Estimate, β ^{&} | Standard error | p |
|--------------------------------------------------|------------------------------------|----------------|------------------------|
| Intercept | 8.57 | 0.24 | <0.0001 [*] |
| Sex ⁺ | -0.19 | 0.10 | 0.05 [*] |
| Intervention group ⁺⁺ | 0.11 | 0.09 | 0.22 |
| Age | -0.01 | 0.004 | 0.01 [*] |
| TSK_27-32 ⁺⁺⁺ | -0.21 | 0.12 | 0.07 [*] |
| TSK_33-37 ⁺⁺⁺ | -0.09 | 0.13 | 0.49 |
| TSK ≥ 38 ⁺⁺⁺ | -0.34 | 0.12 | 0.007 [*] |
| Days | 0.38 | 0.05 | <0.0001 [*] |
| Days squared term | -0.03 | 0.005 | <0.0001 [*] |

[&]Log transformation; ⁺ Women as the reference group; ⁺⁺ “Adjust activity” advice as the reference group; TSK: Tampa Scale, ⁺⁺⁺TSK_19-26 points as the reference group; ^{*} Significance at $p < 0.05$.

Patient’s compliance: The mean and median values (crude) for daily step count were consistently higher in the “Stay active” group on the first day of follow up and over time (Figure 4). After statistical modeling (LMM), the predictions for the mean number of steps were also higher in the “Stay active” group, after controlling for all confounding factors. However, the difference did not reach statistical significance in the final LMM (Table 7).

The average daily number of steps for men was 17% lower than for women, and younger people were more active than older people. Patients who reported traits of fear of movement (TSK ≥ 38) had significantly lower step counts over time, after controlling for all factors, independent of treatment advice ($p < 0.05$; Table 7).

There was no association between baseline TSK score and either pain intensity or sex.

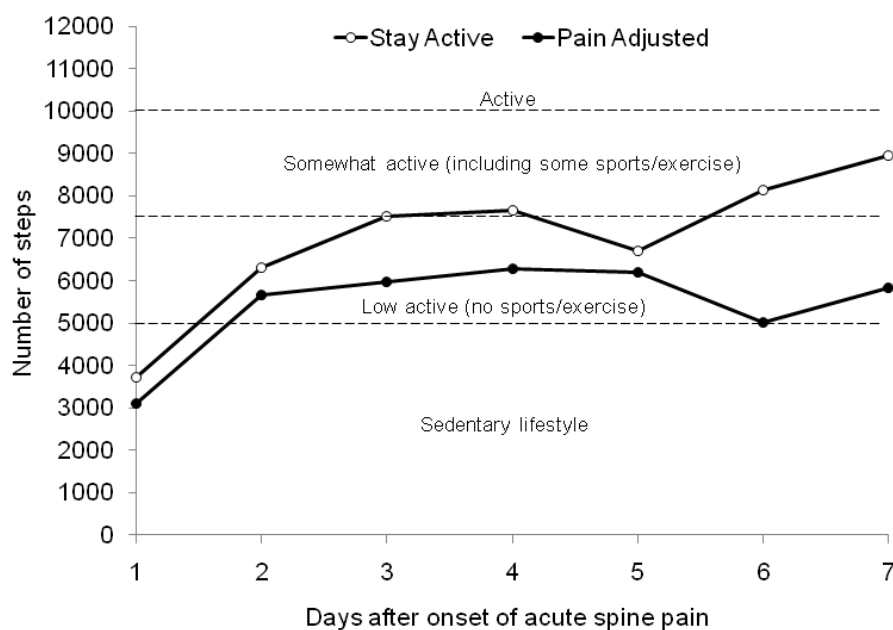


Figure 4. Daily median number of pedometer steps in patients with acute low back pain in the “Stay active” (n=47) and “Adjust activity” (n=52) groups. Dashed lines indicate cut-offs for pedometer-determined levels of physical activity in adults (Tudor-Locke, 2004).

Physical activity and compliance: Step count increased for the whole group with time ($p < 0.001$). However, the “Stay active” group had a greater step count at all times, which seems to reflect compliance with the “Stay active” advice. After seven days of follow up, patients in the “Stay active” group reached the “Somewhat physically active” category, defined for the reported step counts for populations without pain.¹⁶⁶ In contrast, patients in the “Adjust activity” group reached only the “Low activity category” (Figure 4).

4.3 Topic presentation

4.3.1 Severity and duration of pain

Table 8. Pain intensity (VRS) scores and multiple pain sites in studies I-IV.

| Pain intensity (VRS) ¹ | Study I-II n (% within the group) | Study IV ^(2,3,4) n (% within the group) | | |
|----------------------------------------------------------|--------------------------------------|-------------------------------------------------------|----------------|----------------|
| | | 2 ² | 3 ³ | 4 ⁴ |
| Mean/median | 4.0/4.5 | 3.5/4.0 | 3.5/3.0 | 2.0/2.0 |
| Very severe | 30 (19%) | 7 (6%) | 7 (7%) | - |
| Severe | 85 (54%) | 67 (55%) | 39 (41%) | 1 (0.5%) |
| Moderate | 32 (20%) | 25 (21%) | 35 (36%) | 19 (12%) |
| Mild | 11 (7%) | 20 (18%) | 15 (16%) | 41 (25.5%) |
| None | - | - | - | 96 (62%) |
| Pain in several anatomic sites n (% within the group) | 154/174 (88.5%) | 72/144 (50%) | 51/144 (35%) | 21/65 (32%) |

¹VRS: Verbal Rating Scale (1-5) Number of patients who completed the pain questionnaire: ²the “spine sample”, n=119/144; ³the “extremities sample”, n=96/144; ⁴the reference group, n=61/65 patients with pain.

“Very severe” or “Severe” pain (VRS) was reported by 73% of the patients in studies I-III; in 62% of patients in the “spine sample” and 48% of patients in the “extremities sample”. In Study IV, patients with spinal pain had more pain sites than patients with pain in the extremities had (50% vs. 35%, Table 8).

Patients in the “extremities sample” and patients in studies I-III with a non-Swedish background reported higher pain intensity scores. There were no differences in the duration of pain with regard to sex or ethnic background.

Table 9. Quartiles of pain intensity at baseline (VAS) and on (NRS) Days 1, 4, and 7 of the follow up, in patients with acute severe low back pain (Study V).

| Pain intensity | Baseline Score VAS ¹ | Score NRS ² | | |
|------------------------|---------------------------------|------------------------|---------|---------|
| | | Day 1 | Day 4 | Day 7 |
| Quartile 1 (n) | 62.0 | 4.0 | 2.0 | 1.0 |
| Quartile 2 (n) | 79.0 | 5.0 | 3.0 | 2.0 |
| Quartile 3 (n) | 90.0 | 6.0 | 4.0 | 4.0 |
| Quartile 4 (n) | >90.0 | 10.0 | 8.0 | 8.0 |
| Overall mean/median | 72.0/79.0 | 5.0/5.0 | 3.5/3.0 | 2.8/2.0 |
| Total (n) ³ | (102) | (98) | (97) | (69) |

¹VAS: Visual Analogue scale (0-100), ²NRS: Numeric Rating Scale (0-10); ³The numbers vary as some patients did not complete the pain intensity estimation in their diaries because of no pain.

In patients with acute severe LBP (Study V), the median score for pain intensity decreased from 5.0 to 2.0 points (NRS) during the seven days of follow up, (p<0.001; Figure 4, Table 9). Among patients with baseline VAS scores greater than or equal to 90 points (i.e. quartile 3-4), the scores for pain intensity remained higher at the end of the follow up than the scores among patients in the first quartile (4.0 vs. 1.0

respectively; Table 9). Higher scores for pain intensity were seen in both patients with a non-Swedish background compared to Swedish patients, and for men compared to women, on Days 2 and 3 of the follow-up (Mann-Whitney U test; $p \leq 0.03$).

4.3.2 The influence of psychological distress on pain intensity

The prevalence of excessive illness behaviour in Study I and of distress, i.e. depressed mood and anxiety, in Study IV, was greater in patients whose main pain location was the neck/spine (Table 10). In Study I, 16% of the patients exhibited excessive illness behaviour, and the majority of them had chronic neck pain. In studies II-III, psychiatric illness was seen in 84% of patients. In Study IV, the prevalence of distress was significantly greater for patients with pain in the spine (Table 10).

Table 10. Summary of the prevalence (%) of excessive illness behaviour (Waddell signs (WS)), depressed mood (BDI and DAPOS-D), anxiety (STAI and DAPOS-A), and psychiatric disorders for patients in studies I-V with different main pain locations.

| Main pain location | Neck-shoulders n (% within the group) | Low back n (% within the group) | Extremities n (% within the group) | All locations n (% of the total) |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|--------------------------------------|
| Studies I-II Excessive illness behaviour (WS ≥ 3) ¹ Depressed mood BDI ≥ 13 ² | 16 (9) 63 (42) | 8 (5) 28 (19) | 3 (2) 12 (8) | 27 (16) 103 (69) |
| Studies II-III Depression ³ Other psychiatric diagnoses ³ | 29 (35) 21 (25) | 6 (7) 6 (7) | 6 (7) 2 (2) | 41 (49) 29 (34) |
| Study IV Depressed mood BDI ≥ 13 ⁴ Depressed mood DAPOS-D ≥ 9 ⁵ Anxiety DAPOS-A ≥ 5 ⁵ Anxiety STAI S ≥ 35 ⁶ Anxiety STAI T ≥ 35 ⁷ | | 54 (43) 63 (44) 77 (53) 72 (58) 70 (57) | 12 (16) 44 (30) 40 (28) 33 (44) 30 (40) | n.a. n.a. n.a. n.a. n.a. |
| Study V Depressed mood DAPOS-D ≥ 9 ⁸ Anxiety DAPOS-A ≥ 5 ⁸ Fear of movement TSK > 38 ⁹ | | 35 (35) 27 (27) 22 (23) | | 35 (35) 27 (27) 22 (23) |

¹n=174, ²Beck Depression Inventory (BDI) answered by n=149/174 individuals, ³Studies II-III n=70/83

⁴BDI answered by 125 and 74 patients in the "spine sample", and in the "extremities sample", respectively

⁵Depression Anxiety and Positive Outlook Scale (DAPOS) answered by 144 patients in both groups

⁶⁻⁷STAI answered by 124 and 74 patients in the "spine sample" and in the "extremities sample", respectively

⁸DAPOS answered by 101 patients; ⁹TAMPA scale (TSK) answered by 97 patients; n.a: not applicable

In Study IV, participants with a non-Swedish background reported higher scores on the DAPOS-D than the Swedish patients (the mean/median values for patients with a non-Swedish or Swedish background were 10.0/9.0 and 8.4/7.0, respectively), and on the DAPOS-A (mean/median values 6.4/5.0 vs. 5.2/4.0). In Study V, scores on the DAPOS-D and TSK were also higher for participants with a non-Swedish background than they were for those who were Swedish.

In Study V, patients with higher scores on the DAPOS-D (>9 points) and with the treatment advice “Adjust activity” had 1.93 times excess of risk (RR=1.93; CI: 0.77–4.85) of continuing to suffer greater pain-related disability (DRI \geq 32 points) compared to patients with higher scores on the DAPOS-D (>9 points) with the treatment advice “Stay active” (Table 11), at four-day of follow up. Similar results were found regarding anxiety (DAPOS-A >6 points). In addition, the highest DRI scores were observed for patients with the lowest scores on the DAPOS-PO (\leq 10 points), i.e. with a less positive attitude, in the “Adjust activity” group, compared to patients with the lowest scores on the DAPOS-PO (\leq 10 points), in the “Stay active” group, on Days 1 and 4 of the follow up (Table 11).

Table 11. Comparison of the mean DRI scores at baseline and on Days 1 and 4 and scores on the DAPOS-D, DAPOS-A, and DAPOS-PO, in the two groups in Study V.

| DAPOS | DRI baseline Mean (SD) | DRI Day 1 Mean (SD) | DRI Day 4 Mean (SD) | Number n |
|------------------------------------|------------------------|---------------------|---------------------|----------|
| “Stay active” advice | | | | |
| DAPOS-D\leq9 | 75 (16) | 55 (19) | 37 (22) | 36 |
| DAPOS-D$>$9 | 71 (19) | 48 (25) | 33 (18) | 7 |
| “Adjust activity” advice | | | | |
| DAPOS-D\leq9 | 66 (24) | 47 (22) | 29 (19) | 42 |
| DAPOS-D$>$9 | 87 (8) | 70 (12) | 57 (21) | 6 |
| “Stay active” advice | | | | |
| DAPOS-A\leq6 | 75 (17) | 55 (19) | 37 (22) | 35 |
| DAPOS-A$>$6 | 73 (16) | 47 (24) | 31 (18) | 8 |
| “Adjust activity” advice | | | | |
| DAPOS-A\leq6 | 68 (23) | 47 (21) | 30 (18) | 43 |
| DAPOS-A$>$6 | 78 (23) | 68 (25) | 50 (38) | 5 |
| “Stay active” advice | | | | |
| DAPOS-PO\leq10 | 70 (21) | 47 (18) | 41 (18) | 10 |
| DAPOS-PO$>$10 | 76 (15) | 56 (20) | 35 (20) | 33 |
| “Adjust activity” advice | | | | |
| DAPOS-PO\leq10 | 83 (20) | 62 (23) | 49 (23) | 5 |
| DAPOS-PO$>$10 | 67 (23) | 48 (22) | 30 (22) | 43 |

DAPOS: Depression, Anxiety and Positive Outlook Scale. Cut-off: DAPOS-D, >9 points, which was the 90th percentile (5-25 points); DAPOS-A, <6 points, which was the 90th percentile (5-15); DAPOS-PO \leq 10 points, which was the 15 percentile (5-15). Ninety-one patients completed the DAPOS questionnaire.

4.3.3 Disability related to pain intensity, pain duration, and pain location

In studies I-III, the degree of sick leave was significantly associated with higher pain intensity scores, the number of pain sites, while a reduced ability to work was more common in neck pain. However, higher pain intensity scores were partially associated with longer periods of sick leave, and not associated with the duration of pain (*Tables 10- 12*). In Study IV, patients in whom the main pain site was the spine had longer periods of sick leave compared to patients whose main site of pain was another location (*Table 2*). Among the patients with spine pain, the duration of sick leave was positively associated with pain intensity ($p<0.05$) (*Table 12*).

In Study V, baseline VAS scores were significantly negatively correlated with the duration of sick leave (days), i.e. lower baseline VAS score was associated with a shorter period of sick leave ($p<0.05$).

Table 12. Correlations between pain intensity and excessive illness behaviour (Waddell signs), depressed mood (BDI and DAPOS-D), anxiety (STAI and DAPOS-A), number of pain sites, and sick leave in studies I and IV (the “spine sample”).

| Patients with CMP | Pain intensity (VRS) |
|----------------------------|----------------------|
| Study I-II (n=174) | |
| Waddell signs ¹ | 0.220** |
| BDI ² | 0.349** |
| Number of sites of pain | 0.282** |
| Pain duration | ns |
| Sick leave duration | ns |
| Sick leave degree | 0.238** |
| Study IV (n=144) | |
| BDI ² | 0.442** |
| DAPOS-D ³ | 0.380** |
| DAPOS-A ⁴ | 0.414** |
| STAI S ⁵ | 0.332** |
| STAI T ⁶ | 0.370** |
| Number of sites of pain | 0.090 |
| Pain duration | ns |
| Sick leave duration | 0.203* |

**Pearson’s correlation coefficient significant at $p<0.01$ (2-tailed test)

*Pearson’s correlation coefficient significant at $p<0.05$ (2-tailed test)

¹Excessive illness behaviour: Waddell signs; ²BDI: Beck Depression Inventory

³Depression Anxiety and Positive Outlook Scale (DAPOS): DAPOS-D subscale,

⁴DAPOS-A subscale, ⁵Anxiety: STAI S, ⁶Anxiety: STAI T

4.3.4 Disability related to distress

In Study I, excessive illness behaviour was associated with self-perceived disability and inability to work. In Study II, inability to work was more commonly seen in patients suffering from psychiatric illnesses.

In Study V, rates of pain-related disability decreased during the 1-week follow-up period ($p<0.01$); however, patients with depressed mood exhibited more pain-related disability in combination with the treatment advice “Adjust activity” over time (*Tables 5-6*).

5 GENERAL DISCUSSION

The explanation and prediction of the participants' experiences of pain and consequent disability form the cornerstone of this thesis. This work confirms that psychosocial factors play a central role in the prolongation of pain, especially of spine pain. The biopsychosocial approach used in this thesis might enable patients at risk of developing spine pain-related disability to be identified.

I will now address the questions posed in the introduction (Page 6):

- Can the presence of physical symptoms/organic signs alone explain the duration of sick leave in CMP, and pain-related disability in acute musculoskeletal pain?
- How strong is the association between physical symptoms/organic signs and the prolongation of pain in patients on long-term sick leave due to CMP, and disability, in both acute musculoskeletal pain and CMP?

5.1 Physical symptoms that explain pain prolongation, pain intensity, and disability

The results presented here show that the main pain location and the presence and extent of physical signs (number of pain locations) are not correlated with the duration of CMP. It is important to keep in mind that a correlation does not imply causality. However, Studies II-III show that multiple pain sites were associated with worse pain intensity and diminished physical function. Previous studies have found moderate correlations between the number of pain sites and disability, pain severity, and the tendency to focus on and report physical symptoms.¹⁶⁷ The presence of multiple pain sites as a physical comorbidity was frequently seen, especially among patients whose main site of pain was the neck (studies I-IV). The results presented in this thesis agree with the postulation that isolated neck pain is extremely rare.^{7,168} Pain in multiple sites is typically regarded as comorbid to single-site pain,¹⁶⁹ and it is more severe and disabling than single-site pain.¹⁷⁰

The rating of pain intensity decreased over time in acute LBP (Study V), which probably mimics the natural course of acute LBP. However, patients with the highest baseline scores for pain intensity continued with the highest scores on pain intensity during, and at the end of the follow up.

Regarding pain location, patients with pain in the spine were more likely to report "Severe" or "Very severe" pain intensity than patients with primary pain in another location (Table 8, and Studies I-IV). The prevalence of chronic neck pain was 59% in patients on long-term sick leave (Study II), 9.7% in the spine group, and 9.5% in the reference group (Study IV). The prevalence of chronic neck pain in the general population in Sweden is in the range 9 to 22%.^{37,171} The prevalence in other countries is between 24 and

There were no differences in the duration of chronic or acute pain according to sex or ethnic background. The results presented here show that women and patients with a non-Swedish background experience greater pain, which agrees with previous Swedish research.¹⁷⁴⁻¹⁷⁵ Other reports, however, present contradictory results relating to pain severity as a prognostic factor for the chronicity of pain in patients with neck pain and LBP.¹⁷⁶⁻¹⁷⁸ These results indicate that the predictive value of pain intensity varies, which agrees with the results presented in this work.^{20, 86, 179}

5.1.1 Pain analyses: characteristics and effect on disability

The physical symptoms/signs (pain intensity, pain characteristics, number of pain sites, type of diagnosis) did not explain the duration of long-term sick leave in the patients studied in Studies I-III. The duration and degree of disability was related to other factors in most of those who received a psychiatric evaluation. Additionally, pain intensity was positively associated with longer periods of sick leave in Study IV, in the “spine sample” (Table 12). A clinical implication of the relationship between pain intensity and disability is the impact that the duration of sick leave will have on the recovery of patients with CMP. For instance, the preoperative duration of sick leave is the main predictor of both subjective and objective outcomes in patients with disc herniation who receive surgical treatment.¹⁸⁰ Furthermore, higher baseline VAS scores were correlated with sick leave in Study V. In this study, 93% of patients returned to work within a week of the onset of acute LBP, which agrees with previous results.¹⁸¹

In summary, chronic spinal pain, independently of the type of diagnosis (specific or nonspecific), is associated with multiple pain sites, greater pain, longer periods of pain, and occurs more frequently among women. A significant number of patients with CMP have somatic comorbidity, which contributes to substantial disability. We can conclude that a particular combination of parameters rather than a single physical sign, explains the prolongation of pain and disability in these patients.

5.2 Psychosocial factors that explain pain prolongation, pain intensity, and disability

Psychological factors are associated with intensity of pain (Studies I-V, Table 5-12). The identification and modification of psychosocial factors should be an aim in the management of nonspecific CMP.¹⁸²⁻¹⁸⁴ There are people in the primary healthcare system who are experiencing distress and suffering from nonspecific CMP who share the same, or almost the same, psychological profile as patients with other chronic diseases.

5.2.1 Excessive illness behaviour

Excessive illness behaviour compromises an important construct that is relevant in the maintenance of CMP.^{38,116} Objective physical findings that support their complaints of pain are absent for many patients with orthopaedic complaints, and the intensification of their illness behaviour may lead to avoidance behaviour.¹²⁰ One quarter of patients on long-term sick leave in Study I exhibited WS, indicating emotional or psychological distress. Excessive illness behaviour was unrelated to age and was unrelated to loss of physical function, but was related to depressed mood, higher self-rated disability, and greater pain intensity. These results are consistent with those of other studies, which have shown that between 12 and 36% of patients with chronic neck and low back pain exhibit excessive illness behaviour.³⁸ Excessive illness behaviour is a major factor concluding that a patient with CMP is dysfunctional.^{117,185}

5.2.2 Mental health comorbidity

Psychiatric evaluation of patients on long-term sick leave (studies II-III) revealed a high prevalence (84%) of unrecognised/untreated mental health comorbidity. However, 56% of patients who only underwent an orthopaedic evaluation in Study II suffered from depressed mood (BDI \geq 13 points), while 43% of patients from the spine sample in Study IV did so. Individuals with high levels of pain, illness, social and work inactivity and other psychological stressors are more liable to experience pain prolongation and disability.¹⁸⁶⁻¹⁸⁹ Half of the participants who underwent psychiatric evaluation (studies II-III) were non-Swedish patients who were affected by various psychiatric disorders, which agrees with previous Swedish findings.¹⁹⁰ Women with CMP, especially those with spine pain (studies II-III), suffered from mental health comorbidity, particularly depression, more often and this also agrees with previous results.^{46,58}

5.2.3 The effect of distress on pain intensity

The intensity of both chronic and acute pain was associated with psychological distress. Half of the patients with CMP were in a depressed mood, and these patients experienced the greatest pain intensity. Damush et al. found that depression and pain severity in CMP have different effects on self-management practices.¹⁹¹ They showed that the severity of depression is a significant barrier to patients' self-involvement in the management of pain.

Furthermore, this thesis shows that, although pain intensity decreases over time in acute LBP, it can be negatively influenced by distress. The treatment advice "Adjust activity" also affects acute LBP negatively. This result suggests that distress in combination with physical inactivity may play a more important role than pain intensity alone in predicting the duration of acute LBP. A large cohort study has shown that initial pain intensity predicts the duration of pain experience, that the initial level of disability predicts long-term disability, and that the presence of depression initially in the course predicts later depression among patients

with acute LBP.¹⁷⁶ The work presented here supports all of these conclusions. A minority of patients in Study V with LBP exhibited fear of movement. Other studies have shown that patients with LBP and fear of movement develop CMP.^{119,120} However, relationships of fear, anxiety, and depression with physical function have also been observed among patients with knee osteoarthritis.¹⁹²

5.2.4 The effect of distress on disability

Greater experience of pain-related disability was observed with time in patients with LBP who experienced depressed mood (DAPOS-D >9) and who were given the treatment advice “Adjust activity”.

A more intense experience of pain was often associated with disability and a higher degree of sick leave (studies I-III). Psychiatric disorders among patients on long-term sick leave have been frequently unrecognised due to a lack of multidisciplinary team assessment, and a lack of training in how to apply guidelines for assessing the ability to work in CMP.^{57,193} As a consequence, diagnoses and levels of work ability have been difficult to establish for these patients.¹⁹⁴ Furthermore, women with CMP were most likely to remain on long-term sick leave due to mental health comorbidity. This emphasises the need to investigate other factors in nonspecific spine pain, as others have also pointed out.¹⁹⁵ Moreover, long-term sick leave is considerably more common in patients with lumbar disc herniation than it is in, for example, patients with pain in the knee.^{180,196}

In summary, the results suggest that pain intensity, duration of sick leave and an inability to work are associated with psychological distress in CMP (studies I-IV). Distress in acute severe LBP affects pain-related disability, in the presence of low physical activity, in the short- time (Study V).

5.3 Patient’s compliance and physical activity in acute LBP

Patients with acute severe LBP tended to comply with the treatment advice, “Stay active” or “Adjust activity according to pain”, despite the fact that the advice to “Stay active” initially had a negative effect on pain-related disability. Over time, the step counts reported by the “Stay active” group increased to a greater extent than those reported by the “Adjust activity” group. This tendency was especially clear during the final two days of the follow-up. However, some patients with a greater experience of pain avoidance (TSK \geq 38) were more likely to report lower step counts, independently of the advice they received. Furthermore, all subjects in the “Stay active” group, even those with a depressed mood, became physically more active, something not seen in the “Adjust activity” group. Patients in the “Stay active” group were encouraged to be as active as possible and to continue with normal daily activities. Some of them continued with sports, exercise, and work activities, which may explain their greater scores for pain intensity and pain-related disability related to movements in which the spine is actively involved, especially during the first three days of follow up (Figure 3). Previous studies have shown that pedometer users significantly increase their physical activity

when given a step goal. However, this conclusion is based on data from different periods of time and from different populations.¹⁹⁷ Most of patients included in Study V were satisfied with the attention and treatment they received. Patient satisfaction is the most important condition for compliance with advice and in the evaluation of the effectiveness of treatment.¹⁹⁸ It is probable that the extensive physical examination, careful evaluation, and “coaching” given during the first week after the acute phase were convincing, and made the subjects in both groups receptive to the different treatment advice. Informing the patient about clinical findings, and reassuring patients that they do not have a serious disease and that their prognosis is generally favourable, play an important role in the management of acute severe LBP.¹⁹⁹ All patients returned to work within 8 days.

The mechanisms by which patients cope with nonspecific LBP are determined by several factors some of which are not related to physical pathology. Such factors include the experience by the patient of distress, and the attitudes and advice of healthcare givers.^{140-146,200-202} A positive attitude motivates patients to return to work early and stimulates recovery.²⁰³ The work presented here shows the importance of adopting a more biopsychosocial and less biomedical approach to LBP and CMP in general, as others have previously shown.^{184, 204}

5.4 Methodological considerations: strengths and limitations

5.4.1 Epidemiological considerations

The design of an epidemiological study must be appropriate for achieving the objectives, and the selection of the subjects should ensure that the results are valid. The patients included in studies I-III constituted a group that had been selected by the Social Insurance Office and the results obtained from this group cannot be extrapolated to general healthcare settings. They can, however, be extrapolated to other specialised units in Sweden that assess medical conditions and the ability to work. These studies provide specific information and identify factors that are associated with long-term sick leave due to CMP, but they do not prove causality. Thus, mental health comorbidity may cause CMP, or it may be caused by CMP.

The majority of participants in Study V working at private manufacturing companies were men (72%). The proportions of men and women and the proportions of blue-collar and white-collar workers in our study corresponded to the proportions employed at the companies involved. The main advantage of an RCT is the possibility of calculating relative risk. The calculated RR for disability after one week in this study may be applied to any other population working in similar conditions. Moreover, bias in the distribution of confounders was avoided by randomisation and blinding, and by following strict inclusion/exclusion criteria, thus ensuring that the results have internal validity. Results from RCT studies can, however, be biased by volunteer bias.

5.4.2 Considerations when applying statistical models in clinical studies

Research may have clinical significance even if statistical significance is not reached. The power of Study V was affected by the small sample size, and this was probably the main cause of the failure to reach statistical significance when comparing the treatment groups in the final linear mixed models. The target recruitment number was 66 patients per group, which, it had been estimated, was required to achieve sufficient statistical power. However, it was not possible to achieve this number because of our strict definition of acute severe LBP. Nevertheless, the mean daily step count was consistently higher in the “Stay active” group than it was in the “Adjust activity” group. Missing data and loss to follow-up can substantially reduce the sample size in a longitudinal survey, particularly if observations are made on more than two occasions.^{158,205} It cannot be excluded that a type II error has occurred.⁴ The majority of the patients who did not report pain intensity and related disability for Days 6 and 7 in the diary explained that it was because they were free of pain and they did not need to report it.

5.4.3 Considerations regarding the usefulness of self-report questionnaires

Pain and distress questionnaires

Pain and distress are hypothetical constructs and are not directly observable. They can be measured only indirectly through subjective scores. Such scores reflect personal experiences of pain, and measure much more than a purely physical sensation. They can be inflated or diminished by such factors as the intensity of the person’s interest, social requirements, and the spontaneous reaction of the person to the questions.^{206, 207} Nevertheless, a number of studies have demonstrated that self-report questionnaires can accurately measure functional status.¹⁵⁸ Pain is a multidimensional phenomenon, and assessment of mood is necessary to identify sources of hindrance in people suffering from CMP. Most of the assessment instruments used to measure depressed mood, however, have not been designed for populations with CMP.^{208,209}

Validity of scores from a measuring instrument

The agreement between the BDI instrument using a cut-off of 13 and the structured clinical interview for DSM disorders was 80% (Study III). The BDI cut-off was based on previous recommendations regarding the adequacy of the BDI cut-off for patients with CMP.²¹⁰ The prevalence of depression determined by the BDI instrument in the “spine sample” (43%) was very similar to that determined by the DAPOS (44%) (Table 9). Half of the patients in the “extremity sample” did not complete the questionnaires (BDI/STAI), so we could not compare the prevalence of distress assessed by these instruments. These results agree with previous research suggesting that a BDI cut-off stricter than the original one of 10 points should be used.²¹¹

Table 13. DAPOS scores for the different populations.

| <i>Subscale¹</i> | <i>DAPOS-D Mean (SD)</i> | <i>DAPOS-A Mean (SD)</i> | <i>DAPOS-PO Mean (SD)</i> |
|---------------------------------------------------------------------|------------------------------|------------------------------|-------------------------------|
| <i>Study</i> | | | |
| <i>Pincus Study, 2004² Osteopathic clinic sample</i> | 8.6 (3.4) | 5.3 (2.6) | 11.8 (2.4) |
| <i>Pain management sample</i> | 12.4 (5.3) | 7.6 (3.7) | 9.3 (2.9) |
| <i>Pincus Study, 2008³ Pretest</i> | 12.2 (5.1) | 7.5 (3.7) | 8.0 (3.2) |
| <i>Posttest</i> | 9.6 (4.1) | 5.9 (2.9) | 10.2 (2.5) |
| <i>Study IV⁴ Spine sample</i> | 9.2 (4.5) | 6.1 (3.5) | 9.9 (3.2) |
| <i>Extremities sample</i> | 7.9 (3.7) | 4.8 (3.1) | 11.3 (2.9) |
| <i>Control group</i> | 8.3 (2.8) | 4.4 (1.7) | 12.5 (2.5) |
| <i>Study V⁵ “Stay active” group</i> | 7.7 (2.6) | 4.2 (1.6) | 12.1 (2.0) |
| <i>“Adjust activity” group</i> | 6.7 (2.2) | 3.6 (1.2) | 12.8 (1.6) |

¹Depression Anxiety and Positive Outlook Scale (DAPOS): DAPOS-D depression subscale; DAPOS-A, anxiety subscale, DAPOS-PO positive outlook subscale; ²Patients with CMP from two separate centres, a pain-management clinic (n=190) and a self-referral outpatient osteopathic clinic (n=204); ³Patients with CMP from a pain-management clinic (n=83); ⁴Patients with CMP from two different clinical settings—a general orthopaedic setting (n=144) and an occupational orthopaedic setting (n=144)—and a control group (n=161); ⁵Patients with acute LBP (48 patients in the “Stay active” group and 53 in the “Adjust activity” group)

Cross-cultural validation of the DAPOS, Study IV

Many questionnaires used in research are not validated after translation into another language in which they will be used. We have cross-validated the DAPOS in the Swedish language before carrying out the work presented here. The theoretical structure of the original DAPOS is valid also for the Swedish version. Scores on DAPOS for patients with CMP were similar to those reported previously in patients with CMP.^{154,212} Furthermore, participants in the reference group in Study IV, as well as the participants in Study V, reported (as expected) the highest scores on the DAPOS-PO. This confirms the utility of the scale in measuring distress and positive affect in a concise manner in a Swedish cultural setting (Table 13).

Structure invariance of a measuring instrument

An instrument that shows measurement invariance or equivalence in its structure can be applied across different populations because construct validity is ensured. In this work, only measurement invariance was reported. The DAPOS was designed to be used in patients with CMP, and thus we can be even more sure that its construct validity is valid.²¹² The DAPOS subscales are equivalent with respect to sex, and thus the DAPOS assesses the three constructs in the same way in both women and men. It is important to remember that the diagnostic groups were chosen arbitrarily, based on the main site of pain. This probably explains the

results presented here regarding partial invariance across diagnostic groups. Invariance across sex or groups based on site of pain has not previously been reported, and thus there are no results to compare with the results in this thesis. Pincus has reported that some patients find Item 11 difficult to answer,²¹² and, indeed, some of the patients in the “spine sample” also found this.

Construct validity, representativeness, and generalisability of the DAPOS

Confirmatory factor analysis (CFA) considers the covariance of the scores. Thus, results from CFA are valid and may be generalised. The results from the DAPOS obtained in Study IV can probably be generalised to all other patients with CMP in orthopaedic settings in Sweden. Furthermore, information on distress/positive affect obtained from the control group can be extrapolated to the population from which the controls came. Scores on the DAPOS in the control group were compared with scores on the DAPOS in patients with acute LBP (Study V; Table 13). In both groups, the mean/median values for the scores for each subscale were very similar. This information may be used for international comparisons of further normative DAPOS data. The results presented here confirm the usefulness and validity of the scale and agree with previous results.²¹² DAPOS measures distress and positive outlook in patients with CMP: it is quick to apply and has excellent construct validity. Screening for distress in patients with CMP can help to identify those patients with mental health comorbidity who need to be referred for further psychological or psychiatric evaluation and treatment.

5.5 Clinical and research implications

5.5.1 Patients with CMP in focus

The work presented here has confirmed that CMP is a complex multidimensional problem. Understanding this complexity is vital for individualised treatment and for determining how treatment goals can be identified in the best way for each patient on long-term sick leave due to CMP. These aspects have been discussed in previous research.^{213,214} The findings of this thesis show greater pain and long-term disability among patients with nonspecific CMP, many of whom were unemployed, women and immigrants, and of whom half had undiagnosed mental health comorbidity. These findings suggest the need to focus on a target evaluation/treatment of these patients. Screening and diagnosis of mental health comorbidity should be incorporated into the pain analysis routine in primary healthcare and insurance medicine to detect hidden illness and treat it accordingly. Models for the management of acute back pain and CMP are condensed in existing recommendations and guidelines for the management of pain, and they are supported by different approaches.^{147,198,213} They highlight the need to improve interpersonal, behavioural, and cognitive evaluation at the primary healthcare, to interrupt the prolongation of pain.²¹³⁻²¹⁵ Furthermore, the guidelines describe flows to address the multi-professional stepwise management of patients with nonspecific pain, especially in

the spine.^{147,199} They take into account the implications for clinical practice, since mental health comorbidity affects pain intensity and the level of sick leave taken by patients with CMP.

5.5.2 Patients with acute severe LBP in focus

The results of this thesis confirm the usefulness of the “Stay active” advice and of returning early to work. The main contribution of this work is the early identification of the signs of depressed mood and fear avoidance in patients with acute severe LBP, which, over time, leads to passive/avoidance behaviours in some patients.

The “Adjust activity” advice has a negative short-term effect on pain-related disability in patients with distress, and thus focusing on activity rather than pain should help patients with acute severe LBP to cope with their pain and to continue to be as active as possible. Screening for distress in patients with acute LBP may help to target patient self-management and to develop short-term target plans that prevent pain prolongation and disability. A comprehensive pain management regimen with an interdisciplinary team, offering evaluation, information, advice, and treatment, may play an important role in the first contact with a patient with acute severe LBP. Consequently, an effective way to prevent the development of long-lasting problems is to support acute LBP patients who demonstrate signs of distress, particularly when nonspecific pain is of concern.

This work shows that a successful short-term outcome can be expected if the advice “Stay active” is followed.

5.6 Ethical considerations

5.6.1 The long-term use of opioids for the relief of nonspecific CMP

Important clinical issues, such as physical dependency, tolerance, cognitive dysfunction, abnormal pain sensitivity, and dysfunction of the immune and reproductive systems, may be sufficient reasons to limit the long-term use of opioids for the relief of nonspecific CMP in primary care, as previously recommended.⁹⁷ Whether or not to continue with oral opioid therapy for CMP is controversial.¹⁰³ Opioids are not recommended as the first-line treatment to relieve pain in acute LBP.¹⁹⁹ Adverse effects such as dependence, tolerance, and addiction occur in patients with CMP who receive opioids.^{96,217}

It is important to highlight two points regarding the management of CMP. First, long-term oral opioid therapy is not recommended, according to international guidelines, for patients with nonspecific CMP due to the known side effects.^{103,199,217} Second, recovery is not possible in patients with unrecognised mental health comorbidity, while oral opioids are being consumed.

5.6.2 Women with chronic pain in focus

The International Association for Study of Pain recognises that women report more pain than men, and that sex and gender differences in pain experience can guide the clinical management of pain.²¹⁹ In orthopaedics, for example, low-energy vertebral compression fracture has been regarded as a condition with a relatively good prognosis. However, detailed studies showed that women aged 40-85 years reported much worse functional limitation, pain, and quality of life one year after the acute fracture than men did. This contradicted the prevailing belief of a benign prognosis in the great majority of patients with such fractures.²²⁰ We have shown that mental health comorbidity is higher in women than in men with CMP, in agreement with previous results.²²¹ A clear gender difference with respect to chronic back pain, has been previously reported, with more women than men being affected by this condition.²²¹ It has been postulated that women with chronic pain struggle to convince physicians that their pain is real.⁵⁴ The expression “to be taken seriously and to be believed” should contribute to understanding the patient’s experience of CMP, and thus improve the physician’s ability to treat pain in all patients.

5.7 Conclusions

This thesis demonstrates the association between psychological factors and both pain intensity and disability, in both acute severe LBP and CMP. It highlights the need for routine screening for distress in these patients, in both primary healthcare and insurance medicine, to give a better understanding of CMP and more accurate evaluation.

The early identification of distress and fear of movement, and giving the advice to “Stay active” early in the episode of care, may prevent pain-related disability in patients with acute severe LBP.

Study I: Excessive illness behaviour is associated with psychological distress in patients on long-term sick leave due to CMP. Looking for illness behaviour during consultation is useful for targeting other factors that may be important in estimating function and diagnosing symptoms.

Study II: Both somatic and mental health comorbidity are commonly seen in patients on long-term sick leave due to CMP. The ability to work and level of sick leave in these patients is often determined by undiagnosed psychiatric comorbidity; not solely by the orthopaedic complaint. Diagnosis of mental health comorbidity changes the cause of the inability to work from somatic to psychiatric.

Study III: The sensitivity of the BDI is good enough to enable the orthopaedic surgeon to detect symptoms of depression when other psychiatric assessments are not available. The prevalence of undiagnosed psychiatric disorders is high (84%) in patients on long-term sick leave due to CMP.

Study IV: The Swedish version of the DAPOS screens distress and positive outlook in patients with CMP quickly and with excellent construct validity. This makes it possible to screen for distress to identify patients with CMP who may need referral for psychological or psychiatric treatment.

Study V: Pain-related disability is modified differently by distress when patients are given different treatment advice. Patients who experience distress and who are advised to avoid physical activities exhibit greater pain intensity and disability in the short term. Thus, “Stay active” is the appropriate advice for the treatment of acute severe LBP to prevent pain-related disability, even in persons with pronounced distress.

Study V: Treatment advice given in acute severe LBP is complied with. The “Stay active” advice increased physical activity in all subjects. However, the level of physical activity was affected by fear of movement, independently of the treatment advice.

5.8 Future perspectives

The following aspects will be important in future pain analysis research that focuses on nonspecific CMP:

- Evaluation of therapy outcomes for nonspecific CMP in terms of a return to work and pain relief in primary care settings
- Evaluation of the implementation of policies promoting physical activity in special target groups with nonspecific CMP, focusing on acceptance and self-involvement in the management of pain
- Investigation of compliance with international guidelines in the management of first-time acute LBP, recurrent LBP, and chronic LBP, in primary healthcare, particularly the evaluation of the international recommendations for the management of acute and chronic spinal pain in Sweden
- Performance of international comparisons of further normative DAPOS data.

6 SVENSK SAMMANFATTNING

Syfte: Syftet var att identifiera faktorer som påverkar upplevelsen av smärta och funktionsförmåga hos patienter med akut och kronisk muskuloskeletal smärta (KMS), och att validera den svenska versionen av DAPOS-skalan (Depression, Anxiety, and Positive Outlook Scale). Ett ytterligare syfte var beskriva den konceptuella strukturen för smärta i rörelseapparaten, ff. i ryggen, och dess hantering i primärvården.

Metod: I tre tvärsnittsstudier (I–III) inkluderades 174 patienter, varav 51 % var kvinnor och 46 % var icke-svenska patienter, som var långtidssjukskrivna på grund av KMS. Medelåldern var 45 (23–62) år. Alla var sjukskrivna på grund av en somatisk diagnos (M 00–99) och remitterade från Försäkringskassan för en bio-psyko-social funktionsanalys för bedömning av diagnos och arbetsförmåga. Alla patienterna genomgick en ortopedisk undersökning och besvarade följande frågeformulär före läkarbesöket: Verbal Rating Scale skattar smärtintensitet, Disability Rating Index skattar egen funktionsförmåga och Beck Depression Inventory mäter stämningsläge. Abnormalt smärtbeteende mättes med sex Wadells tecken under besöket hos ortoped. Försäkringskassan remitterade 83/174 patienter för en ytterligare psykiatrisk undersökning. **I:** Associationen mellan abnormalt smärtbeteende och kliniskt status, smärtintensitet, depression, egenskattad funktionsförmåga, kön, och sjukfrånvarons varaktighet undersöktes (174/174). **II:** Förekomst av somatisk och psykisk samsjuklighet hos patienter i långvarig sjukskrivning på grund av KMS studerades. Patientens förmåga att arbeta före utvärderingen jämfördes med förmågan att arbeta a) efter enbart ortopedisk bedömning (91/174) och b) efter teambedömning gjord av ortoped och psykiater (83/174). **III:** Sänkt stämningsläge mätt med Beck Depression Inventory (BDI) jämfördes med diagnosen depression fastställd av psykiater (71/83). **IV:** I en valideringsstudie undersöktes de psykometriska egenskaperna hos den svenska versionen av DAPOS, 11 frågor, med hjälp av konfirmatorisk faktoranalys hos 288 patienter med KMS och 161 kontroller. **V:** I en randomiserad kontrollerad studie av 109 patienter med akut ländryggsmärta undersöktes hur stämningsläge, oro och rörelserädsla påverkar smärtintensitet, funktionsförmåga och fysisk aktivitet. Följsamheten till rådet "håll dig aktiv" trots smärta jämfört med "anpassa din aktivitet" till smärta mättes med hjälp av en dagbok under 7 dagar. I dagboken noterade patienten sin smärtintensitet, funktionsförmåga och antal steg per dag mätt med stegräknare.

Resultat: I: Abnormalt smärtbeteende påvisades hos 27 % av patienterna. De hade högre grad av sänkt stämningsläge, högre smärtintensitet och längre sjukfrånvaro.

II: Nacksmärta var den vanligaste huvuddiagnosen (103/174). Nästan alla patienter (99 %) med huvudsaklig nacksmärta hade 2 eller flera smärtlokalisationer. De rapporterade högre smärtintensitet, större egenskattad funktionsnedsättning och fler av dem var helt sjukskrivna. Av de patienter som undersöktes enbart av ortoped bedömdes 99 % (90/91) kunna återgå till arbete i olika grad. Av dem hade 56 % sänkt stämningsläge (BDI \geq 13).

Av de patienter som genomgick teambedomning hade 84 % (70/83) psykiatriska diagnoser, och 93 % av dem hade tidigare odiagnostiserade psykiatriska sjukdomar. Depression var den vanligaste orsaken till funktionsnedsättande samsjuklighet, särskilt bland kvinnor och invandrare.

Av de patienter som genomgick teambedomning hade 63 % (52/83) full arbetsförmåga om den baserades på resultaten från fysisk undersökning. Tidigare odiagnostiserad psykiatrisk sjukdom ändrade huvudorsaken till oförmåga att arbeta hos 69 % (36/52) av dem. En tredjedel av patienterna rapporterade långtidsmedicinering med opioider (55/174). **III:** Överensstämmelsen mellan BDI och diagnosen depression fastställt av psykiater var 80 %. Sensitiviteten var 88 % hos BDI att korrekt identifiera depression hos dessa patienter. **IV:** Den svenska versionen av DAPOS uppvisade god tillförlitlighet och validitet för att mäta stämningsläge, ångest och positiv livsinställning hos patienter med KMS. De tre delskalorna av DAPOS var invarianta med avseende på kön, dvs. DAPOS fångade på samma sätt stämningsläge, ångest och positiv livsinställning hos kvinnor och män. **V:** Smärtintensitet och funktionsnedsättning minskade snabbt över tid för alla patienter med akut svår ländryggsmärta ($P < 0,001$). Alla patienter återgick i arbetet inom 8 dagar. Patienter med sänkt stämningsläge (DAPOS-D > 9) och som fick rådet "anpassa din aktivitet" till smärtan rapporterade högre smärtintensitet och funktionsnedsättning följande dagar jämfört med patienter med sänkt stämningsläge som fick rådet "håll dig aktiv" trots smärta (relativ risk RR=1,93 CI=0,77–4,85). Patienter utan rörelserädsla (TSK < 38 poäng) uppvisade större fysisk aktivitet, dvs. fler steg, oavsett vilket råd de fick.

Slutsatser: Att mäta antal Wadells tecken under konsultation hjälper ortopederna att upptäcka andra faktorer som påverkar smärtintensitet och sjukfrånvaro hos patienter med KMS. Odiagnostiserad psykiatrisk samsjuklighet är vanligt förekommande hos patienter med långvarig sjukskrivning på grund av KMS. BDI är ett lämpligt instrument att använda inom somatisk sjukvård för att bekräfta sänkt stämningsläge. Den svenska versionen av DAPOS kan ersätta de 61 frågorna från BDI och STAI frågeformulären. Rutinmässig bio-psycho-social funktionsanalys av patienter med smärta i rörelseapparaten skulle kunna öka förståelsen för denna patientgrupp och möjliggöra andra behandlingsalternativ i primärvården. Vid KMS är de psykologiska faktorerna associerade med smärtintensitet, funktionsnedsättning, och arbetsförmåga. Vid akut ländryggsmärta påverkar de psykologiska faktorerna smärtintensitet, funktionsnedsättning, och fysisk aktivitetsnivå. Rådet "håll dig aktiv" trots smärta är det lämpligaste rådet för att undvika smärtrelaterade funktionsnedsättning de närmaste dagarna hos patienter med akut ländryggsmärta.

Nyckelord: smärtanalys, muskuloskeletal smärta, psykiatrisk samsjuklighet, smärtintensitet, funktionsförmåga, ryggsmärta, ländryggsmärta, arbetsförmåga, sänkt stämningsläge oro, följsamhet

7 APPENDIX

| | |
|---------------|---------------------|
| Personnummer: | |
| Namn: | Yrkesortopeden SU/S |

Nedan följer olika erfarenheter som andra patienter delgivit oss. Var vänlig och ringa in lämplig siffra från 1-5 för varje påstående. Läs och besvara varje påstående så gott Du kan i Din nuvarande livssituation.

| | Nästan Aldrig | | | | Nästan hela tiden |
|-------------------------------------------------------------------------|------------------|---|---|---|----------------------|
| 1. Jag känner mig misslyckad | 1 | 2 | 3 | 4 | 5 |
| 2. Jag får en skrämmande känsla av att något hemskt är på väg att hända | 1 | 2 | 3 | 4 | 5 |
| 3. Jag har skuldkänslor | 1 | 2 | 3 | 4 | 5 |
| 4. Jag kan skratta och se den roliga sidan av saker och ting | 1 | 2 | 3 | 4 | 5 |
| 5. Jag är besviken på mig själv | 1 | 2 | 3 | 4 | 5 |
| 6. Jag får en skrämmande känsla, som en klump i magen | 1 | 2 | 3 | 4 | 5 |
| 7. Jag känner mig glad | 1 | 2 | 3 | 4 | 5 |
| 8. Jag lägger ständigt skulden på mig själv | 1 | 2 | 3 | 4 | 5 |
| 9. Jag får en plötslig känsla av panik | 1 | 2 | 3 | 4 | 5 |
| 10. Jag ser fram emot saker och ting med glädje | 1 | 2 | 3 | 4 | 5 |
| 11. Jag har tänkt på att skada mig själv | 1 | 2 | 3 | 4 | 5 |

8 REFERENCES

1. **Kline RB**. Principles and practice of structural equation modeling. New York: 2nd Edition, Guilford Press; 2005. p. 63-90.
2. **Indrayan A**. Medical biostatistics. Boca Raton, FL: 2nd Edition, Chapman & Hall/CRC; 2008. p. 439-522.
3. **Loeser JD, Treede RD**. The Kyoto protocol of IASP Basic Pain Terminology. *Pain*. 2008;137:473-477.
4. **Gross Portney L, Watkins M**. Foundations of clinical research: applications to practice. Upper Saddle River, New Jersey: 2nd Edition, Prentice Hall; 2008. p. 347-351.
5. **Rustoen T, Wahl AK, Hanestad BR, Lerdal A, Paul S, Miaskowski C**. Prevalence and characteristics of chronic pain in the general Norwegian population. *Eur J Pain*. 2004;8:555-565.
6. **Picavet HS, Schouten JS**. Musculoskeletal pain in the Netherlands: prevalences, consequences and risk groups, the DMC(3)-study. *Pain*. 2003;102:167-178.
7. **Carnes D, Parsons S, Ashby D, Breen A, Foster NE, Pincus T, Vogel S, Underwood M**. Chronic musculoskeletal pain rarely presents in a single body site: results from a UK population study. *Rheumatology (Oxford)*. 2007;46:1168-1170.
8. **Demyttenaere K, Bonnewyn A, Bruffaerts R, Brugha T, De Graaf R, Alonso J**. Comorbid painful physical symptoms and depression: prevalence, work loss, and help seeking. *J Affect Disord*. 2006;92:185-193.
9. **Keeley P, Creed F, Tomenson B, Todd C, Borglin G, Dickens C**. Psychosocial predictors of health-related quality of life and health service utilisation in people with chronic low back pain. *Pain*. 2008;135:142-150.
10. **Huijnen IP, Verbunt JA, Peters ML, Delespaul P, Kindermans HP, Roelofs J, Goossens M, Seelen HA**. Do depression and pain intensity interfere with physical activity in daily life in patients with Chronic Low Back Pain? *Pain*. 2010;150:161-166.
11. **Truchon M, Cote D, Schmouth ME, Leblond J, Fillion L, Dionne C**. Validation of an adaptation of the stress process model for predicting low back pain related long-term disability outcomes: a cohort study. *Spine (Phila Pa 1976)*. 2010;35:1307-1315.
12. **Thomee P, Wahrborg P, Borjesson M, Thomee R, Eriksson BI, Karlsson J**. [Self-belief--basis for successful rehabilitation. Confidence in one's own ability a strong predictor in orthopedic injury]. *Lakartidningen*. 2009;106:1975-1977.
13. **Turk DC, Flor H**. Chronic pain: a biobehavioral perspective. In: Gatchel RJ, Turk DC, Eds. *Psychosocial factors in pain: critical perspectives*. New York: Guilford Publications; 1999. p. 18-34.
14. **Wasiak R, Young AE, Dunn KM, Cote P, Gross DP, Heymans MW, von Korff M**. Back pain recurrence: an evaluation of existing indicators and direction for future research. *Spine (Phila Pa 1976)*. 2009;34:970-977.
15. **Hansson EK, Hansson TH**. The costs for persons sick-listed more than one month because of low back or neck problems. A two-year prospective study of Swedish patients. *Eur Spine J*. 2005;14:337-345.
16. **Maetzel A, Li L**. The economic burden of low back pain: a review of studies published between 1996 and 2001. *Best practice & research*. 2002;16:23-30.
17. **Wadell G**. Preventing incapacity in people with musculoskeletal disorders. *Br Med Bull*. 2006;(77-78):55-69.
18. **Andren D**. Long-term absenteeism due to sickness in Sweden. How long does it take and what happens after? *Eur J Health Econ*. 2007;8:41-50.
19. **Croft PR, Macfarlane GJ, Papageorgiou AC, Thomas E, Silman AJ**. Outcome of low back pain in general practice: a prospective study. *BMJ (Clinical research ed)*. 1998;316:1356-1359.
20. **Demmelmaier I, Lindberg P, Asenlof P, Denison E**. The associations between pain intensity, psychosocial variables, and pain duration/recurrence in a large sample of persons with nonspecific spinal pain. *Clin J Pain*. 2008;24:611-619.
21. **Henschke N, Maher CG, Refshauge KM, Herbert RD, Cumming RG, Bleasel J, York J, Das A, McAuley JH**. Prognosis in patients with recent onset low back pain in Australian primary care: inception cohort study. *BMJ*. 2008 Jul 7;337:a171.
22. **Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, Mannion AF, Reis S, Staal JB, Ursin H, Zanoli G**. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. *Eur Spine J*. 2006;15 Suppl 2:S192-300.
23. **Turk DC, Dworkin RH, McDermott MP, Bellamy N, Burke LB, Chandler JM, Cleeland C, Cowan P, Dimitrova R, Farrar J, Hertz S, Heyse JF, et al**. Analyzing multiple endpoints in clinical trials of pain treatments: IMMPACT recommendations. Initiative on Methods,

- Measurement, and Pain Assessment in Clinical Trials. *Pain*. 2008;139:485-493.
24. **Jorgensen CK, Fink P, Olesen F.** Psychological distress among patients with musculoskeletal illness in general practice. *Psychosomatics*. 2000;41:321-329.
25. **Geusens PP, Lems WF, Verhaar HJ, Leusink G, Goemaere S, Zmierczack H, Compston.** Review and evaluation of the Dutch guidelines for osteoporosis. *J Eval Clin Pract*. 2006;12:539-548.
26. **Pencharz JN, Grigoriadis E, Jansz GF, Bombardier C.** A critical appraisal of clinical practice guidelines for the treatment of lower-limb osteoarthritis. *Arthritis Res*. 2002;4:36-44.
27. **Tsang A, Von Korff M, Lee S, Alonso J, Karam E, Angermeyer MC, Borges G, Bromet E, Demyttenaere K, de Girolamo G, de Graaf R, Gureje O, et al.** Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. *J Pain*. 2008;9:883-891.
28. **Sullivan MJ, Feuerstein M, Gatchel R, Linton SJ, Pransky G.** Integrating psychosocial and behavioral interventions to achieve optimal rehabilitation outcomes. *Journal of occupational rehabilitation*. 2005; Dec;15(4):475-489. Review.
29. **Thieme K, Flor H, Turk DC.** Psychological pain treatment in fibromyalgia syndrome: efficacy of operant behavioural and cognitive behavioural treatments. *Arthritis Res Ther*. 2006;8:R121.
30. **Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC.** The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull*. 2007;133:581-624.
31. **Crombie IK CP, Linton SJ, LeResche L, Von Korff M.** *Epidemiology of pain*. Seattle, WA: IASP Press; 1999.
32. **Deyo RA, Weinstein JN.** Low back pain. *N Engl J Med*. 2001 Feb 1;344(5):363-370. Review.
33. **Williams DA, Feuerstein M, Durbin D, Pezzullo J.** Health care and indemnity costs across the natural history of disability in occupational low back pain. *Spine (Phila Pa 1976)*. 1998;23:2329-2336.
34. **Rogerson MD, Gatchel RJ, Bierner SM.** A cost utility analysis of interdisciplinary early intervention versus treatment as usual for high-risk acute low back pain patients. *Pain Pract*. 2010;10:382-395.
35. **Danneskiold-Samsøe B.** Idiopathic low back pain: classification and differential diagnosis. *JMP*. 2004;12:93-99.
36. **Lindgren H, Bergman S.** Chronic musculoskeletal pain predicted hospitalisation due to serious medical conditions in a 10 year follow up study. *BMC Musculoskelet Disord*. 2010;11:127.
37. **Bergman S, Herrstrom P, Hogstrom K, Petersson IF, Svensson B, Jacobsson LT.** Chronic musculoskeletal pain, prevalence rates, and sociodemographic associations in a Swedish population study. *J Rheumatol*. 2001;28:1369-1377.
38. **Waddell G.** *The back pain revolution*. Edinburgh: 2nd Edition, Churchill Livingstone. 2004. p. 74-75, 179-202.
39. **van Tulder MW, Koes B, Malmivaara A.** Outcome of non-invasive treatment modalities on back pain: an evidence-based review. *Eur Spine J*. 2006;15 Suppl 1:S64-81.
40. **Papageorgiou AC, Croft PR, Thomas E, Ferry S, Jayson MI, Silman AJ.** Influence of previous pain experience on the episode incidence of low back pain: results from the South Manchester Back Pain Study. *Pain*. 1996;66:181-185.
41. **Brooks P.** Issues with chronic musculoskeletal pain. *Rheumatology (Oxford)*. 2005;44:831-833.
42. **Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D.** Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain*. 2006;10:287-333.
43. **Carroll LJ, Hogg-Johnson S, van der Velde G, Haldeman S, Holm LW, Carragee EJ, Hurwitz EL, Cote P, Nordin M, Peloso PM, Guzman J, Cassidy JD.** Course and prognostic factors for neck pain in the general population: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976)*. 2008;33:S75-82.
44. **Blyth FM, March LM, Brnabic AJ, Jorm LR, Williamson M, Cousins MJ.** Chronic pain in Australia: a prevalence study. *Pain*. 2001;89:127-134.
45. **Greenspan JD, Craft RM, LeResche L, Arendt-Nielsen L, Berkley KJ, Fillingim RB, Gold MS, Holdcroft A, Lautenbacher S, Mayer E, Mogil JS, Murphy A, Traub RJ.** Studying sex and gender differences in pain and analgesia: a consensus report. *Pain*. 2007; 132 Suppl 1:S26-45.
46. **Svedberg P, Salmi P, Hagberg J, Lundh G, Linder J, Alexanderson K.** Does multidisciplinary assessment of long-term sickness absentees result in modification of sick-listing diagnoses? *Scand J Public Health*. 2010;38:657-663.
47. **Eriksen J, Jensen MK, Sjogren P, Ekholm O, Rasmussen NK.** Epidemiology of chronic non-malignant pain in Denmark. *Pain*. 2003;106:221-228.
48. **LeResche L.** Epidemiologic perspectives on sex differences in pain. In: Fillingim R, ed. *Sex, Gender and Pain*. Seattle, WA: IASP Press; 2000:233-249.
49. **Smith BH, Elliott AM, Chambers WA, Smith WC, Hannaford PC, Penny K.** The impact of

- chronic pain in the community. *Fam Pract*. 2001;18:292-299.
50. **Cote P, Cassidy JD, Carroll LJ, Kristman V.** The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain*. 2004;112:267-273.
51. **Jensen AL, Harder I.** The osteoporotic pain experience. *Osteoporos Int*. 2004;15:204-208.
52. **Papageorgiou AC, Macfarlane GJ, Thomas E, Croft PR, Jayson MI, Silman AJ.** Psychosocial factors in the workplace--do they predict new episodes of low back pain? Evidence from the South Manchester Back Pain Study. *Spine*. 1997;22:1137-1142.
53. **Werner A, Isaksen LW, Malterud K.** 'I am not the kind of woman who complains of everything': illness stories on self and shame in women with chronic pain. *Social science & medicine* (1982). 2004 Sep;59(5):1035-1045.
54. **Skuladottir H, Halldorsdottir S.** Women in chronic pain: sense of control and encounters with health professionals. *Qual Health Res*. 2008;18:891-901.
55. **Ekberg K, Bjorkqvist B, Malm P, Bjerre-Kiely B, Karlsson M, Axelson, O.** Case-control study of risk factors for disease in the neck and shoulder area. *Occup Environ Med*. 1993;51:4: 262-6.
56. **Sundquist J, Ostergren PO, Sundquist K, Johansson SE.** Psychosocial working conditions and self-reported long-term illness: a population-based study of Swedish-born and foreign-born employed persons. *Ethn Health*. 2003;8:307-317.
57. **Salmi P, Svedberg P, Hagberg J, Lundh G, Linder J, Alexanderson K.** Multidisciplinary investigations recognize high prevalence of comorbidity of psychiatric and somatic diagnoses in long-term sickness absentees. *Scand J Public Health*. 2009;37:35-42.
58. **Linder J, Svensson O.** The impact of pain and depression on assessment of rehabilitation need: a cross-sectional study in long-term sick-listed patients. *Int J Rehabil Res*. 2007;30:255-260.
59. **Penfield W.** Forward. In: White J, Sweet WH. *Pain and neurosurgeon: A 40-year experience*. Springfield, Illinois. Charles C Thomas, Publisher. 1969.
60. **Melzack R, Wall PD.** Pain mechanisms: a new theory. *Science*. 1965;150:971-979.
61. **Melzack R.** From the gate to the neuromatrix. *Pain*. 1999;Suppl 6:S121-126.
62. **Melzack R.** Pain and the neuromatrix in the brain. *J Dent Educ*. 2001;65:1378-1382.
63. **Melzack R.** Evolution of the neuromatrix theory of pain. The Prithvi Raj Lecture: presented at the third World Congress of World Institute of Pain, Barcelona 2004. *Pain Pract*. 2005;5:85-94.
64. **Diatchenko L, Slade GD, Nackley AG, Bhalang K, Sigurdsson A, Belfer I, Goldman D, Xu K, Shabalina S, Shagin D, Max M, Makarov S, Maixner W.** Genetic basis for individual variations in pain perception and the development of a chronic pain condition. *Hum Mol Genet*. 2005;14:135-143.
65. **Ala-Kokko, L.** Genetic risk factors for lumbar disc disease. *Ann Med*. 2002;34:42-7.
66. **Turk DC, Okifuji A.** Psychological factors in chronic pain: evolution and revolution. *J Consult Clin Psychol*. 2002;70:678-690.
67. **Turk DC, Okifuji A.** Assessment of patients' reporting of pain: an integrated perspective. *Lancet*. 1999;353:1784-1788.
68. **Blyth FM, Macfarlane GJ, Nicholas MK.** The contribution of psychosocial factors to the development of chronic pain: the key to better outcomes for patients? *Pain*. 2007;129:8-11.
69. **Currie SR, Wang J.** Chronic back pain and major depression in the general Canadian population. *Pain*. 2004;107:54-60.
70. **Dersh J, Gatchel RJ, Polatin P, Mayer T.** Prevalence of psychiatric disorders in patients with chronic work-related musculoskeletal pain disability. Comment in: *J Occup Environ*. 2002 Oct;44(10):888-9.
71. **Sullivan MJ, Thibault P, Andrikonyte J, Butler H, Catchlove R, Lariviere C.** Psychological influences on repetition-induced summation of activity-related pain in patients with chronic low back pain. *Pain*. 2009;141:70-78.
72. **Woby SR, Roach NK, Urmston M, Watson PJ.** The relation between cognitive factors and levels of pain and disability in chronic low back pain patients presenting for physiotherapy. *Eur J Pain*. 2007;11:869-877.
73. **Von Korff M, Moore JE, Lorig K, Cherkin DC, Saunders K, Gonzalez V, Laurent D, Rutter C, Comite F.** A randomized trial of a lay person-led self-management group intervention for back pain patients in primary care. *Spine (Phila Pa 1976)*. 1998;23:2608-2615.
74. **Morley S, Williams AC.** RCTs of psychological treatments for chronic pain: progress and challenges. *Pain*. 2006;121:171-172.
75. **Jensen MP, Turner JA, Romano JM, Karoly P.** Coping with chronic pain: a critical review of the literature. *Pain*. 1991;47:249-283.
76. **Turner JA, Mancl L, Aaron LA.** Brief cognitive-behavioral therapy for temporomandibular disorder pain: effects on daily electronic outcome and process measures. *Pain*. 2005;117:377-387.

77. **Villemure C, Bushnell MC.** Cognitive modulation of pain: how do attention and emotion influence pain processing? *Pain.* 2002;95:195-199.
78. **Keefe FJ, Somers TJ.** Psychological approaches to understanding and treating arthritis pain. *Nat Rev Rheumatol.* 2010;6:210-216.
79. **Shaw W, Hong QN, Pransky G, Loisel P.** A literature review describing the role of return-to-work coordinators in trial programs and interventions designed to prevent workplace disability. *J Occup Rehabil.* 2008;18:2-15.
80. **Woolf CJ.** Pain: moving from symptom control toward mechanism-specific pharmacologic management. *Ann Intern Med.* 2004;140:441-451.
81. **Flor H, Diers M.** Sensorimotor training and cortical reorganization. *NeuroRehabilitation.* 2009;25(1):19-27.
82. **Chapman CR, Tuckett RP, Song CW.** Pain and stress in a systems perspective: reciprocal neural, endocrine, and immune interactions. *J Pain.* 2008;9:122-145.
83. **Arendt-Nielsen L, Graven-Nielsen T.** Muscle pain: sensory implications and interaction with motor control. *Clin J Pain.* 2008;24:291-298.
84. **Merskey HB, N.** Classification of Chronic Pain. Seattle, WA: IASP Press 1994.
85. **Turk DC, Rudy TE.** The robustness of an empirically derived taxonomy of chronic pain patients. *Pain.* 1990;43:27-35.
86. **Von Korff M, Dunn KM.** Chronic pain reconsidered. *Pain.* 2008;138:267-276.
87. **Von Korff M, Miglioretti DL.** A prognostic approach to defining chronic pain. *Pain.* 2005;117:304-313.
88. **Dunn KM, Croft PR, Main CJ, Von Korff M.** A prognostic approach to defining chronic pain: replication in a UK primary care low back pain population. *Pain.* 2008;135:48-54.
89. **Foster NE, Mullis R, Young J, Doyle C, Lewis M, Whitehurst G, Hay M, Study Team, I. B.** IMPaCT Back study protocol. Implementation of subgrouping for targeted treatment systems for low back pain patients in primary care: a prospective population-based sequential comparison. *BMC Musculoskelet Disord.* 2010;11:186.
90. **Burton AK BF, Cardon G, Eriksen HR, Henrotin Y, Lahad A, Leclerc A, Muller G, van der Beek AJ.** European Guidelines for Prevention in Low Back Pain. *Eur Spine J.* 2004;15 (suppl 2):S136-168.
91. **Coste J, Spira A, Ducimetiere P, Paolaggi JB.** Clinical and psychological diversity of non-specific low-back pain. A new approach towards the classification of clinical subgroups. *J Clin Epidemiol.* 1991;44(11):1233-1245.
92. **Pengel LH, Herbert RD, Maher CG, Refshauge KM.** Acute low back pain: systematic review of its prognosis. *BMJ (Clinical research ed).* 2003;327:323.
93. **Lakke SE, Soer R, Takken T, Reneman MF.** Risk and prognostic factors for non-specific musculoskeletal pain: a synthesis of evidence from systematic reviews classified into ICF dimensions. *Pain.* 2009;147:153-164.
94. **Picavet HS, Hazes JM.** Prevalence of self reported musculoskeletal diseases is high. *Ann Rheum Dis.* 2003;62(7):644-650.
95. **Trescot AM, Helm S, Hansen H, Benyamin R, Glaser E, Adlaka R, Patel S, Manchikanti L.** Opioids in the management of chronic non-cancer pain: an update of American Society of the Interventional Pain Physicians' (ASIPP) Guidelines. *Pain Physician.* 2008;11:S5-S62.
96. **Breivik H.** Opioids in cancer and chronic non-cancer pain therapy-indications and controversies. *Acta Anaesthesiol Scand.* 2001;45:1059-1066.
97. **Chapman CR, Lipschitz DL, Angst MS, Chou R, Denisco C, Donaldson W, Fine P, Foley K, Gallagher R, Gilson A, Haddox J, Horn SD, et al.** Opioid Pharmacotherapy for Chronic Non-Cancer Pain in the United States: A Research Guideline for Developing an Evidence-Base. *J Pain.* 2010;11:807-829.
98. **Kalso E, Allan L, Dellemijn PL, Faura C, Ilias K, Jensen S, Perrot S, Plaghki H, Zenz M.** Recommendations for using opioids in chronic non-cancer pain. *Eur J Pain.* 2003;7:381-386.
99. **Sachs CJ.** Oral analgesics for acute nonspecific pain. *Am Fam Physician.* 2005;71:913-918.
100. **Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E.** Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. *CMAJ.* 2006;174:1589-1594.
101. **Abs R, Verhelst J, Maeyaert J, Van Buyten P, Opsomer F, Adriaensen H, Verlooy J, Van Havenbergh T, Smet M, Van Acker K.** Endocrine consequences of long-term intrathecal administration of opioids. *J Clin Endocrinol Metab.* 2000;85:2215-2222.
102. **Daniell HW.** Opioid endocrinopathy in women consuming prescribed sustained-action opioids for control of nonmalignant pain. *J Pain.* 2008;9:28-36.
103. **Rhodin A, Stridsberg M, Gordh T.** Opioid endocrinopathy: a clinical problem in patients with chronic pain and long-term oral opioid treatment. *Clin J Pain.* 2010;26:374-380.
104. **Hutchinson K, Moreland AM, de CWAC, Weinman J, Horne R.** Exploring beliefs and practice of opioid prescribing for persistent non-cancer pain by general practitioners. *Eur J Pain.* 2007;11:93-98.

105. **Keefe FJ, Gil KM.** Behavioral concepts in the analysis of chronic pain syndromes. *J Consult Clin Psychol.* 1986;54:776-783.
106. **Truchon M, Cote D, Fillion L, Arsenault B, Dionne C.** Low-back-pain related disability: an integration of psychological risk factors into the stress process model. *Pain.* 2008;137:564-573.
107. **Fordyce WE, Roberts AH, Sternback RA.** The Behavioral management of chronic pain: A response to critics. *Pain.* 1985;22:113-125.
108. **Keefe FJ, Lumley M, Anderson T, Lynch T, Studts JL, Carson KL.** Pain and emotion: new research directions. *J Clin Psychol.* 2001;57:587-607.
109. **Sullivan MJ, Adams H, Tripp D, Stanish WD.** Stage of chronicity and treatment response in patients with musculoskeletal injuries and concurrent symptoms of depression. *Pain.* 2008;135:151-159.
110. **Brown T, Nemiah J, Barr J, Barry H.** Psychological factors in low-back pain. *N Engl J Med.* 1954;251:123-128.
111. **Craig KP, KM. Eckstein Grunau, R.** The facial expression of pain. In: Turk DC and Melzack R Eds. *Handbook of pain assessment.* New York: 2nd Edition, Guilford Press; 2001:153-169.
112. **Keefe FW, DA. Smith SJ.** Assessment of pain behaviours. In: Turk DC and Melzack R Eds. *Handbook of pain assessment.* New York: 2nd Edition, Guilford Press; 2001:170-190.
113. **Jensen M.** Validity of self-report and observation measures. In: Jensen TS TJ, Wiesenfeld-Hallin Z, Eds. *Progress in pain research and management.* Seattle, WA: IASP Press; 1997:637-661.
114. **Mechanic DV, EH.** Stress, illness and the sick-role. *Am Sociol Rev.* 1961;26:51-58.
115. **Waddell G, Pilowsky I, Bond MR.** Clinical assessment and interpretation of abnormal illness behaviour in low back pain. *Pain.* 1989;39:41-53.
116. **Apeldoorn AT, Bosselaar H, Blom-Luberti T, Twisk JW, Lankhorst GJ.** The reliability of nonorganic sign-testing and the Waddell score in patients with chronic low back pain. *Spine (Phila Pa 1976).* 2008;33:821-26.
117. **Dickens C, Jayson M, Creed F.** Psychological correlates of pain behaviour in patients with low back pain. *Psychosomatics.* 2002;43:42-48.
118. **Prkachin KM, Hughes E, Schultz I, Joy P, Hunt D.** Real-time assessment of pain behavior during clinical assessment of low back pain patients. *Pain.* 2002;95:23-30.
119. **Vlaeyen JW, Linton SJ.** Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. *Pain.* 2000;85:317-332.
120. **Leeuw M, Goossens ME, Linton SJ, Crombez G, Boersma K, Vlaeyen JW.** The fear-avoidance model of musculoskeletal pain: current state of scientific evidence. *J Behav Med.* 2007;30:77-94.
121. **Burton AK, Tillotson KM, Main CJ, Hollis S.** Psychosocial predictors of outcome in acute and subchronic low back trouble. *Spine (Phila Pa 1976).* 1995;20:722-728.
122. **Geisser ME, Roth RS, Theisen ME, Robinson ME, Riley JL, 3rd.** Negative affect, self-report of depressive symptoms, and clinical depression: relation to the experience of chronic pain. *Clin J Pain.* 2000;16:110-120.
123. **Cassidy JD, Cote P, Carroll LJ, Kristman V.** Incidence and course of low back pain episodes in the general population. *Spine.* 2005;30:2817-2823.
124. **Rush AJ, Polatin P, Gatchel RJ.** Depression and chronic low back pain: establishing priorities in treatment. *Spine (Phila Pa 1976).* 2000;25:2566-2571.
125. **Truchon M.** Determinants of chronic disability related to low back pain: towards an integrative biopsychosocial model. *Disabil Rehabil.* 2001;23:758-767.
126. **Polatin PB, Kinney RK, Gatchel RJ, Lillo E, Mayer TG.** Psychiatric illness and chronic low-back pain. The mind and the spine--which goes first? *Spine.* 1993;18:66-71.
127. **Truchon M, Fillion L.** Biopsychosocial determinants in chronic disability and low-back pain: a review. *J Occup Rehab.* 2000;10:117-142.
128. **Fleten N, Johnsen R, Forde OH.** Length of sick leave - why not ask the sick-listed? Sick-listed individuals predict their length of sick leave more accurately than professionals. *BMC Public Health.* 2004;4:46.
129. **Katon WJ, Walker EA.** Medically unexplained symptoms in primary care. *J Clin Psychiatry.* 1998;59 Suppl 20:15-21.
130. **Mason V.** The prevalence of low back pain in Great Britain. London: Office of Population Censuses and Surveys Social Survey Division; 1994.
131. **Soucy I, Truchon M, Cote D.** Work-related factors contributing to chronic disability in low back pain. *Work.* 2006;26:313-26.
132. **Van der Weide WV, JH. Salle, HJ. van Dijk, FJ.** Prognostic factors for chronic disability from acute low-back pain in occupational health care. *Environ Health Perspect.* 1999;25:50-56.
133. **Vaez MH, J. Alexanderson, K.** The panorama of future sick-leave diagnoses among young adults initially long-term sickness absent due to neck, shoulder, or back diagnoses. An 11-year prospective cohort study. *BMC Musculoskeletal Disord.* 2009;10:84.

134. **Loisel P, Hong QN, Imbeau D, Lippel K, Guzman J, Maceachen E, Corbiere M, Santos R, Anema JR.** The Work Disability Prevention CIHR Strategic Training Program: program performance after 5 years of implementation. *J Occup Rehabil.* 2009;19:1-7.
135. **Lund T, Christensen KB, Vaez M, Labriola M, Josephson M, Villadsen E, Voss M.** Differences in sickness absence in Sweden and Denmark: the cross national HAKNAK study. *Eur J Public Health.* 2009;19(3):343-349.
136. **Costa L da C, Maher C, McAuley J, Hancock J, Herbert D, Refshauge M, Henschke N.** Prognosis for patients with chronic low back pain: inception cohort study. *BMJ (Clinical research ed.)* 2009;339:b3829.
137. **Hestbaek L, Leboeuf-Yde C, Manniche C.** Low back pain: what is the long-term course? A review of studies of general patient populations. *Eur Spine J.* 2003;12:149-165.
138. **Schiottz-Christensen B, Nielsen GL, Hansen VK, Schodt T, Sorensen HT, Olesen F.** Long-term prognosis of acute low back pain in patients seen in general practice: a 1-year prospective follow-up study. *Fam Pract.* 1999;16:223-232.
139. **Coudeyre E, Rannou F, Tubach F, Baron G, Coriat F, Brin S, Revel M, Poiraudaud S.** General practitioners' fear-avoidance beliefs influence their management of patients with low back pain. *Pain.* 2006;124:330-337.
140. **Bishop A, Thomas E, Foster NE.** Health care practitioners' attitudes and beliefs about low back pain: a systematic search and critical review of available measurement tools. *Pain.* 2007;132:91-101.
141. **Indahl A, Velund L, Reikeraas O.** Good prognosis for low back pain when left untampered. A randomized clinical trial. *Spine (Phila Pa 1976).* 1995;20:473-477.
142. **Hagen EM, Svensen E, Eriksen HR.** Predictors and modifiers of treatment effect influencing sick leave in subacute low back pain patients. *Spine (Phila Pa 1976).* 2005;30:2717-2723.
143. **Bishop A, Foster NE, Thomas E, Hay EM.** How does the self-reported clinical management of patients with low back pain relate to the attitudes and beliefs of health care practitioners? A survey of UK general practitioners and physiotherapists. *Pain.* 2008;135:187-195.
144. **Dey P, Simpson CW, Collins SI, Hodgson G, Dowrick F, Simison J, Rose J.** Implementation of RCGP guidelines for acute low back pain: a cluster randomised controlled trial. *Br J Gen Pract.* 2004;54:33-37.
145. **Fullen BM, Baxter GD, O'Donovan BG, Doody C, Daly L, Hurley DA.** Doctors' attitudes and beliefs regarding acute low back pain management: A systematic review. *Pain.* 2008;136:388-396.
146. **Linton SJ, Vlaeyen J, Ostelo R.** The back pain beliefs of health care providers: are we fear-avoidant? *J Occup Rehabil.* 2002;12:223-232.
147. **Rossignol M, Poitras S, Dionne C, et al.** An interdisciplinary guideline development process: the Clinic on Low-back pain in Interdisciplinary Practice (CLIP) low-back pain guidelines. *Implement Sci.* 2007;2:36.
148. **Pincus T, Foster NE, Vogel S, Santos R, Breen A, Underwood M.** Attitudes to back pain amongst musculoskeletal practitioners: a comparison of professional groups and practice settings using the ABS-mp. *Manual therapy.* 2007;12:167-175.
149. **Main CJ, Waddell G.** Behavioral responses to examination. A reappraisal of the interpretation of "nonorganic signs". *Spine.* 1998;23:2367-2371.
150. **Sobel JB, Sollenberger P, Robinson R, Polatin PB, Gatchel RJ.** Cervical nonorganic signs: a new clinical tool to assess abnormal illness behavior in neck pain patients: a pilot study. *Arch Phys Med Rehabil.* 2000;81:170-175.
151. **Högstedt CBM, Marklund S, Palmer E, Theorell T.** Den höga sjukfrånvaron—sanningen och konsekvens. Stockholm: Sandviken Publisher; 2004.
152. **Salen BA, Spangfort EV, Nygren AL, Nordemar R.** The Disability Rating Index: an instrument for the assessment of disability in clinical settings. *J Clin Epidemiol.* 1994;47:1423-1435.
153. **Beck AT, Steer RA.** Internal consistencies of the original and revised Beck Depression Inventory. *J Clin Psychol.* 1984;40:1365-1367.
154. **Pincus T, Williams AC, Vogel S, Field A.** The development and testing of the depression, anxiety, and positive outlook scale (DAPOS). *Pain.* 2004;109:181-188.
155. **Pincus T, Santos R, Morley S.** Depressed cognitions in chronic pain patients are focused on health: evidence from a sentence completion task. *Pain.* 2007;130:84-92.
156. **Spielberger CD, Gorsuch RL, RE L.** Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1970.
157. **Lundberg M, Styf J, Jansson B.** On what patients does the Tampa Scale for Kinesiophobia fit? *Physiotherapy theory and practice.* 2009;25:495-506.
158. **Jensen M and Karoly P.** Measurement of pain: Self-report scales and procedures for assessing pain in adults. In: Turk DC and Melzack R Eds. *Handbook of pain assessment.* New York: 2nd Edition, Guildford Press; 2001.p. 15-34, 760.

159. **Urban BJ, Keefe FJ, France RD.** A study of psychophysical scaling in chronic pain patients. *Pain.* 1984;20:157-168.
160. **Schneider PL, Crouter SE, Bassett DR.** Pedometer measures of free-living physical activity: comparison of 13 models. *Med Sci Sports Exerc.* 2004;36:331-335.
161. **Kelsey JL, Thompson D, Evans A.** Methods in observational epidemiology. New York: Oxford University Press. 1986. p. 288-291.
162. **Briggs SR CJ.** The role of factor analysis in the development and evaluation of personality scales. *J Pers.* 1986;54:106-148.
163. **Twisk JW, de Vente W.** The analysis of randomised controlled trial data with more than one follow-up measurement. A comparison between different approaches. *Eur J Epidemiol.* 2008;23:655-660.
164. **Azuero A, Pisu M, McNees P, Burkhardt J, Benz R, Meneses K.** An application of longitudinal analysis with skewed outcomes. *Nurs Res.* 2010;Jul-Aug;59(4):301-7.
165. **Beaton DE, Bombardier C, Guillemin F, Ferraz MB.** Guidelines for the process of cross-cultural adaptation of self-report measures. *Spine (Phila Pa 1976).* 2000;25:3186-3191.
166. **Tudor-Locke C, Bassett DR, Jr.** How many steps/day are enough? Preliminary pedometer indices for public health. *Sports medicine (Auckland, NZ).* 2004;34(1):1-8.
167. **Ohlund C, Eek C, Palmblad S, Areskoug B, Nachemson A.** Quantified pain drawing in subacute low back pain. Validation in a nonselected outpatient industrial sample. *Spine (Phila Pa 1976).* 1996;21:1021-1030; discussion 1031.
168. **Carroll LJ, Cassidy JD, Peloso PM, Giles-Smith L, Cheng S, Greenhalgh W, Haldeman S, van der Velde G, Hurwitz E, Cote P, Nordin M, Hogg-Johnson S, Holm L, Guzman J, Carragee EJ.** Methods for the best evidence synthesis on neck pain and its associated disorders: the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976).* 2008;33:S33-38.
169. **Kamaleri Y, Natvig B, Ihlebaek CM, Bruusgaard D.** Does the number of musculoskeletal pain sites predict work disability? A 14-year prospective study. *Eur J Pain.* 2009;13:426-430.
170. **Natvig B, Bruusgaard D, Eriksen W.** Localized low back pain and low back pain as part of widespread musculoskeletal pain: two different disorders? A cross-sectional population study. *J Rehabil Med.* 2001;33:21-25.
171. **Guez M, Hildingsson C, Nasic S, Toolanen G.** Chronic low back pain in individuals with chronic neck pain of traumatic and non-traumatic origin: a population-based study. *Acta Orthop Suppl.* 2006 Feb;77(320):132-137.
172. **Evans TH, Mayer TG, Gatchel RJ.** Recurrent disabling work-related spinal disorders after prior injury claims in a chronic low back pain population. *Spine J.* 2001;1:183-189.
173. **Carroll LJ, Hogg-Johnson S, Cote P, van der Velde G, Holm L, Carragee E, Hurwitz E, Peloso P, Cassidy JD, Guzman J, Nordin M, Haldeman S.** Course and prognostic factors for neck pain in workers: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine (Phila Pa 1976).* 2008;33:S93-100.
174. **Ektor-Andersen J, Janzon L, Sjölund B.** Chronic pain and the sociodemographic environment: results from the Pain Clinic at Malmö General Hospital in Sweden. *Clin J Pain.* 1993;9(3):183-8.
175. **Wiking E, Johansson SE, Sundquist J.** Ethnicity, acculturation, and self-reported health. A population based study among immigrants from Poland, Turkey, and Iran in Sweden. *J Epidemiol. Community Health.* 2004;58:574-582.
176. **Epping-Jordan JE, Wahlgren DR, Williams RA, Pruitt S, Slater M, Patterson T, Grant I, Webster J, Atkinson JH.** Transition to chronic pain in men with low back pain: predictive relationships among pain intensity, disability, and depressive symptoms. *Health Psychol.* 1998;17:421-427.
177. **Hunter J.** Physical symptoms and signs and chronic pain. *Clin J. Pain.* 2001;17:S26-32.
178. **Miedema HS, Chorus AM, Wevers CW, van der Linden S.** Chronicity of back problems during working life. *Spine (Phila Pa 1976).* 1998;23:2021-2028; discussion 2028-2029.
179. **Elliott AM, Smith BH, Hannaford PC, Smith WC, Chambers WA.** Assessing change in chronic pain severity: the chronic pain grade compared with retrospective perceptions. *Br J Gen Pract.* 2002;52:269-274.
180. **Silverplatt K, Lind B, Zoega B, Halldin K, Gellerstedt M, Brisby H, Rutberg L.** Clinical factors of importance for outcome after lumbar disc herniation surgery: long-term follow-up. *Eur Spine J.* 2010;19:1459-1467.
181. **Coste J, Delecoeuillerie G, Cohen de Lara A, Le Parc JM, Paolaggi JB.** Clinical course and prognostic factors in acute low back pain: an inception cohort study in primary care practice. *BMJ.* 1994 Feb 26;308(6928):577-80.
182. **Bendix AF, Bendix T, Vaegter K, Lund C, Frolund L, Holm L.** Multidisciplinary intensive treatment for chronic low back pain: a randomized, prospective study. *Cleve Clin J Med.* 1996;63:62-69.
183. **Hazard RG, Fenwick JW, Kalisch SM, Redmond J, Reeves V, Reid S, Frymoyer JW.**

- Functional restoration with behavioral support. A one-year prospective study of patients with chronic low-back pain. *Spine (Phila Pa 1976)*. 1989;14:157-161.
184. **Jellema P, van der Windt DA, van der Horst HE, Blankenstein AH, Bouter LM, Stalman WA.** Why is a treatment aimed at psychosocial factors not effective in patients with (sub)acute low back pain? *Pain*. 2005;118:350-359.
185. **Waddell G, Main CJ, Morris EW, Di Paola M, Gray IC.** Chronic low-back pain, psychologic distress, and illness behavior. *Spine*. 1984;9:209-213.
186. **Linton SJ.** An overview of psychosocial and behavioral factors in neck-and-shoulder pain. *Scand J Rehabil Med Suppl*. 1995;32:67-77.
187. **Linton SJ, Buer N.** Working despite pain: factors associated with work attendance versus dysfunction. *Int J Behav Med*. 1995;2(3):252-262.
188. **Ariens GA, van Mechelen W, Bongers PM, Bouter LM, van der Wal G.** Psychosocial risk factors for neck pain: a systematic review. *Am J Ind Med*. 2001;39:180-193.
189. **Talo S, Rytokoski U, Puukka P.** Patient classification, a key to evaluate pain treatment: a psychological study in chronic low back pain patients. *Spine*. 1992;17:998-1011.
190. **Robertson E, Iglesias E, Johansson SE, Sundquist J.** Migration status and limiting long-standing illness: a longitudinal study of women of childbearing age in Sweden. *Eur J Public Health*. 2003;13:99-104.
191. **Damush TM, Wu J, Bair MJ, Sutherland JM, Kroenke K.** Self-management practices among primary care patients with musculoskeletal pain and depression. *J Behav Med*. 2008;31:301-307.
192. **Scopaz KA, Piva SR, Wisniewski S, Fitzgerald GK.** Relationships of fear, anxiety, and depression with physical function in patients with knee osteoarthritis. *Arch Phys Med Rehabil*. 2009;90:1866-1873.
193. **Stein MB, Cox BJ, Afifi TO, Belik SL, Sareen J.** Does co-morbid depressive illness magnify the impact of chronic physical illness? A population-based perspective. *Psychol Med*. 2006;36:587-596.
194. **Norrefalk JR.** Effect on work ability after team evaluation of functioning regarding pain, self-rated disability, and work ability assessment. *J Multidiscip Healthc*. 2010;3:155-159.
195. **Coste J, Schiano PJ, Leparc JM, Paolaggi JB.** Clinical and psychological classification of non-specific low-back pain. A new study in primary care practice. *Revue d'epidemiologie et de sante publique*. 1995;43:127-138.
196. **Johansson AC, Cornefjord M, Bergkvist L, Ohrvik J, Linton SJ.** Psychosocial stress factors among patients with lumbar disc herniation, scheduled for disc surgery in comparison with patients scheduled for arthroscopic knee surgery. *Eur Spine J*. 2007;16:961-970.
197. **Bravata DM, Smith-Spangler C, Sundaram V, Gienger A, Lin N, Lewis R, Stave C, Olkin I, Sirard JR.** Using pedometers to increase physical activity and improve health: a systematic review. *Jama*. 2007;298:2296-2304.
198. **Bombardier C.** Outcome assessments in the evaluation of treatment of spinal disorders: summary and general recommendations. *Spine (Phila Pa 1976)*. 2000;25:3100-3103.
199. **Koes BW, van Tulder M, Lin CW, Macedo LG, McAuley J, Maher C.** An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. *Eur Spine J*. 2010.
200. **Foster NE, Thomas E, Bishop A, Dunn KM, Main CJ.** Distinctiveness of psychological obstacles to recovery in low back pain patients in primary care. *Pain*. 2010;148:398-406.
201. **Lee PW, Chow SP, Lieh-Mak F, Chan KC, Wong S.** Psychosocial factors influencing outcome in patients with low-back pain. *Spine (Phila Pa 1976)*. 1989;14:838-843.
202. **Saunders KW, Von Korff M, Pruitt SD, Moore JE.** Prediction of physician visits and prescription medicine use for back pain. *Pain*. 1999;83:369-377.
203. **Coste J, Lefrancois G, Guillemin F, Pouchot J.** Prognosis and quality of life in patients with acute low back pain: insights from a comprehensive inception cohort study. *Arthritis and rheumatism*. 2004;51:168-176.
204. **Linton SJ, van Tulder MW.** Preventive interventions for back and neck pain problems: what is the evidence? *Spine*. 2001;26:778-787.
205. **Von Korff M.** Epidemiological and survey methods: assessment of chronic pain. In: Turk DC, Melzack R, eds. *Handbook of pain assessment*. New York: The Guilford Press; 2001. p. 603-618.
206. **Miller CH, Quick BL.** Sensation seeking and psychological reactance as health risk predictors for an emerging adult population. *J Health Commun*;25:266-275.
207. **Quick BL, Bates BR.** The use of gain- or loss-frame messages and efficacy appeals to dissuade excessive alcohol consumption among college students: a test of psychological reactance theory. *J Health Commun*. 2010;15:603-628.
208. **Pincus T, Williams A.** Models and measurements of depression in chronic pain. *J Psychosom Res*. 1999;47:211-219.

209. **Read J, Pincus T.** Cognitive bias in back pain patients attending osteopathy: testing the enmeshment model in reference to future thinking. *Eur J Pain.* 2004;8:525-531.
210. **Richter P, Werner J, Heerlein A, Kraus A, Sauer H.** On the validity of the Beck Depression Inventory. A review. *Psychopathology.* 1998;31:160-168.
211. **Geisser ME, Roth RS, Robinson ME.** Assessing depression among persons with chronic pain using the Center for Epidemiological Studies-Depression Scale and the Beck Depression Inventory: a comparative analysis. *Clin J Pain.* 1997;13:163-170.
212. **Pincus T, Rusu A, Santos R.** Responsiveness and construct validity of the depression, anxiety, and positive outlook scale (DAPOS). *Clin J Pain.* 2008;24:431-437.
213. **Gatchel RJ, Turk DC.** Criticisms of the biopsychosocial model in spine care: creating and then attacking a straw person. *Spine (Phila Pa 1976).* 2008;33:2831-2836.
214. **McDonough SM, Tully MA, O'Connor SR, Boyd A, Kerr D, O'Neill S, Delitto A, Bradbury I, Tudor-Locke C, Baxter D, Hurley DA.** The Back 2 Activity Trial: education and advice versus education and advice plus a structured walking programme for chronic low back pain. *BMC Musculoskelet Disord.* 2010;11:163.
215. **Estabrooks PA, Glasgow RE.** Translating effective clinic-based physical activity interventions into practice. *Am J Prev Med.* 2006;31:S45-56.
216. **Linton SJ, Boersma K.** Early identification of patients at risk of developing a persistent back problem: the predictive validity of the Orebro Musculoskeletal Pain Questionnaire. *Clin J Pain.* 2003;19:80-86.
217. **Kalso E, Edwards JE, Moore RA, McQuay HJ.** Opioids in chronic non-cancer pain: systematic review of efficacy and safety. *Pain.* 2004;112:372-380.
218. **Koes BW, van Tulder MW, Ostelo R, Kim Burton A, Waddell G.** Clinical guidelines for the management of low back pain in primary care: an international comparison. *Spine.* 2001;26:2504-2513; discussion 2513-2504.
219. **Collett BJ, Berkley K.** The IASP Global Year against pain in women. *Pain.* 2007;132 Suppl 1:S1-2.
220. **Suzuki N, Ogikubo O, Hansson T.** The course of the acute vertebral body fragility fracture: its effect on pain, disability and quality of life during 12 months. *Eur Spine J.* 2008;17:1380-1390.
221. **Munce SE, Stewart DE.** Gender differences in depression and chronic pain conditions in a national epidemiologic survey. *Psychosomatics.* 2007;48:394-399.

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