Classification and targeted treatment of patients with Non Specific Chronic Low Back Pain

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In loving memory of my mother Wenche Fersum

Contents

Scientific environment

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List of papers

This thesis is based on the following papers, referred to in the text by their Roman numerals.

I Fersum K, Dankaerts W, O'Sullivan P, Maes J, Skouen JS, Bjordal JM, Kvåle A. Integration of sub-classification strategies in RCTs evaluating manual therapy treatment and exercise therapy for non-specific chronic low back pain (NSCLBP): A systematic review. British Journal of Sports Medicine 2010; 44:1054-1062. doi:10.1136/bjsm.2009.063289

II Fersum K, O'Sullivan P, Kvåle A, Skouen JS. The inter-examiner reliability of a classification system for patients with non-specific low back pain. Manual Therapy 2009;14:555-561.

III Fersum K, O'Sullivan P, Skouen JS, Smith A, Kvåle A. Efficacy of classification based 'cognitive functional therapy' in patients with Non Specific Chronic Low Back Pain (NSCLBP) – A randomized controlled trial. Submitted

Abstract

Non-specific chronic low back pain (NSCLBP) disorders have proven highly resistant to change in spite of enormous resources directed at them. There is lack of evidence for single treatment interventions for patients with NSCLBP despite the substantial amount of Randomised Controlled Trials (RCT) evaluating treatment outcome for this disorder. It has been hypothesised that this vacuum of evidence is caused by the lack of sub-classifying the heterogeneous population of patients with chronic LBP for outcome research. Another reason suggested for the limited evidence is the lack of sub-grouping and managing the disorder from a biopsychosocial perspective. There is growing evidence that NSCLBP is associated with maladaptive cognitive, movement and lifestyle behaviours that act to promote a vicious cycle of pain. Few classification systems reflecting a bio-psycho-social model have been validated and tested in RCTs for the management of NSCLBP disorders. The O'Sullivan Classification System (OCS) has been developed and validated over many years and subgroups patients based on their maladaptive cognitive, movement and lifestyle behaviours.

This thesis consists of three papers and the work for these papers was performed from 2005 till 2009. In paper I a systematic review with a meta-analysis was undertaken to determine how the integration of sub-classification strategies with matched interventions in RCTs evaluating manual therapy treatment and exercise therapy for NSCLBP was performed in the literature. A structured search for relevant studies in Embase, Cinahl, Medline, PEDro and the Cochrane Trials Register database, was followed by a hand search of all relevant studies in English up till December 2008. A large number of RCTs (n= 767) was retrieved, and 68 of these focused on the efficacy of manual therapy and exercise and were looked at in more detail. However, only five out of 68 studies (7.4%) sub-classified patients beyond applying general inclusion and exclusion criteria. In the few studies where classification and matched interventions have been utilised, our meta-analysis showed a statistical

difference in favour of the classification based intervention for reductions in pain (P=0.004) and disability (P=0.0005), both for short and long-term reduction in pain (P=0.001). Effect sizes ranged from moderate (0.43) short term, to minimal (0.14) for long-term. However, the data should be interpreted with caution, as the numbers are insufficient to definitively quantify the effect of sub-classification strategies for the treatment of NSCLBP. Also, out of the five papers using a classification system in the meta-analysis only three considered all dimensions of LBP within a biopsychosocial perspective. We concluded that a better integration of sub-classification strategies in NSCLBP outcome research was needed.

This led us in paper II to examine the inter-tester reliability of clinician's ability to independently classify patients with non-specific low back pain, utilizing the mechanism-based OCS. Here 26 patients underwent a full examination by four different physiotherapists (O'Sullivan and three others) independently. The therapists underwent a multilevel decision making process, based on disorder classification, primary directional pain provocation and the detection of dominant psychosocial factors. Percentage agreement and Kappa-coefficients were calculated for six different levels of decision-making. For levels 1-4, percentage agreement had a mean of 96% (range 75-100%). In the 5th level, deciding the directional pattern of provocation, Kappa agreement could be calculated. For the primary direction of provocation, Kappa and percentage agreement had a mean between the four testers of 0.82 (range 0.66-0.90) and 86% (range 73-92%) respectively. Increased familiarity with the system increased the reliability scores. In the final decision making level, the scores for detecting psychosocial influence gave a mean Kappa-coefficient of 0.65 (range 0.57-0.74) and a mean agreement of 87% (range 85-92%). Our findings confirmed some of the previous work on the classifications system, suggesting that the inter-tester reliability of the system is moderate to substantial for a range of patients within the NSLBP population. These findings were considered an important step towards implementing targeted interventions programs for subgroups with NSLBP.

In paper III we performed a RCT to investigate the efficacy of the intervention called 'cognitive functional therapy' (CFT) utilised in the OCS. The intervention aims to address the behaviours often seen in NSCLBP in a targeted, functionally specific and patient focused manner. The RCT was a two-armed study comparing classification based CFT (CB-CFT) with patients receiving traditional manual therapy and exercise (MT-EX). 121 patients with mechanically provoked NSCLBP (>52 weeks) were randomized to either CB-CFT (n= 62) or MT-EX (n= 59). A linear mixed model was used to estimate the group differences in treatment effect and also in the change in outcome from 3 and 12-month follow-up. Primary outcomes were change in Oswestry Disability Index (ODI) score and pain intensity measured with numerical rating scale (PINRS) at 12 months follow-up. Secondary outcomes were the Fear Avoidance Behaviour Questionnaire, the Orebro multidimensional questionnaire, the Hopkins symptoms check list and time off work due to their disorder. After adjustment for baseline scores, the CB-CFT group displayed superior outcomes supported by both statistically and clinically significant differences, compared to the MT-EX group. The degree of improvement in the CB-CFT group for ODI score was 13.7 points from baseline (95% CI, 11.4 to 16.1, $P<0.001$) and for PINRS scores 3.2 (95% CI, 2.5 to 3.9, $P<0.001$). In the MT-EX group, the improvement for ODI score was 5.5 points (95% CI, 2.8 to 8.3, $P<0.001$) and 1.5 for PINRS (95% CI, 0.7 to 2.2, $P<0.001$). There were also clinically and statistically significant reductions in fear avoidance behaviours (physical activity and work), the Orebro multidimensional questionnaire, the Hopkins symptoms check list and reduced need for ongoing care in favour of CB-CFT. The subjects in the CB-CFT group also reported a 3 times less likelihood to have time off work due to their disorder when compared to the MT-EX group. The results supported the use of classification based 'cognitive functional therapy' for NSCLBP as it produced superior outcomes compared to traditional physical therapies.

In conclusion, this thesis support the need for sub-classification and targeted treatment for NSCLBP based on a biopsychosocial construct. Further studies are needed to confirm these results also in those with higher levels of pain and disability and in other cultural groups to determine the generalizability of the findings.

Abbreviations

CB-CFT	Classification based cognitive functional therapy
CLBP	Chronic low back pain
CS	Classification Systems
FABQ	Fear Avoidance Beliefs Questionnaire
HSCL	Hopkins Symptoms Checklist
LBP	Low back pain
MT-EX	Manual therapy and exercise
NSCLBP	Non-specific chronic low back pain
OCS	O'Sullivan Classification System
ODI	Oswestry Disability Index
PINRS	Pain Intensity Numerical Rating Scale
RCT	Randomised Controlled Trial
REK	The Regional Ethics Committee
QTF	Quebec Task Force
SD	Standard Deviation
VESC	Vertebral Endplate Signal Changes

1. INTRODUCTION

1.1 Incidence

Low back pain (LBP) in the Western industrialised countries represents a common and very costly health problem (Waddell 2004). Incidence of LBP in the Nordic population during a lifetime ranges from 60-65%, and 40-55% experience pain within a 12-month period (Leboeuf-Yde et al. 1996). Some authors suggest that most patients with back pain will recover rapidly, regardless of treatment method (Spitzer 1987; Deyo 2002), however nearly half of pain sufferers have symptoms which persist and debilitate them for years (Carette 1994), and recurrence is very common. Improvement of back pain is apparent for most patients up till about 3 months. Thereafter levels for pain, disability and return to work remains almost constant. Six months after an episode, 60-70% of patients will have experienced relapses of pain, and up to 16% will be sick-listed. After 12 month, as many as 62% will still be experiencing pain (Hestbaek et al. 2003). More than 5% of the population that experience LBP, remains disabled with chronic LBP (Anderson 1981; Dillingham 1995; Waddell 2004; Breivik et al. 2006). However, in a recent study from North Carolina, US, it was concluded that chronic LBP (CLBP) is on the rise (Freburger et al. 2009). According to the study, 3 to 9% of North Carolina residents surveyed in 1992 said that they had debilitating CLBP. That number rose to 10.2% by 2006. Among people reporting ongoing, serious LBP in 1992, about 73% said they had seen a physician, physical therapist or chiropractor at least once during the past year. In 2006, 84% said they had done so. The fraction of people with back pain who ever had back surgery increased only slightly, from 22.3% in 1992 to 24.8% in 2006. In Norway, a recent study showed that there has been a marked decrease in work absenteeism related to LBP (Brage et al. 2010). This decrease has also been evident in other European countries, Great Britain in particular (Waddell et al. 2002). Suggested reasons for this change has been the increased focus to stay active and the recommendations that patients return to work as quickly as possible from health care workers and guidelines. Musculoskeletal pain was considered the main reason in 35% of sick listing in Norway in 2008 and in 30% of the new cases of disability pension in 2006. LBP was the dominant reason both in work absenteeism and disability pension. Two thirds of low back pain related work absenteeism was related to localised back pain without referred pain, the rest was back pain with referred pain. In the cases of disability pensioners, disc prolapses in the lumbar with nerve root compression accounted for 50% of the payments (Brage et al. 2010).

1.2 Diagnosis

In spite of a large number of pathological conditions that is capable of causing back pain, a definite diagnosis is difficult to achieve in most cases (85%) (Waddell 2004). Patients with uncomplicated LBP without an underlying malignancy or neurological deficit are defined as non-specific low back pain (NSLBP) (Deyo et al. 1996). As a result of not getting a specific diagnosis in the majority of cases, uncertainty in the treatment of this group of patients also seems to be very evident (Cherkin et al. 1998). As new and improved radiological examinations procedures continue to evolve, increasing our knowledge about associations or lack of associations between findings on MR and low back pain, the percentages of NSLBP may vary according to different studies. An example of this is the reported prevalence of ‘‘vertebral endplate signal changes’’ (VESC – including Modic changes) and its association with LBP. The wide range in reported prevalence rates and associations with LBP could be explained by differences in the definitions of VESC, LBP, or study sample (Jensen et al. 2008).

The most common neurologic impairment associated with back pain is herniated disc, and 95% of disc herniations occur at the lowest two lumbar intervertebral levels. The minority are diagnosed either as having nerve root pain (< 5%) (Laerum et al. 2007; Grovle et al. 2010) or LBP (< 1%) associated with serious underlying pathology (i.e. fractures, metastatic cancer, spinal osteomyelitis, and epidural abscess) (Henschke et al. 2009).

1.3 Transition from acute to chronic pain

Back pain is usually described by the length of time symptoms persist: Acute LBP lasts less than 6 weeks. Sub-acute LBP lasts between 6 and 12 weeks and chronic LBP persists for more than 12 weeks. For those, whose conditions have transitioned from acute to chronic pain (pain persisting) for 3 months or longer (1986), there are often few physical abnormalities. Integrating the cognitive and trauma literatures into our understanding of pain may elucidate the mechanism(s) through which chronicity develops from acute pain (less than 6 weeks duration) (1996). Although it may seem clear that psychosocial factors play a role in chronic pain, most studies are cross-sectional or retrospective. The few prospective studies using acute pain samples have not identified specific pathways linking psychosocial factors to pain perpetuation. In terms of prognostic indicators for poor outcome there have been extensive research over the last years. However, few studies have looked at whether prognostic indicators are similar across different subgroups of the back pain population. Factors that cause acute pain to become chronic can also act as a barrier to recovery of chronic pain and have been suggested as one reason for this limited research (Grotle et al. 2010). Two studies from Australia have supported this view by showing large overlaps in prognostic indicators for recovery in acute (Henschke et al. 2008) and chronic LBP (Costa et al. 2009). Grotle et al. (Grotle et al. 2006) also showed similar findings among first time consulters in primary care with acute LBP and secondary care consulters with CLBP. On the other hand, this overlap in prognostics indicators for recovery does not mean that the risk factors for development of chronic pain will be the same to those, which cause pain to persist. The injury type and severity of an acute low back pain episode might influence why it become long standing. However, as time passes and healing occurs, the influence of other factors such as fear avoidance behaviours, coping, stress and depression may play a more critical role in pain persistence (Grotle et al. 2010).

1.4 Underlying pain mechanisms

A number of factors need to be considered when looking at the different mechanism underlying NSCLBP and must be considered individually, and their weighting differ according to each different patient (Dankaerts et al. 2005).

Pathoanatomical

One of the oldest and most traditional approaches to diagnosis and understanding of the underlying mechanisms of LBP is from a pathoanatomical perspective (Nachemson 1999). Studies have reported findings of intervertebral disc (IVD) and facet joint degeneration, IVD prolapse, spondylolisthesis, foraminal spinal stenosis and Modic changes, and such findings are commonly assumed to be related to LBP (Nachemson 1999; Jarvik et al. 2002; Kjaer et al. 2005). This assumption does sound feasible if the underlying mechanism was pathology, however, the problem with an assumed underlying pathoanatomical diagnoses for NSCLBP is that in the pain free population there are also a considerable number of abnormal pathoanatomical findings which correlates poorly with levels of pain and disability (Jarvik 2003). Modic changes have been suggested to be the most clinically relevant single MRI finding in relation to LBP (Kjaer et al. 2005).

The confounding impacts of psychosocial, neuro-physiological and physical factors are often given little consideration regarding their contribution to the underlying basis of these disorders. In a prospective study looking at the three-year incidence of low back pain in an initially asymptomatic cohort, the authors found that depression was the highest predictor of any of the baseline variables and there were no association between new LBP and type 1 endplate changes (Modic), disc degeneration, annular tears, or facet degeneration (Jarvik et al. 2005).

Physical factors

CLBP has been found to be associated with numerous etiologic factors that have been linked to the condition: obesity, increased lumbar lordosis, reduced spinal mobility, tight hamstrings, and leg length inequality (Pope et al. 1985). Individual physical factors such as where in its range a spinal articulation is loaded, reduced trunk muscle strength and endurance, impaired flexibility, ligamentous laxity and motor control dysfunction have also shown to influence and be associated with LBP (Abenhaim et al. 2000; McGill 2004; Dankaerts et al. 2005; Dankaerts et al. 2006; Dankaerts et al. 2006; Dankaerts et al. 2009). Trunk muscle strength and endurance has been extensively studied in relation to CLBP (Ito et al. 1996; Mannion et al. 2001; Verbunt et al. 2005; Urzica et al. 2007; Mitchell et al. 2010). Although some studies have questioned the importance of the strength of spinal and abdominal muscles in LBP (Addison et al. 1980), the majority of researchers have found this to be an important physical factor in developing and predicting CLBP (Bayramoglu et al. 2001; Mitchell et al. 2010). Obesity has been suggested to be both a direct and indirect factor in CLBP, however, specific evidence is lacking (Mellin 1987). Certain physical factors such as sustained end range spinal loading, exposure to vibration, lifting in end range positions (ie flexion and rotation) and specific sporting activities involving cyclical end range loading of the spine (especially combined with rotation), can negatively impact the musculoskeletal system and have the potential to cause ongoing peripheral nociceptor sensitization (Adams et al. 1999; Abenhaim et al. 2000; Burnett et al. 2004; McGill 2004). This may support the efficacy of including ergonomic advice as part of the management of LBP.

“Motor control is defined as the ability to regulate or direct mechanisms essential to movement” (Shumway-Cook et al. 2007). This involves mechanisms like how does the central nervous system organize the many individual muscles into coordinated functional movements? How is the sensory information from the environment and the body used in order to select and control movement? How is our movement behaviour influenced by the perceptions, of ourselves, the tasks we perform and the environment in which we are moving (Shumway-Cook et al. 2007). Lack of motor control as an underlying mechanism for back pain has been suggested by several authors as a cause of CLBP (Richardson et al. 1995; O'Sullivan et al. 1997; O'Sullivan 2000; Dankaerts et al. 2009), but to what extent it is an underlying mechanism is still unclear as motor control are highly variable and the presence does not establish cause and effect (O'Sullivan 2005).

Apart from changes in mean muscle activity, LBP appears to be accompanied by various task-specific changes in muscular control which become manifest as altered patterns of muscle recruitment (Grabiner et al. 1992; Hodges 2001; Hubley-Kozey et al. 2002). In some individuals with LBP gait can also be disordered. Although it appears to be a consistent finding that individuals with LBP walk more slowly than pain-free individuals (Keefe et al. 1985; Lamoth et al. 2002; Spenkelink et al. 2002), it is at present not clear why LBP is accompanied by slower walking. It has been suggested that slower walking is a reflection of the presence of pain and/or fear-avoidance behaviour associated with pain and may reflect an attempt to reduce pain by restricting movements of the spine (Ahern et al. 1988; Vlaeyen et al. 2000). Individuals with acute induced pain as well as those with chronic LBP show increased activity levels of the lumbar erector spinae during the swing phase of gait, whereas this muscle is normally hardly active (Arendt-Nielsen et al. 1996). These changes in muscle activity are often assumed to ‘‘guard’’ or ‘‘splint’’ the spine in individuals with LBP (Lund et al. 1991; Arendt-Nielsen et al. 1996; Vogt et al. 2003). Nevertheless, individuals with LBP exhibit a normal range of movement during walking despite the presence of pain (Lamoth et al. 2002) and walking for about 10 min has been found to actually decrease the pain during acute LBP (Taylor et al. 2003). In a previous study on the impact of induced acute pain in healthy individuals, it was found that acute pain does not alter the trunk coordination during walking at different velocities (Lamoth et al. 2004). However, acute pain affects muscular control in terms of increased (residual) variability, reflecting timing deficits and changes in the frequency content while leaving the global pattern of lumbar erector spinae activity intact. In contrast, fear induced in healthy individuals has no effect at all on gait coordination. These findings appear to contradict the assumption that individuals with LBP alter motor control by way of protective guarding or splinting (Arendt-Nielsen et al. 1996; Main et al. 1996; Vogt et al. 2003). Alternatively, one may hypothesize that individuals with LBP have difficulty in adequately controlling their movements, and hence in dealing with perturbations, and therefore adapt a slower walking velocity allowing more precise control. Under normal circumstances, walking is a highly flexible and adaptive activity that is continuously altered so as to meet both environmental and internal requirements. In normal walking, coordinated patterns of trunk and pelvis rotations and trunk muscle activity are important for the maintenance of dynamic equilibrium, to reduce the energy cost and to effectively deal with perturbations during locomotion (Thorstensson et al. 1987; Stokes et al. 1989; White et al. 2002).

Altered motor behavior as a response to pain has also been reported in specific low back pain disorders such as neurogenic and radicular pain, neuropathic, centrally mediated pain and inflammatory conditions. However, this response is often considered to be an adaptive or protective response (Elvey 1997; Hall et al. 1999; Elvey et al. 2004). Similarly there are also psychological processes such as stress, fear, anxiety, depression, and somatization that are known to disrupt motor behavior (Hodges et al. 2003). Attempting to treat these conditions with physical interventions is likely to be ineffective due to the non-mechanical underlying mechanisms of these disorders (O'Sullivan 2005).

Lifestyle factors

The prevalence of back pain has been examined in a number of studies, however there are fewer studies that describe the associations between lifestyle factors and LBP. It is important to know from a health perspective whether lifestyle factors, such as physical activity, smoking, body mass index, sleep and stress are associated with LBP (Bjorck-van Dijken et al. 2008; Mitchell et al. 2010). Also the additional understanding of LBP in adolescence and the risk factors for developing chronic low back pain in adult life may have implications for early interventions and management (Astfalck et al. 2010). The transition from childhood into adulthood involves major lifestyle and psychological changes (LeResche et al. 2005). The spine also undergoes substantial changes in periods of growth and development (Grimmer et al. 2000), hence it may not be appropriate to extrapolate the research on LBP in the adult population to adolescence (Astfalck et al. 2010).

Different levels of physical activity have been suggested to predispose patients to LBP. In a population-based study from Sweden, researchers found that there was an association between physical activity and LBP, especially in individuals with physical demanding jobs, but with low physical activity during leisure time (Bjorck-van Dijken et al. 2008). There has also been shown a dose-response relationship between both short and long-term LBP and increasing workload (Hartvigsen et al. 2001). Also increased physical workload, such as manual material handling, bending and twisting, as well as a working environment involving whole-body vibration, constitute an increased risk for LBP (Hoogendoorn et al. 1999; Thorbjornsson et al. 2000). There is also evidence of a gender difference, that these physical demands have a more profound effect on women when exposed to similar heavy loads as men (Macfarlane et al. 1997).

A recent systematic review (Kelly et al. 2010) also addresses the issue of sleep in relations to CLBP. Prevalence studies indicate that more than 50% of CLBP patients complain of sleep disturbance (Marin et al. 2006;Tang et al. 2007). Sleep disturbance for patients with CLBP encompasses many factors and can be manifested in many different ways: poor quality sleep, reduced sleep efficiency and duration, delayed sleep onset, increased activity or movement during sleep or fragmentation of sleep architecture (the 5 stages of sleep – non rapid eye movement (REM), stage 1-4 and REM sleep). In the study by Tang et al. (2007), 70 patients with CLBP reported significant alterations in sleep onset and maintenance when compared with age and sex-matched controls (Tang et al. 2007). A larger Norwegian study showed similar findings among 457 CLBP patients reporting significant sleep problems compared with controls (Hagen et al. 2006). Sleep is also vital for tissue restoration, growth, and energy conservation (Adam et al. 1977; Adam et al. 1983). Sleep deprivation can also cause pain to become more and more severe, resulting in a hyperalgesic response.

Psychological and social factors

Personal qualities such as coping, environmental factors such as life adversity and social support have been postulated to have the capacity to influence chronic pain states. Social factors such as the compensation system, work place disputes, work and family tensions and cultural issues affecting beliefs, reinforce the psychological factors that can increase the central drive of pain (Nachemson 1999). An increasing number of studies have investigated these factors in relation to its impact on the central nervous system and pain mediated via the forebrain (Linton 2000; Zusman 2002). Coping strategies such as negative thinking, pathological fear and abnormal anxiety regarding pain, avoidant behaviour, catastrophizing and hypervigilance have been shown to be associated with high levels of pain, disability and muscle guarding (Frymoyer et al. 1985; Main et al. 1996; Linton 2000). Some of the research relating personal and environmental factors for chronic pain have been criticised for its clinical and empirical attempts to classify patients into subgroups along independents paths (Klapow et al. 1995; Frymoyer et al. 1985). Psychosocial factors are often considered in isolation or only in relation to one dimension of the clinical picture, i.e. pain or mood (Weickgenant et al. 1993). Despite this advanced knowledge regarding the relative contribution of these factors to negatively impact pain disorders, there is considerable debate whether these factors predispose or are as a result of a pain disorder. Positive factors such as adaptive coping strategies, appropriate pacing and distraction (reduced hypervigilance) on the other hand, can have a descending inhibitory effect on pain via the forebrain (Zusman 2002). There is evidence that cognitive behavioural interventions reduce disability and are cost effective in specific groups with NSCLBP (Woby et al. 2004; Linton et al. 2006), however, there appears to be a growing trend within physiotherapy to classify most patients with non-specific CLBP as primarily psychosocial driven due to a lack of an alternative diagnosis. Although there seems to be psychological and social cognitive issues related to most CLBP it appears that only a small sub-group exists where these factors become the dominant or primary pathological basis for the disorder (O'Sullivan 2005).

Neuro-physiological factors

The changes suggested to occur in chronic pain states in the peripheral as well as central parts of the nervous system, can also give an insight into some of the underlying mechanisms commonly seen in NSCLBP patients (Zusman 2004). It has been postulated that two interdependent mechanisms contribute to chronicity-nociceptive (humoral and immune-related dysfunction that stimulates nociceptive structures and body tissues) and non-nociceptive (cognitive-evaluative) mechanisms. In either case there is an increase in the conviction of the central nervous system that body tissue is in danger and therefore there is an increase in the activity of the pain neuromatrix (Moseley 2003). The pain neuromatrix being the combination of cortical mechanisms that when activated produce pain (Melzack 1990). In chronic pain states the nociceptive system undergoes profound changes both peripherally and centrally. Alterations of wide dynamic range second-order nociceptors are particular relevant as these dominates the ascending connections to the brain areas, identified as key components of the pain neuromatrix. In CLBP patients a reorganization of the primary sensory motor cortices, with marked implications across pain dimensions have been shown (Flor et al. 1997). Also an imbalance of the descending modulatory systems could lead to an increase in endogenous facilitation resulting in innocuous input being perceived as painful imbalance. Such an imbalance may cause pain of diffuse nature and amplification of persistent pain (Dubner et al. 1999). Also the tight interdependence of body perception and movement repertoire that can be seen in amputees learning to perform normally impossible movements of their phantom arm (Moseley et al. 2009), may also give an indication of the movement abnormalities observed in people with CLBP, as a manifestation of a disruption of the working body schema. This proposition has been supported, by the close association between lumbar tactile acuity and performance on motor control tests (Luomajoki et al. 2010)

1.5 Current evidence for management of NSCLBP

The current evidence for management of non-specific chronic low back pain (NSCLBP) reveals that interventions such as manual therapy, exercise, acupuncture, spinal injections and cognitive behavioural therapy as single interventions are not superior to each other, have a limited long-term impact on the disorder and small effect sizes (Assendelft 2004; Furlan AD 2005; Hayden et al. 2005; Ostelo 2005; Staal JB 2008). Exercise is widely used in the rehabilitation of NSCLBP patients. However, no consensus exists as to the most effective programme design based on RCTs and systematic review (Liddle 2004). This review also (Liddle 2004) highlighted the diversity of exercise programmes offered to patients with CLBP. Further, no form of exercise has been shown to be more efficacious than another (Van Tulder 2000). The review by Assendelf et al. (2004) concluded that there is no evidence that spinal manipulative therapy is superior to other standard treatments for patients with acute or chronic low back pain (Assendelft 2004). A study comparing the efficacy of general exercise, motor control exercises and spinal manipulation concluded that there is little basis on which to prefer (Ferreira et al. 2007). It has been stated that caring for chronic LBP, is one of the most difficult and unrewarding problems in clinical medicine (Leclere 1990), as no treatment has been shown to be clearly effective (Mannion et al. 2001; Assendelft 2004; Hayden et al. 2005; Ostelo 2005), highlighting the resistance of this disorder to change. An obvious explanation could be that there actually is no difference in effect between the different treatment options.

The reasons for the failure of current clinical practice to effectively manage NSCLBP are proposed to lie in two main domains:

1. The failure to adequately deal with NSCLBP within a multidimensional biopsychosocial framework in order to address the vicious cycle of pain (Leeuw et al. 2007).

2. The lack of sub-grouping and targeted management. NSCLBP subjects can be sub-grouped based on cognitive (Turk 2005), physical (Dankaerts et al. 2009), neurophysiological (Woolf et al. 1998) and lifestyle behaviours (Mitchell et al. 2010). Few clinical trials exist utilizing multidimensional classification systems or targeted interventions for NSCLBP (Fersum et al. 2010). All this evidence lends to the need for a biopsychosocial person centred CS to target management (Leboef-Yde 2001; O'Sullivan 2005; Fersum et al. 2010).

1.6 Classification of low back pain

Classification systems (CS) are defined as devices for sorting the complex elements of reality into reasonable and logical entities (Petersen et al. 1999; Petersen 2003). Ideally, the objectives of a diagnostic classification are to find a label that indicates the cause of the disease, predicts outcome, predicts responses to specific therapies, and can be used to describe the disease in communicating experience or research. Current approaches or models used for the diagnosis and classification of CLBP have tended to only focus on a single dimension of the disorder, limiting their validity (Ford et al. 2003). Outcomes are likely to be determined by the interactive effects of multiple factors, as single factors may not account for a statistically significant or clinically meaningful proportion of the variance in outcome. In studies that have included measures of both physical and psychological functioning interactive effects of biopsychosocial factors on the outcomes have been reported (Mayer et al. 1987) suggesting that multidimensional rather than unidimensional classifications should be attempted for a problem as complex as chronic pain (Turk 1988). It has been proposed that we need a broader conceptualisation of patients with chronic pain (Turk 2005). There is growing evidence and support for psychological factors importance in pain, suffering and disability (Gatchel et al. 1986). Flor and Turk (1988) discovered that in patients suffering from LBP cognitive appraisals of helplessness and hopelessness were much more predictive of both self- report of pain impact and behavior in response to pain than physical factors predicting pain severity, life interference, or physician visits (Flor et al. 1988). Jensen et al. (2001) also supported this in their findings that perceptions of control over pain and decreased beliefs about being disabled and catastrophizing, were associated with reductions in pain intensity, depression, number of physician visits, and physical disability (Jensen et al. 2001). According to Turk (2005) these data suggest that greater attention should be given to identifying the characteristics of patients who improve and those who fail to improve when treated with the same approach. A number of studies have focused on empirically identifying patient subgroups based on psychological characteristics and psychopathology using the Minnesota Multiphasic Personality Inventory (MMPI) (Swimmer et al. 1992) and Symptom Check List-90R (Hutten et al. 2001).

Turk and Rudy performed a cluster analysis using the West Haven-Yale Multidimensional Pain Inventory (MPI) identifying 3 relative homogeneous groups:

1) “Dysfunctional (DYS)”, patients who perceived the severity of their pain to be high, reported that pain interfered with much of their lives, reported a higher

degree of psychologic distress due to pain, and reported low levels of activity; 2) "Interpersonally Distressed (ID)," patients with a common perception that significant others were not very supportive of their pain problems; and
3) "Adaptive Copers (AC)," patients who reported high levels of social support, relatively low levels of pain and perceived interference, and relatively high levels of activity.

Several studies in Europe have been conducted afterwards to confirm their findings using different measures of the constructs assessed by the MPI (Talo et al. 1992; Jamison et al. 1994; Strong et al. 1994).

Developing a consensus regarding the classification of pain from a neurophysiological perspective also possess some great challenges. Current methods of classifying pain, is believed to have a number of major limitations. Pain syndromes are usually identified by parts of the body, duration, and causative agent. An anatomical based classification of pain is believed to limiting because the innervation of distinct anatomical regions is often analogous, bearing in mind differences of the target organ innervated (e.g. skin vs. viscera), length of axon and myelination (Woolf et al. 1998). There are a couple of crucial features that needs be addressed when developing a successful classification system: (1) The CS needs a truly operational criteria, and (2) the use of inclusion and exclusion criteria. The first feature is a must even if the level of knowledge of the mechanisms is good. The second feature holds because there is bound to be some degree of nosologic overlap. A classification system should also have validity, and this can difficult to achieve at this moment in time, validity is an estimate of the degree to which the classification system corresponds to the underlying biology of the disorder being studied. Validity is traditionally defined with reference to some gold standard. The challenge in different fields of classification is the absence of a gold standard. The alternative approach is to use an iterative, fallible process of searching for and identifying symptom clusters, biological markers, history and treatment response.

1.7 Current classification systems

In order to be able to treat patients effectively and with a good outcome, there has been an increasing demand and need for sub-classification of the NSLBP population. Numerous CS have been proposed (McKenzie 1981; Spitzer et al. 1987; Delitto et al. 1995; Sahrmann 2001; Petersen et al. 2003; O'Sullivan 2005). However, only a few are found sufficiently reliable and valid (Petersen et al., 1999), and even fewer consider the disorder from a biopsychosocial perspective (Petersen et al. 1999; Ford et al. 2003; McCarthy et al. 2004; O'Sullivan 2005; Dankaerts et al. 2006; Fersum et al. 2010). The following overview is not meant to be exhaustive but highlight some of the strength and weaknesses of the different CS (See table 1)

The Quebec Task Force CS was designed by a panel of international experts in the field of LBP management. It was developed to use classification of all LBP patients to help with clinical decision making, providing a prognosis and evaluating treatment effectiveness (Spitzer 1987). The classification in this system is by a method of classifying patterns based on clinical features. It is by many considered to be the first 'multidimensional classification system,' as it considers biomedical, psychological and social considerations in the classification process (McCarthy et al. 2004). The developers of the QTF classification system argued that because the most LBP patients presents with a disorder with an unidentified etiology, a classification system should be designed based primarily on pain data (Spitzer 1987). The task force also argued that only in the minority of cases can the origin of the pain be identified (i.e. the pathology causing the disability can be determined). A classification system, therefore, should be composed of data collected from a variety of sources, including 1 a combination of signs and symptoms (pain and neurological examination data), (2) radiological data, (3) Previous response to treatment (surgical or conservative treatment), (4) work status (working, not working), and (5) symptom duration. The QTF consists of 11 groupings and considers pathoanatomical diagnosis (specific, non specific or 'red flags'), signs and symptoms (area of pain referral), social factors and the stage of the disorder (acute, sub-acute and chronic). The work status and symptom duration data were used to form 2 additional axes of classification. By adding these two separate axes the developers of the QTF system believed that prognosis is influenced by both symptom duration and work status, evident from data collected on patients by the Quebec Worker's Compensation Board (Spitzer et al. 1987). The developers of the QTF system apparently believed that the addition of a radiological test confirming the presence of a compressed nerve root required a separate category. From the perspective of prognosis and physical therapy treatment, patients in these 2 categories may not differ. From the spine surgeon's perspective, the patient with a radiologically confirmed nerve root compression may be considered a candidate for surgery, whereas the patient with identical signs and symptoms but no radiologically confirmed nerve root compression will likely not be a surgical candidate. The QTF classification system was designed to account for those patients who may be candidates for surgery. Several authors have evaluated the clinical categories, looking at the discriminant and predictive validity. Results from these studies suggest that it has good predictive and discriminate validity (Marras et al. 1995; Frank et al. 2000; Loisel et al. 2002). However, some studies have also pointed out limitations of the QTF it has not been tested for reliability and does not consider the underlying mechanism, except for differentiating somatic from radicular pain (Dankaerts et al. 2006). Within this system there is no subgrouping of NSLBP except on the basis of pain area, and no specific treatment is advocated for this large group of patients other than general exercise, therefore limiting its use for physiotherapy assessment and treatment (Padfield 2002).

McKenzie’s system is based on information from history taking, and symptom response to patient or therapist generated loading of the lumbar spine. It has been reported as the most commonly used system by physiotherapists (Battie et al. 1994).

The McKenzie system is a clinical guideline index designed for most, but not all, patients with LBP (Riddle 1998). The medical history consists of questions related to symptom onset and symptom behavior associated with several different postures. The examination requires the therapist to observe the patient's posture and the alignment of several bony landmarks. Trunk movements are observed for limitations and frontal-plane deviations. Observations are made of trunk movements and the patient is simultaneously questioned about the effect of these movements have on symptom location and intensity. In addition, a complete a neurological examination and examination the patient's hip and sacroiliac joints is performed. McKenzie's classification system requires the clinician to classify the patient's problem into 1 of 13 categories The most commonly discussed categories are the postural syndrome, the 4 dysfunction syndromes, and the 7 derangement syndromes. In addition, there is a category exists for those patients classified as having a hip or sacroiliac joint problem. The dysfunction syndrome is further subdivided into flexion dysfunction, extension dysfunction, side-gliding dysfunction, and adherent nerve root dysfunction. The derangement syndrome is subdivided into 7 derangement syndromes that are numbered consecutively from 1 to 7, each with a different set of criteria of symptom distribution. McKenzie described these various syndromes because he believed that each syndrome required a different treatment strategy. Although it was suggested in his work that that patients also can be classified as having a sacroiliac joint or hip problem, he did not describe the examination procedures or treatments for these conditions (McKenzie 1981). The system was originally based on the clinical experience of the author and whilst there was no data regarding the reliability and validity from its origin, subsequent studies have investigated these issues (Riddle et al. 1993; Donahue et al. 1996; Karas et al. 1997). The system as a whole has been tested for reliability, and has substantial inter-tester agreement according to the criteria of Landis and Koch (1977) when applied by trained examiners (Kappa coefficients ranging from 0.6 to 0.7: (Landis et al. 1977; Kilpikoski et al. 2002). A number of studies have supported the validity of the system’s ability to predict outcome of treatments with McKenzie-therapy or active rehabilitation for patients whose symptoms have centralised, i.e. abolished from their most distal location, following the McKenzie examination procedures (Donelson 1990; Donelson et al. 1990; Karas et al. 1997). A randomised controlled trial investigating treatment-related validity of the McKenzie system, i.e. ability to categorise patients in a way that might result in selection of the most effective treatment, have shown conflicting results (Cherkin et al. 1998). The McKenzie’s biomechanical explanations as the basis for the classification and treatment, has also been questioned in terms of validity (Edmondston et al. 2000).

Delitto et al. (1995) has developed a classification system proposed to be a clinical guideline index designed to guide treatment for patients with LBP (Delitto et al. 1995). The system classifies patients into four main categories using information gathered from history taking and clinical examination. The system requires the therapist to collect historical and disability questionnaire data to aid in determining whether the patient's condition is amenable to physical therapy intervention or requires care of another practitioner. Examination procedures are designed to assess the effect of movements on symptom behavior and to assess the alignment of various body structures. The classification system has 3 levels involving different types of clinical decision-making. The first level requires the therapist to use various instruments to decide whether the patient (1) can be managed independently by a physical therapist, (2) cannot be managed by a physical therapist, or (3) can be managed by a physical therapist in consultation with another practitioner. The second level of clinical decision making requires the therapist to stage the patient into 1 of 3 groups (stage I, stage II, or stage III) based on the presence and severity of various functional limitations and disabilities, scores on a disability scale and work status information. When making decisions at the second level, therapists can only use historical and disability data obtained from the patient. The examination is not done until the therapist is prepared to make clinical decisions at the third level. The third level of clinical decision-making involves the assignment of the patient, after being assigned to a stage, and syndromes (categories) accordingly described for each stage (Delitto et al. 1995). Intertester reliability of single categories has been questioned (Delitto et al. 1995; Riddle et al. 2002), however, the system as a whole has been shown to have moderate intertester reliability (Kappa coefficient 0.56) (Delitto et al. 1995; Fritz et al. 2000; Riddle et al. 2002). Two randomised controlled trials have, with regard to choice of treatment, shown validity of one of the seven categories of the system (Delitto et al. 1993; Erhard et al. 1994). In addition, a recently published trial has shown that treatment based on the classification system as a whole, was more beneficial for acute NSLBP patients, than treatment based on clinical practice guidelines (Fritz et al. 2003). As the population of patients with long-lasting NSLBP differs very much from the acute NSLBP, this classification system may not be valid for patients with non-specific chronic low back pain (NSCLBP).

The development of the Petersen system was based on the review of the literature (Petersen et al. 1999) and proposed criteria for categorization presented in a paper regarding classification (Laslett et al. 1999) The initial version of the Petersen system was initially evaluated by five Danish back specialists. Minimum criteria for placing patients within particular categories were discussed and comments from the specialists were incorporated in the final version of the system.

The development phase followed three steps. In step one, pathoanatomic categories that could be derived from evidence were included, (reducible disc syndrome , irreducible disc syndrome, non-mechanical disc syndrome, nerve root compression syndrome, spinal stenosis syndrome, zygapophisial joint syndrome, and sacroiliac joint syndrome). The next step included two additional categories widely assumed within the physiotherapy profession to be pathoanatomically oriented, (adherent nerve root syndrome, nerve root entrapment syndrome, myofascial pain syndrome, and adverse neural tension syndrome) or indicated pain producing connective tissue, although not specific to certain anatomical structures, (postural syndrome and dysfunction syndrome), were included. In step three they included a category widely assumed to indicate that patient responses during clinical examination should be re-evaluated, (abnormal pain syndrome). Adherent nerve root and nerve root entrapment have been excluded from the system later due to low intertester reliability (Petersen et al. 2004). This CS attempts to connect a symptomatic response to key orthopedic tests and an assumed underlying pathologic structure to direct the treatment strategy. The syndromes are defines by symptom location and effect of mechanical loading (Petersen 2003). The intertester reliability of this CS was tested out on ninety patients with chronic low back pain, each patient being examined by two physiotherapists. Four physiotherapists conducted all the assessments in total. Percentage of agreement and kappa coefficients were calculated for each category. The overall rate of agreement was 72% and the kappa coefficient was 0.62 for the mutually exclusive syndromes in the classification system. Agreement rates for each of the syndromes ranged from 74% to 100% and kappa coefficients ranged from 0.44 to 1.00. These findings suggest the inter-tester reliability for some of the categories to be acceptable. The relatively modest level of total agreement (39%) for the system as a whole might indicate that the utility of the system for general screening purposes is limited, compared with the utility in identification of particular syndromes. It has been suggested that due to low prevalence of positive findings in some of the syndromes, future work should focus on testing reliability on a larger sample of patients, and testing of validity and feasibility of the system as a whole (Petersen et al. 2004).

Van Dillen and coworkers have developed a classification system comprising five categories based on testing of muscular stability, alignment, asymmetry, and flexibility of the lumbar spine, pelvis, and hip joints (Maluf et al. 2000). Of particular interest to the system is the recording of movements and activities in daily functioning that provokes the patients' familiar symptoms. The CS was designed in an effort to aid clinicians in identifying the primary movement problem toward which the physical therapy intervention should be directed. Therefore, each category of the CS is named for the specific direction of spinal movement or alignment that is found to be consistently associated with an increase in LBP during testing.

An underlying assumption of this approach is that daily repetition of similar movements and postures result in habitual movement of the lumbar spine in a specific direction, which then may contribute to the development, persistence, or recurrence of mechanical LBP (Maluf et al. 2000). The direction of spinal motion associated with an increase in low back-related symptoms is though to reflect movement strategies and postures that are repeated by a given individual throughout each day. If you are a painter primarily painting overhead you can be inclined to develop a symptom, causing predisposition for motion of the lumbar spine into a direction of extension, however somebody with a office job may be more likely to develop symptoms associated with lumbar flexion. Presumably, individuals may develop habitual movements and postures in response to functional activity demands that may contribute to LBP and that may be identified and corrected through the evaluation of alignments and motions of the lumbar spine (Maluf et al. 2000; Harris-Hayes et al. 2009). In order to a patient into 1 of the 5 categories (flexion, extension, rotation, rotation with flexion, rotation with extension) the clinician should attempt to identify a consistent pattern of signs i.e., direction-specific motions and alignments of the lumbar spine) and symptoms (i.e., reproduction of low back–related complaints, including numbness, tingling, or pain in the back or lower extremities) in response to items performed in several different test positions (i.e. standing or sitting). Confirmation that the symptom-provoking spinal motion or alignment has been correctly identified occurs by restricting that motion or alignment and noting whether there is a reduction of symptoms (Maluf et al. 2000). Reliability of the individual tests used in criteria for classification has been shown to vary from fair to almost perfect (Kappa coefficients ranging from 0.21 to 1.00) (Van Dillen et al. 1998; Harris-Hayes et al. 2009). However, in the most recent study only 3 out of the 5 categories could be reliably tested as there were no flexion or extension patients in their study sample (Harris-Hayes et al. 2009). The use of the system has been illustrated by a case report by Maluf et al. (2000) and the effect on pain of modified patient preferred movement by Van Dillen et al. (2003). Also 3 factors relating to the validity of 3 out of the 5 categories have been identified and validated (Van Dillen et al. 2003). However, no data have been published supporting or refuting the validity of the system concerning its ability to categorise patients in a way that might result in selection of the most effective treatment.

To summarise, although data on reliability and validity have been published indicating usefulness of some of these classification systems, to date evidence is lacking to support their application in identifying subgroups of patients with better outcomes from a specific treatment compared to others common clinical approaches. Therefore, there is a need for an improved classification system with prescriptive validity for patients with low back pain.

1.8 The O’Sullivan classfication system

Since 1997 Peter O’Sullivan has developed a novel system, the O’Sullivan Classification System (OSC) based on the Quebec Task Force Classification (QTFC), incorporating multiple dimensions in the classification of patients into subgroups based on proposed underlying pain mechanisms. The classification system fits within the QTFC as it uses many of the same criteria set by the QTFC. Both these systems use categories as ´non-specific´ LBP patients without radiation below the gluteal folds`, absence of `red and dominant yellow flags` and absence of neurological signs`. Rather than replacing existing CS this multi-dimensional mechanism-based CS is an additive, attempting to sub-classify the large proportion of patients that sits within the NSCLBP. The OCS incorporates the biopsychosocial model, which subgroups patients based on identification of cognitive (negative back pain beliefs, fear, hypervigilance, anxiety, low mood), lifestyle behaviours (activity avoidance, poor pacing) associated with the disorder and maladaptive movement (loss of movement control and awareness, protective and avoidance behaviours) (O'Sullivan 2000; O'Sullivan 2005). The classification is based on a systematic examination process (subjective history, objective examination and available medical information), using several different classification levels based on the proposed driving mechanism behind the disorder (O'Sullivan 2005; Fersum et al. 2009). This system differentiates between specific LBP, including red flag disorders (i.e. cancer, infection, inflammatory disorders, fractures) versus NSLBP. NSLBP is further split into either centrally mediated back pain or peripherally mediated back pain. The centrally mediated back pain is split into dominant psychosocial or non-dominant psychosocial. The peripherally mediated disorders are split into pelvic girdle pain or low back pain. The pelvic girdle pain is split into either reduced force closure or excessive force closure. The pelvic girdle pain group has been described in detail elsewhere (O'Sullivan et al. 2007; O'Sullivan et al. 2007). For the low back pain group, the next level of classification divides it into either control impairment disorder or a movement impairment disorder. A control impairment disorder is represented with a loss of functional control of a spinal region, with a resultant loading and movement based pain disorder. These disorders will often present with no impairment to range of movement in their pain provocative direction. Altered dynamic control of the spinal region leaves the spine vulnerable to tissue strain, from repetitive end range strain and abnormal loading.

Pain associated with a functional loss of regional spinal control may be manifested as:

1. "through range movement pain" due to non-physiological loading of the spinal region
2. "loading based pain" due to non-physiological loading of the spinal region in certain positions
3. "end of range pain" or "overstrain" due to repetitive strain of the spinal region at the end of range.

According to the work O'Sullivan (2000, 2005), the control impairment group differs from the movement impairment group in that the symptomatic structure may have normal movement parameters in the direction of pain provocation, but becomes sensitised from abnormal loading and strain (O'Sullivan 2000; O'Sullivan 2005).

Directional subgroups also exists either into flexion, passive or active extension, a lateral shift or a combination of these in which case it is classified as multidirectional (O'Sullivan 2000; Dankaerts et al. 2006; Dankaerts et al. 2009). A group of patients with spondylolisthesis and a classification of control impairment have been successfully managed previously (O'Sullivan et al. 1997), but to date this approach has not been trailed adequately in subjects with NSLBP.

Movement impairment disorders are associated with a painful loss of normal physiological movement about a spinal region. This could occur secondary to connective tissue changes and / or more likely to muscle guarding around the sensitised spinal region. These patients will generally avoid moving into the painful range and this can be related to flexion, extension, lateral flexion or it can be multidirectional (O'Sullivan 2005). The movement impairment is usually both active and passive. Within the movement impairment disorders some patients present with a multisegmental and multidirectional movement impairment associated with high levels of co-contraction of the abdominal wall and back muscles. This reflects high levels of trunk muscle co-contraction and fear avoidance behaviour with regards to spinal movement.

A model has been suggested for accumulating evidence in the validation process of a classifications system (Dankaerts et al. 2004). This model involves a structured build up and consists of different stages of validation, each step dealing with different criteria. See figure 1. The first process involves a hypothesis behind the classification system. Initially this was through the formulation and definition of the 5 distinct subgroups with motor control impairment (MCI) (O'Sullivan 2000). The next step involved testing clinicians ability to discriminate the different patterns and the CS has good inter-tester reliability (Dankaerts et al. 2006; Fersum et al. 2009) and validity based on provocative movement behaviours (Dankaerts et al. 2005; O'Sullivan 2005;

Dankaerts et al. 2007; O'Sullivan et al. 2007; O'Sullivan et al. 2007; Beales et al. 2009; Dankaerts et al. 2009), as well as cognitive domains (Fersum et al. 2009). Once a generally accepted diagnostic classification system has been developed, outcome studies are required to determine the most effective treatments for particular categories of patients.

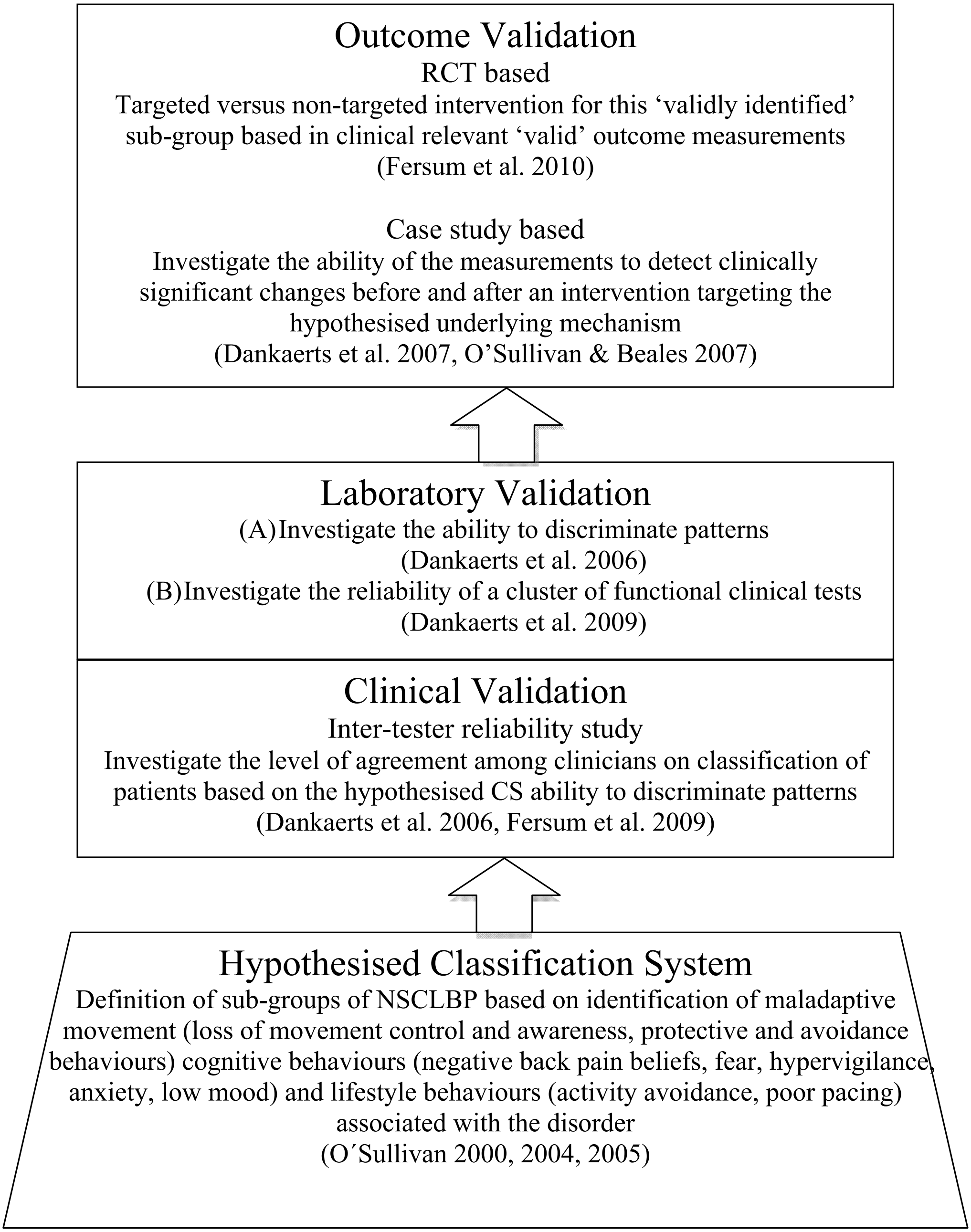
The next level of the outcome validation have been through a series of case studies (Dankaerts et al. 2007; O'Sullivan et al. 2007; O'Sullivan et al. 2007) adding further validation to this multidimensional CS. The intervention, named classification based ‘cognitive functional therapy’ (CB-CFT). CB-CFT directly challenges these maladaptive behaviours in a cognitive and functionally targeted manner to break the vicious cycle of pain and disability. However, this classification and management system for NSCLBP disorders has not been formally tested in a randomized controlled trial until now.

Table 1. Overview of current classification models for NSCLBP

Author	Description	Biopsychosocial perspective?	Validated for NSCLBP?	Reliable?
McKenzie (1981)	1. Postural Syndrome 2. Dysfunction 3. Derangement 4. Other	☹ (No)	☺ (Partial)	☺ (Yes)
QTF Spitzer et al. (1987)	1. Low back pain without radiation of pain below gluteal folds 2. Low back pain with radiation not beyond knee, no neurological signs 3. Low back pain with radiation below knee, no neurological signs 4. Low back pain with lower-extremity radiation and neurological signs 5. Presumptive compression of nerve root based on radiographic tests 6. Compression of nerve root confirmed by imaging tests 7. Spinal stenosis confirmed by radiological test 8. Postsurgical status < 6 months following surgery 9. Postsurgical status > 6 months following surgery 10. Chronic pain syndrome 11. Other diagnoses (metastases, visceral disease etc.)	☺ (Yes)	☺ (Partial)	☺ (Partial)
Delitto et al. (1995)	1. Specific exercise 2. Manipulation 3. Stabilization 4. Traction	☺ (Partial)	☹ (No)	☺ (Partial)
Petersen et al. (2003)	1. Disc syndrome 2. Nerve root compression 3. Spinal stenosis 4. Zygopohyseal joint 5. Postural 6. Sacroiliac joint 7. Dysfunction 8. Myofascial pain 9. Adverse neural tension 10. Abnormal pain 11. Inconclusive	☺ (Partial)	☺ (Partial)	☺ (Partial)
Van Dillen et al. (1998)	1. Rotation with extension 2. Rotation with flexion 3. Rotation 4. Extension 5. Flexion	☹ (No)	☺ (Partial)	☺ (Yes)
O'Sullivan (2005)	1. a. Specific (adaptive/maladaptive) b. Non-Specific 2. Centrally mediated pain a. Dominant psychosocial b. Non-dominant psychosocial 3. Peripherally mediated pain 4. Pelvic girdle pain a. Excessive force closure b. Decreased force closure 5. Low back pain a. Control impairment b. Movement impairment 6. Contribution of psychosocial factor	☺ (Yes)	☺ (Yes)	☺ (Yes)

☺ = Yes ☺ = Partial ☹ = No ☹ = Unknown

Fig. 1.
Flow chart of validation model for the O´Sullivan Classification System. Adapted and reprinted with permission from Dankaerts & O’Sullivan.



2. AIMS OF STUDY

- Review the literature for patients with non-specific low back pain to examine to what extent sub-grouping and targeted treatment have been used previously, and furthermore examine if use of classification systems influenced the outcome.
- Establish the inter-tester reliability of the broader OSC system.
- Examine the efficacy of classification based cognitive functional therapy (CB-CFT) for patients with non-specific chronic low back pain (NSCLBP) compared to manual therapy and exercise.

The aims of the separate papers were:

Paper I

Review the literature on RCTs evaluating manual therapy treatment and exercise therapy for patients with NSCLBP. More specific, the aim was to investigate both the level of integration of sub-classification in these RCTs, as well as summarise the effects of the studies that had sub-classified and matched treatments accordingly based on a meta-analysis.

Paper II

Examine the inter-tester reliability in a clinical setting of therapists' ability to independently classify a wide range of patients with NSLBP, utilising an extended mechanism-based classification method developed by O'Sullivan.

Paper III

Compare the outcome of CB-CFT with current practice (manual therapy and exercise (MT-EX)) in patients with NSCLBP in a randomised controlled study.

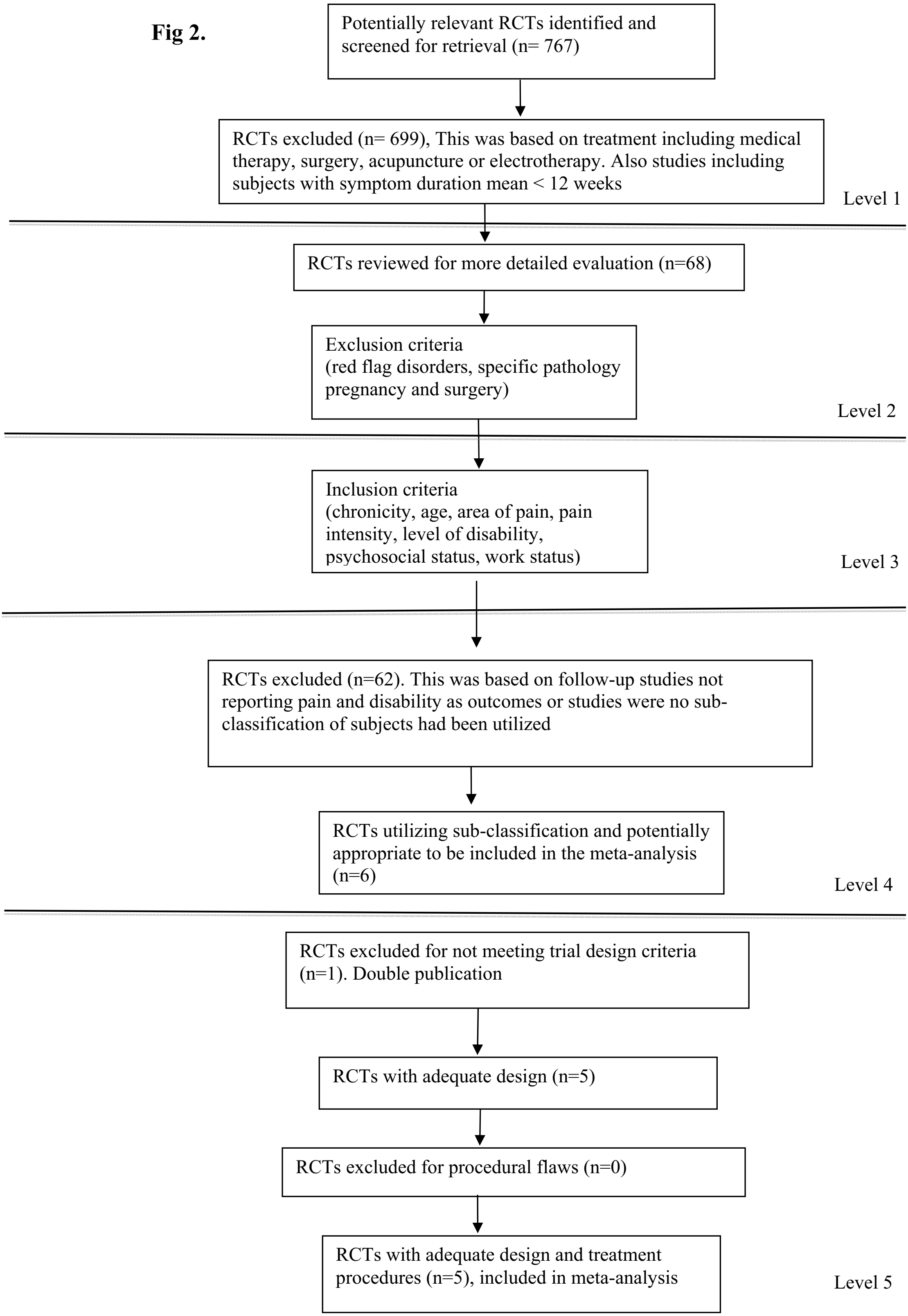
3. MATERIAL AND METHODS

3.1 Material

3.1.1 Paper I

Two independent reviewers conducted searches and assessed randomised controlled trials and out of 767 only 68 utilised manual therapy and exercise. The titles and abstracts of these papers were further screened for suitability for inclusion. Disagreements were resolved with a consensus meeting between reviewers. Many of the studies had included a mix of patients with acute, sub-acute and chronic LBP, as well as included patients with specific LBP disorders. Following the screening, data about age, chronicity, area of pain, level of pain/disability, psycho-social status, work-status, any form of compensation of the participants from the included papers were extracted. Of the 68 studies, only five had attempted a specific sub-classification strategy beyond general inclusion and exclusion criteria in line with the inclusion criteria. From these studies short and long-term data for the outcomes of interest (pain and disability), means and standard deviations (SD) were extracted. With these data a meta-analysis was performed. Figure 2 shows the inclusion process of the papers.

Fig 2.



Potentially relevant RCTs identified and screened for retrieval (n= 767)
RCTs excluded (n= 699), This was based on treatment including medical therapy, surgery, acupuncture or electrotherapy. Also studies including subjects with symptom duration mean < 12 weeks
Level 1
RCTs reviewed for more detailed evaluation (n=68)
Exclusion criteria (red flag disorders, specific pathology pregnancy and surgery)
Level 2
Inclusion criteria (chronicity, age, area of pain, pain intensity, level of disability, psychosocial status, work status)
Level 3
RCTs excluded (n=62). This was based on follow-up studies not reporting pain and disability as outcomes or studies were no sub-classification of subjects had been utilized
RCTs utilizing sub-classification and potentially appropriate to be included in the meta-analysis (n=6)
Level 4
RCTs excluded for not meeting trial design criteria (n=1). Double publication
RCTs with adequate design (n=5)
RCTs excluded for procedural flaws (n=0)
RCTs with adequate design and treatment procedures (n=5), included in meta-analysis
Level 5

3.1.2 Paper II

Four physiotherapists participated in the examination of the inter-tester reliability of the classification system, each with several years of experience in examination and treatment of LBP patients (mean 12 years, range 7–20 years). Three of the four testers were physiotherapists with a Masters degree in manual therapy. One was the developer of the classification system. All the examiners had been educated by Peter O'Sullivan in the classification system during several workshops with him, and were using it in their clinical practice. Prior to the study, O'Sullivan further explained the systems procedures and classifications were discussed using a series of case studies. The examiners also underwent a pilot training period where O'Sullivan examined and classified six patients, while the three others observed. The aim was to refine the specific criteria for assessment, as well as making testers more familiar with the system. The estimated training time for each therapist ranged from 69 to 140 hours, the average being 106.3 hours (workshops and pilot study included).

The patients participating in the inter-tester reliability study were recruited consecutively from physiotherapy clinics around Bergen and from the Outpatient Multidisciplinary Spine Clinic, Haukeland University Hospital (HUS). After recruitment, a telephone screening was performed, and the first 30 patients that fit the inclusion criteria, were tested. The included patients should have had non-specific LBP pain for ≥ 6 weeks, localised primarily in the area from T12 to gluteal folds, and the pain should respond to mechanical provocation such as postures, movement and activities. Furthermore, the pain intensity, measured on a numerical rating scale (PINRS), should be > 2/10. Since the patients were tested twice on each of the two visits, a 0–10 pain numerical rating scale was conducted prior to each testing. If a patient's pain score changed 2 levels between two examinations on the same day, this was considered to be a threat to the classification validity as it is partly based on symptom response to movements and postures and the patient would then be excluded. Four patients were excluded after further examination: three did not fulfil the inclusion criteria (sick-listed > 4 months, radicular pain, lumbar surgery, etc.) and one reported a two-level change in pain between examinations on the given day. This left 26 patients participating in the study.

3.1.3 Paper III

The patients in the randomised controlled trial comparing CB-CFT and MT-EX were recruited from March 2006 till June 2008 from private physiotherapy practices, GPs and the Outpatient Spine Clinic, HUS. In addition, six advertisements were placed in the local newspaper. The participants were eligible for the study if they were between the ages of 18-65 years and had had NSLBP for > 3 months. They could be on sick-leave or not, but pain had to be provoked with postures, movement and activities, primarily localised in the area from T12 to gluteal folds, and with an intensity over the last 14 days, measured by PINRS, > 2/10. Their disability, measured with ODI, had to be higher than 14%.

The exclusion criteria were continuous sick-leave duration > 4 months; acute exacerbation of LBP (pain increasing with more than 2 points on PINRS from their average pain level) within last 3 months); radicular pain; any low limb surgery in the last 3 months; surgery involving the lumbar spine (fusion); pregnancy; diagnosed psychiatric disorders; widespread non-specific pain disorder (no primary LBP focus); specific diagnoses: active rheumatologic disease, progressive neurological disease, serious cardiac or other internal medical condition, malignant diseases, acute traumas, infections, or acute vascular catastrophes.

3.2 Methods

3.2.1 Data collection

Paper I

In the systematic review and meta-analysis, the electronic databases Medline (1966 to December 2008), Cinahl (1982 to December 2008), Embase (1988 to December 2008) and the Cochrane Central Register of Controlled Trials (4th Quarter 2008) were searched via Ovid to identify all relevant trials. This is in line with the recommendations from Minozzi el al. 2000 (Minozzi et al. 2000), and Woods & Treewheellar 1998 (Woods et al. 1998), were both Medline and Embase are suggested to be used to ensure a comprehensive literature search because the overlap between these two databases is small. We also followed minimum search strategy as suggested by van Tulder et al. 2003 (Van Tulder et al. 2003). The search was limited to articles in English and pertaining to human subjects. All reference lists of trials were identified through electronic searching with both MeSH-Terms and single terms and searched recursively until no more trials were identified. Keywords and combinations were: Low back pain, chronic pain AND manipulative medicine, kinesiotherapy, exercise therapy AND randomized controlled trial, RCT, clinical trial. The next phase of the search strategy involved manual selection of the obtained search results.

Paper II

A test–retest design was utilised. O'Sullivan developed a classification manual prior to the inter-tester reliability study. The patients underwent a comprehensive interview and full physical examination by each of the four physiotherapists independently. Rather than assess the reliability of individual tests, this system involved making a disorder classification based on compilation of subjective and physical examination findings in relation to other medical tests and radiological imaging. The subjective assessment included pain area (pain drawing), intensity and nature, pain behaviour (aggravating/easing movements), identification of primary impairments, disability levels, avoidance behaviours, pain coping and pain beliefs. The examination involved assessment of spinal range of movement, analysis of the patient's primary physical impairments (pain provocative and easing postures, movements and functional tasks). Specific muscle and movement tests were performed to identify the relationship between the control of the lumbo-pelvic region and the pain disorders (O'Sullivan, 2000), as well as specific articular tests for the lumbar spine and pelvic region as indicated to identify the structural source of pain and the presence of movement impairments (MI). These are important elements in the classification of the pain disorder and in determining whether the habitual movements or postures are provocative or protective (O'Sullivan 2000; O'Sullivan 2005; O'Sullivan et al. 2007; O'Sullivan et al. 2007).

The process consists of several stages before reaching a classification (Fig 3):

1. The first part involves screening; determining if the condition is specific LBP or NSLBP (O'Sullivan 2005).
2. The second stage considers whether specific LBP disorders have an adaptive or maladaptive response to the disorder (O'Sullivan 2005). If the disorder is classified as non-specific, then consideration of whether the disorder is predominantly centrally or peripherally mediated is made. The presence of localised and anatomically defined pain, associated with specific and consistent mechanical aggravating and easing factors, suggests that physical/mechanical factors are likely to dominate the disorder resulting in a peripheral nociceptive drive. Constant, non-remitting widespread pain, not influenced by mechanical factors, could on the other hand indicate inflammatory or centrally driven pain (O'Sullivan 2005).
3. Centrally mediated pain can then be further sub-classified into the presence of non-dominant or dominant psychosocial factors. Peripherally mediated disorders are sub-classified into either LBP or a pelvic girdle pain disorders.
4. Peripherally mediated lumbar spine pain disorders are divided into MI or MCI disorders, and peripherally mediated pelvic girdle pain into excessive or deficit of force closure. Both these classifications have been described in detail

elsewhere (O'Sullivan 2005; O'Sullivan et al. 2007; O'Sullivan et al. 2007).

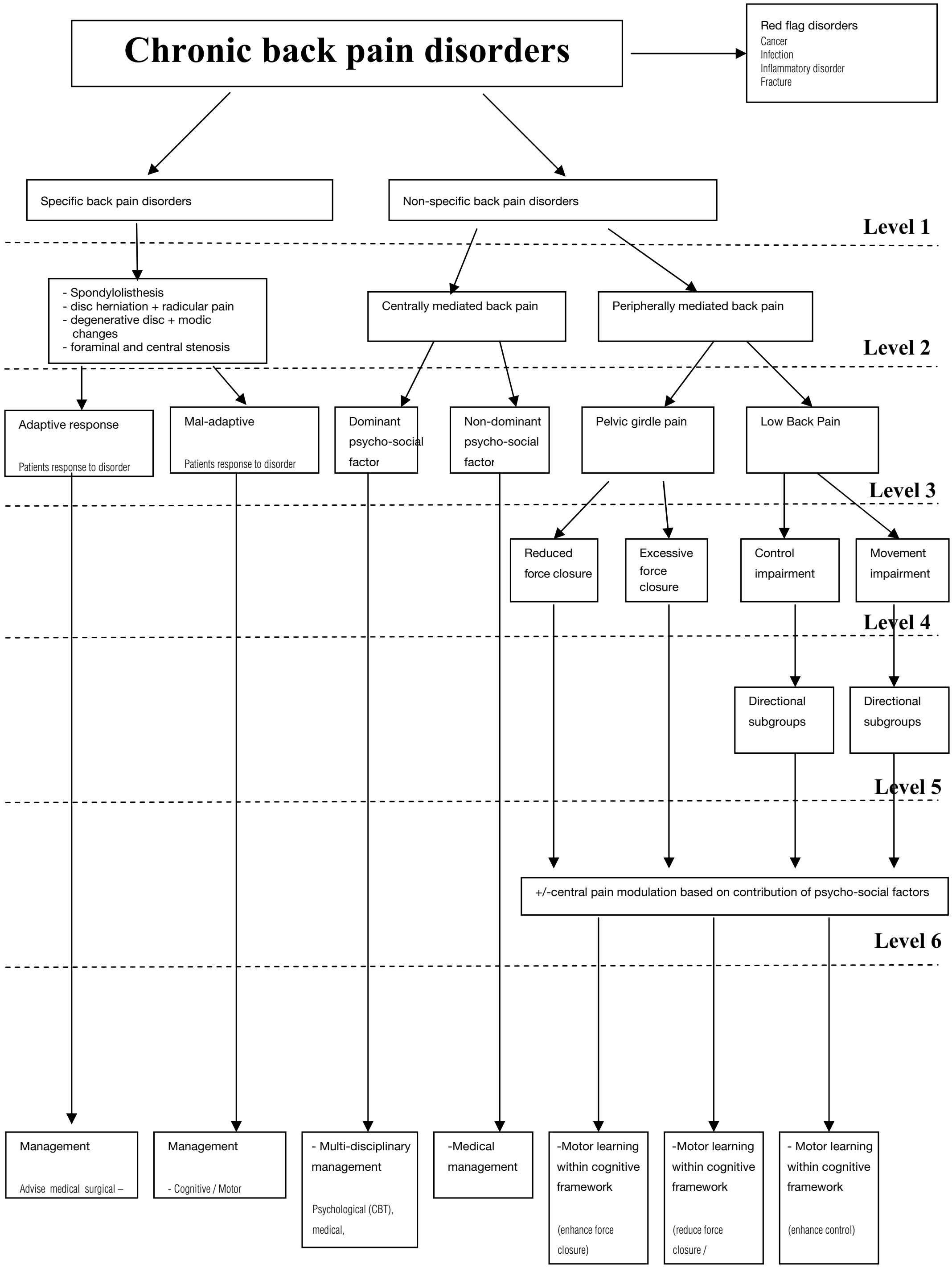
5. If the lumbar spine is the source of pain, the primary directional provocation bias as well as the symptomatic spinal level is noted.

6. The final decision is to indicate if significant psychosocial factors are associated with the disorder, based on all information from the examination process. The evaluation of psychosocial factors considers the presence of underlying fear avoidance behaviour, as well as psychological and social drivers considered to contribute to the pain disorder. Within this reasoning process, consideration is given to whether the patient has adapted in a positive (confrontation, active coping and minimal avoidance behaviours) or negative manner (passive coping and fear avoidance).

Each testing took about 1 hour. The patient was examined independently twice on two days, within a 1-week period. Each therapist filled out a classification form and put it in a sealed opaque envelope after their patient assessment. After examination the patient completed several questionnaires to formally assess their disorder. This included a pain drawing, the Oswestry Disability Index (ODI), Hopkins Symptoms Check List (HSCL), Fear Avoidance Beliefs Questionnaire (FABQ) and Ørebro Musculoskeletal Pain Screening Questionnaire (Ørebro MSPSQ).

Figure 3

Classification process adapted from Peter O'Sullivan



Paper III

The study was a randomised controlled trial (RCT) with an examiner blinded to end-point adjudication. All subjects first underwent a comprehensive interview and full physical examination at the Department of Public Health and Primary health Care, University of Bergen (UiB) by the main author. The aim of the interview was to let subjects tell their story regarding their pain disorder and the impact that it was having on their life. During the interview subjects were guided in questioning to inform: their history of pain, pain area and nature, pain behaviour (aggravating/easing movements and activities), their primary functional impairments, disability, activity levels and sleep patterns. Inquiries were also made regarding their level of fear of pain and any avoidance of activities, work and social engagement. Their degree of pain focus, pain coping strategies, stress responsiveness and its relationship to pain and their pain beliefs were also questioned as was any history of anxiety and depression. Finally their beliefs and goals regarding management of their disorder were ascertained. The physical examination involved analysis of the subject's primary functional impairments (pain provocative movements and functional tasks), assessment of their body control and awareness, as well as easing postures and movements (O'Sullivan 2005). This examination is important in order to classify each subject based on their provocative postures and movement behaviours, lifestyle behaviours and cognitive behaviours (O'Sullivan 2005; O'Sullivan et al. 2007; O'Sullivan et al. 2007). Another assessor blinded to the physical findings and sub-grouping of each patient, assessed spinal range of motion (ROM) with an inclinometer and distributed and explained how to fill in a set of questionnaires: Oswestry Disability Index (ODI), Pain Intensity Numerical Rating Scale (PINRS), Hopkins Symptoms Checklist (HSCL), Fear Avoidance Beliefs Questionnaire (FABQ), Ørebro Pain Screening. At the 3 months follow-up examination a Patient satisfaction questionnaire was also filled in.

When the patients had been examined and classified, and the patient had completed the questionnaires, they were introduced to a third person unfamiliar with the content of the study. A person independent of the study had developed a randomization schedule and produced 160 sealed opaque envelopes containing each participant’s allocation. Randomization was performed in permuted blocks of 16. The randomization took place at the Department of Public Health and Primary Health Care, UiB. The patients drew the envelope containing their allocation and details of procedure in relation to their allocation and were randomised to either CB-CFT or MT-EX.

The intervention lasted 12-weeks and was performed at three different private clinics. Patients were followed up immediately and 12 months post intervention. All the treating physiotherapists prior to the intervention underwent half a day of training with a clinical psychologist regarding the concepts of best practice cognitive approach to managing back pain (Indahl et al. 1995). Therapy in both groups was pragmatic and discontinued if the therapist deemed the participant had no further need of treatment before the 12-weeks were completed, as is standard clinical practice. See figure 4 for flow-chart depicting partcipant recruitment into the RCT study.

Primary outcomes:

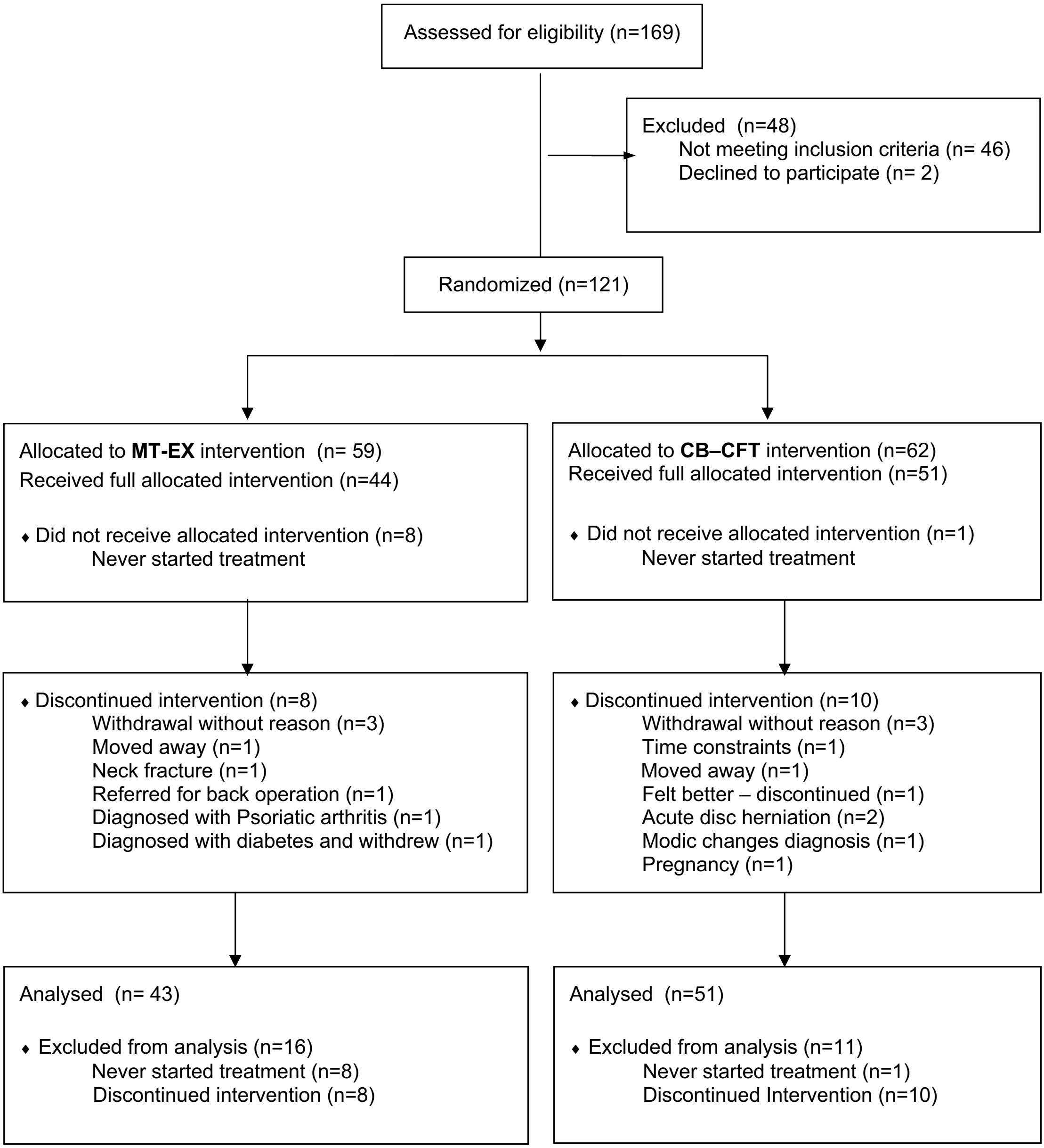
- Oswestry Disability Index questionnaire (ODI) (Roland et al. 2000)
- Pain Intensity Numerical Rating Scale (PINRS) (Jensen et al. 1986) (Pain intensity in the previous week).

Secondary outcome measures:

- Hopkins Symptoms Checklist (HSCL) (Derogatis et al. 1974)
- Fear Avoidance Beliefs Questionnaire (FABQ) (Waddell et al. 1993)
- Ørebro Pain Screening Questionnaire (Linton et al. 1998)
- Total spinal range of motion measured by hand held inclinometer
- Patient satisfaction questionnaire (Ware et al. 1983)
- Sick leave days (Ørebro Pain Screening Questionnaire)
- Pain level – (Ørebro Pain Screening Questionnaire)
- Pain episodes - (Ørebro Pain Screening Questionnaire)
- Ongoing care

Fig 4.

Flow-chart depicting partcipant recruitment and final enrollment for the two treatment groups: Manual therapy and exercise (MT-EX) and Classification-based cognitive functional therapy (CB-CFT)



3.2.2 Treatment

Manual Therapy and Exercise

Within the physical therapy profession, manual therapy is defined as a clinical approach utilizing skilled, specific hands-on techniques, including but not limited to manipulation/mobilization, used by the physical therapist with postgraduate training to diagnose and treat soft tissues and joint structures for the purpose of modulating pain; increasing range of motion (ROM); reducing or eliminating soft tissue inflammation; inducing relaxation; improving contractile and non-contractile tissue repair, extensibility, and/or stability; facilitating movement; and improving function (Cookson 1979; Farrell et al. 1992). The participants allocated to the comparison group were treated with joint mobilization or manipulation techniques applied to the spine or pelvis consistent with best current manual therapy practice in Norway. These therapists were specialists in orthopaedic manual therapy in average 25.7 years with no prior training in the use of the OCS or CB-CFT. The particular dose and techniques were at the discretion of the treating therapist, based on each participant's examination findings. In addition, most patients (82.5%) in this group were given exercises or a home exercise program. This could include general exercise or motor control exercise, but not based on the specific OSC system. The motor control exercise involved isolated contractions of the deep abdominal muscles in different functional positions (Hides et al. 2006).

Classification based cognitive functional therapy

Depending on the classification, each patient received a specific targeted intervention directed at changing their individual cognitive, movement and lifestyle behaviours considered to be provocative and maladaptive of their disorder (O'Sullivan 2000; O'Sullivan 2005; Dankaerts et al. 2007; O'Sullivan et al. 2007; O'Sullivan et al. 2007).

Four main components are matched to the classification;

1. *Cognitive component*. For each patient a vicious cycle of pain is outlined in a diagram explaining how their lack of awareness of pain mechanisms, negative beliefs, fear, hyper-vigilance, poor pacing, avoidance and protective behaviours, reinforced behaviours of muscle guarding, altered movement patterns and body postures, and activity avoidance that in fact provoked their pain further, feeding a vicious cycle of pain and disability.

2. *Specific movement based exercises.* All patients receive targeted functional movement training based on the activities that they nominated they either avoided due to pain or that provoked their pain or both. This approach follows a graduated exposure model where the patient are exposed to the previously pain provocative task, but in a non-provocative manner (O'Sullivan 2000). An example of this could be a patient with a classification of flexion control impairment (O'Sullivan 2000), where the patients often complain of pain with flexion activities or postures (i.e. sitting, bending, lifting). After the patient have been explained the mechanisms of the ongoing pain sensitization, they will be educated on the mechanics of the spine, the nature of ongoing tissue sensitization with their habitual adoption of end range postures (i.e. flexion of the caudal part of lumbar spine in sitting and bending) and the importance of the muscle system of the lumbo-sacral region to control spinal motion segments and minimize strain. In this what we call the cognitive stage the patient is made aware of how the postures and patterns of movements that they have adopted in fact results in maintaining their pain. They will often have to be made aware of the lack of control, or sense of their neutral spine positions. The first part of the specific movement based exercise can be learning to control their lumbo-pelvic region through the mid-range independently from the thorax (i.e. in supine or side lying). If their sitting posture is provocative they will also be instructed to change their sitting posture in line with the first exercise learning to maintain a neutral lordosis and relax the thoraco-lumbar region. If they are able to perform this in a controlled and non-painful manner, it can then be progressing into other painful activities (i.e. bending). Again the

focus will be on moving the lumbo-pelvic region in a relaxed non-painful manner.

Once they have the ability to assume a neutral lordosis in weight bearing (sitting, sit to stand and standing) it can be incorporated into static holding tasks and dynamic tasks such as single leg stand, sit–stand, squat and lifting. This stage is called the associative stage. The final stage in the specific movement based exercise component, is called the autonomous stage and is usually when the patient can perform these functional movement tasks with a low degree of attention. The patients will always have to achieve each stage before it is progressed. This graded exposure challenges the patient to perform functional activities that they nominate as pain- and fear-provoking and which they previously have avoided – but in a mindful, controlled relaxed manner and without pain behaviours such as grimacing, breath holding, guarding, propping with hands etc. They are instructed to change pain behaviours and to reinforce their new behaviours with practical demonstration by the therapist. This is done with the use of mirrors, written instruction and body diagrams.

3. *Functional integration.* The exercises in stage 2 are integrated functionally, specific to their nominated pain provocative functional impairments in activities of daily life. The aim is to restore normal functional movement capacity, reduce avoidance, pain behaviours and fear by means of pain control and confrontation in daily life. In this manner their functional capacity are gradually increased and patients are challenged to perform previously pain provocative habitual postures and movements, but in a normal pain free controlled manner. Where required this is integrated into a conditioning program to build strength and endurance within these tasks.

4. *Cardiovascular exercise*. Patients are encouraged to carry out cardiovascular exercise 3-5 times a week if they weren't previously doing so (20-40 min). All patients are asked to fill in a compliance questionnaire regarding each aspect of the intervention and present it each session.

Based on this cognitive functional approach, patients with a movement impairment disorder can be treated accordingly with a graduated approach to facilitate normal physiological movement. This is based on a cognitive behavioural framework, and first involves education, reduction in fear, and graduated exposure to the impaired pain provocative movement.

3.2.3 Statistical methods

Paper I

Trials were assessed for clinical heterogeneity with respect to their inclusion and exclusion criteria. In order to do a meta-analysis (MA) of the effectiveness of classification based manual therapy and/or exercise we extracted the group means and SD for each comparison using the outcome measure (pain and disability) in these studies that had attempted sub-classification. In two of the studies included in the MA (Vollenbroek-Hutten 2004; Riipinen 2005) were sub-classification had been made based on the Multidimensional Pain Inventory, the data were extracted and plotted for each of the different subgroups to show the effect for each of these independently (see figure 3-5 in Article I). In cases of missing data where studies failed to report SD, we calculated SD from other variance data or imputed a reasonable SD value (Furukawa 2006). Pain intensity on a 100 mm visual analogue scale (VAS) was defined as the pooled estimate of the difference in change between the means of the treatment and the placebo / control groups, weighted by the inverse of the pooled SD of change for each study, i.e. weighted mean difference (WMD) of change between groups. The variance was calculated from the trial data and with 95% confidence intervals [CI] in mm on VAS.

Due to the possibility of the outcome measurement by different disability scales, these were defined as unit less pooled estimate of the difference in change between the mean of treatment and control group, weighted by the inverse of the pooled SD of change for each study, i.e. standardised mean difference (SMD) of change between groups using Review Manager 5.0.18 (2008). The variance was calculated from the trial data with 95% CI. Results were considered significant if $p<0.05$. For reasons relating to generalizability and given this review investigated NSCLBP, we considered it appropriate to conduct MA both for short and long-term outcomes. Four MA were performed (short and long-term for both pain and disability). As the treatment periods and long-term follow-up varied, end of treatment and long-term of 36-52 weeks were chosen as measurement points. The statistical heterogeneity (genuine differences underlying the results of the trials in the review) of the results of the trials was measured using the quantity I^2. Using the p-value as a measure for heterogeneity ($P<0.10$) has been known to be poor at detecting true heterogeneity among studies as significant. It has been suggested that the quantity I^2 should be used instead (Higgins 2003). This value can be calculated as $I^2 = 100\% (Q-df)/Q$ where Q is Cochran's heterogeneity statistics and df the degrees of freedom (where n is the number of trials and therefore degrees of freedom equals number of studies minus one). The Cochran's Q is computed by summing the squared deviations of each trial's estimate and a p-value from the overall meta-analytical estimate and a P-value obtained by comparing the statistic with a X^2 distribution with k-1 degrees of freedom (where k is the number of studies) (Higgins 2003). Trials in the MA were considered to have low statistical heterogeneity if $I^2 < 25\%$, and in such instances a fixed effect model should be used. This assumes that the true effect of treatment is the same value in every trial. In contrast, random effects MA model assumes that the effects being estimated in the different studies are not identical, but follow a similar distribution.

Paper II

After the therapists individually had completed examinations of the 26 patients, the results were logged and compared. The developer's classification of each patient was used as the gold standard to which the other results were compared. Kappa coefficients and percentage of agreement were calculated using SPSS 13.0 for Windows. Cohen's Kappa statistic was used to calculate inter-tester reliability and Landis and Koch's (1977) values for interpretation of the reliability scores were used. Kappa values <0.20 indicate poor agreement, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, and 0.81–1.00

indicate almost perfect agreement. The data was analysed based on agreement of overall classification (specific LBP vs NSLBP), centrally or peripherally mediated, adaptive or maladaptive movement disorders, and whether it was considered to be a pelvic girdle pain or LBP disorder. Kappa agreement of the primary directional pain provocation, the spinal level of pain provocation and the presence of psychosocial influence on their LBP disorder was calculated.

Paper III

A linear mixed model was used to estimate the group differences in treatment effect at both time points and also in the change in outcome from 3 and 12-months follow-up, with baseline values included as the only covariate. Age, gender, BMI, LBP duration and work status were evaluated as possible confounders but did not need to be included in final models. Bootstrapped standard errors were estimated to adjust for departures from normality as some outcome measures displayed slightly skewed distributions. Models were examined to confirm the absence of influential outlying observations. Statistical significance was set at P=0.050.

Two subjects (1 CB-CFT and 1 MT-EX) were missing data at 3-month follow-up but provided 12-month follow-up data, and five subjects (2 CB-CFT and 3 MT-EX) were missing 12-month follow-up data but provided 3-month data. These cases were included in the model, as the linear mixed model used is a likelihood-based estimation procedure resulting in non-biased estimates provided data are missing at random. One subject randomised to MT-EX withdrew from the study before 3-months, and was not included in the analysis. However, a sensitivity analysis performed by imputing the best score of the primary outcome measures at each follow-up for this case confirmed effect size estimates remained similar (within 0.4 for ODI and 0.1 for PINRS) and highly statistically significant (P<0.001).

Statistically significant group differences in sick-leave days and patient satisfaction were assessed using two-sample Wilcoxon rank-sum (Mann-Whitney) test. In the case of sick-leave days, the original variable from Ørebro

Screening questionnaire collapsed down for tabular display but analysed using original 10-category variable, i.e 0, 1-2, 3-7…etc. days.

In addition, change pre- to post-treatment was estimated in both treatment groups using paired t-tests and the change in ODI and PINRS was calculated for each study participant, in terms of absolute change from baseline, and tabulated with reference to consensus values for minimally important change in these outcomes.

4. RESULTS

4.1 Paper I

A total of 767 RCTs published between 1982 to December 2008 that administered conservative treatment for LBP were identified and screened for eligibility**.** However, only 68 studies had focused on the efficacy of manual therapy or exercise and reported outcomes based on levels of disability and pain in subjects with NSLBP and was therefore included in for further review. 11 studies (16.2%) did not report the exclusion of red flags or specific spinal pathology as defined. 14 RCTs (20.6%) did not exclude or subgroup subjects with nerve root irritation / pathology. 29 RCTs (42.6%) had not listed pregnancy as an exclusion criterion. 23 studies (33.8%), did not exclude subjects if they had undergone surgery for their LBP. We also found that 7 studies (10.3%) had not specified a timeframe for LBP duration in their inclusion criteria. 14 studies (20.6%) had included patients with < 3 months durations of symptoms. However in the characteristics of these 21 studies, over 90% of the patients had pain lasting > 3 months. The remaining 47 studies (69.1%) had specified in the inclusion that symptoms durations had to be > 3 months. For age, the majority of the studies 56 (82.3%) specified that the patients had to be between 18-65 years old. Only one study included patients over 65 years old and 11 studies (16.2%) did not specify age. Psychosocial status was only specified in one study (1.5%), work status in 14 (20.6%) and compensation in 11 (16.2%). 11 studies (16.2%) specified pain intensity level and 23 (33.8%) specified disability level as an outcome. Only 6 (8.8%) out of the 68 studies had performed some form of sub-classification according to definitions described previously in the methods. One of these studies was a double publication (Cambron 2006) and therefore only the original study (Gudavalli 2006) was included in the next level. These studies were therefore included in the meta-analysis, providing information on altogether 432 participants for disability and 359 participants for pain. The data from the meta-analysis showed a statistical difference in favour of the classification-based intervention for reductions in pain (P=0.004) and disability (P=0.0005), both for short and long-term reduction in pain (P=0.001). Disability did not reach statistical significance (P=0.07) for long-term outcome. Effect sizes ranged from moderate (0.43) at short-term, to minimal (0.14) for long-term.

4.2 Paper II

In the first part of the classification process, all patients were classified with NSLBP with 98% agreement for this level. All patients in the study had pain arising from a peripheral pain source, with 99% agreement for this. One patient was classified by all four testers as having pelvic girdle pain (100% agreement); the rest were classified as LBP disorders (99% agreement). The fourth level considered increased or decreased force closure for pelvic pain (one patient, 100% agreement), MCI (24 patients, 99% agreement) or MI (one patient, 75% agreement) for low back. In the fifth level, Kappa agreement could be calculated, deciding the directional pattern of provocation. For the primary direction of provocation, Kappa (K) and percentage agreement had a mean between the four testers of 0.82 (range 0.66–0.90) and 86% (range 73–92%) respectively. Increased familiarity with the system also increased the reliability results (<100 h K 1⁄4 0.66, >100 h K 1⁄4 0.90). In the final level of decision making, the mean Kappa coefficient for detecting psychosocial influence was 0.65 (range 0.57–0.74) and the mean agreement 87% (range 85–92%).

4.3 Paper III

Out of the 169 patients that were initially enrolled, 121 patients met the inclusion criteria and were found eligible. In the randomized cohort, 62 patients were assigned to the CB-CFT group, and 59 were assigned to the MT-EX group.

Study participants in the two treatment arms were comparable in terms of baseline characteristics, with the exception of small but significant differences in HSCL, FABQ-Physical and the Ørebro Pain Screening Questionnaire. Both groups significantly improved with the respective therapeutic interventions. After adjustment for baseline scores, the CB-CFT group displayed superior outcomes supported by both statistically and clinically significant differences when compared to the MT-EX group. This was evident both immediately after and at 12-months post-intervention for both primary and secondary outcomes. This was demonstrated by the degree of improvement in the CB-CFT group for ODI score being 13.7 points from baseline (95% CI, 11.4 to 16.1, P<0.001) and for PINRS scores 3.2 (95% CI, 2.5 to 3.9, P<0.001). In the MT-EX group, the mean improvement for ODI score was 5.5 points (95% CI, 2.8 to 8.3, P<0.001) and 1.5 for PINRS (95% CI, 0.7 to 2.2, P<0.001).

The improvements for all secondary outcomes showed similar effects with the CB-CFT group demonstrating significantly greater change when compared to the MT-EX group across all the different outcomes, except for total lumbar range of motion. There was maintenance of treatment effect over the 3 to 12-months follow-up time for both groups, with no significant main effect or group/time interaction effect identified in the linear mixed model.

5. DISCUSSON

5.1 Paper I

Research question: To what extent does the literature and especially RCTs reflect the fact that several back forums have made calls for research to be based on valid and reliable classification systems?

The view that high quality randomized controlled trials are a key benchmark for new knowledge in the field of primary care research on LBP continues to be dominant in the field of research (Cherkin et al. 2009). There is evidence that intensive multidisciplinary biopsychosocial rehabilitation with a functional restoration approach can reduce pain and improve function in NSCLBP patients However, these disorders have proven highly resistant to clinically significant change in RCTs using single interventions such as manual therapy, exercise, acupuncture, spinal injections and cognitive behavioural therapy. One of the suggested reasons for the lack of evidence treating these disorders is the lack of sub-grouping and managing these disorders from a biopsychosocial perspective. As the subject of this thesis is classification and targeted treatment of NSCLBP, it was of great interest to explore the extent to which classification strategies based on a biopsychosocial construct had been advocated in the literature up until now.

The available evidence provides little guidance to clinicians who need to decide which interventions to implement for NSCLBP. Both exercise and spinal manipulative therapy is widely used in the rehabilitation of NSCLBP patients. A review by Liddle et al. (2004) highlighted the diversity of exercise programmes offered to patients with CLBP. Based on RCTs and systematic reviews, no form of exercise has been shown to be more efficacious than another (Liddle 2004; Hayden et al. 2005). The review by Assendelf et al. (2004) also concluded that there is no evidence that spinal manipulative therapy is superior to other standard treatments for patients with acute or chronic low back pain (Assendelft 2004). The authors of an RCT comparing these two interventions directly also conclude that there is little basis on which to prefer for NSCLBP (Ferreira et al. 2007).

The aim of the first paper was to review the literature on RCTs, evaluating manual therapy treatment and exercise therapy for CLBP. We wanted to look at both the level of integration of sub-classification in these RCTs as well as summarising the effects in the studies that had sub-classified and matched treatment to specific subgroups. To our knowledge no studies had systematically reviewed this until now.

Some of our findings were surprising. Inclusion and exclusion criteria are the most basic form for classification. Despite the fact that the diagnostic triage, separating red flag and specific pathological disorders from NSLBP as suggested by the QTF (Spitzer 1987), 16.2% of the studies identified, had not made a distinction to exclude red flag disorders and 20.6% had not excluded or identified patients with nerve root irritation/pathology. This would perhaps be acceptable, except for the fact that these studies claimed they had looked at treatment for NSCLBP. As many as 42.6% did not exclude pregnant subjects and 33.8% did not exclude patients if they had undergone surgery. While it is quite well accepted that pregnancy related pelvic girdle pain represents a specific subgroup of musculoskeletal disorders (O'Sullivan et al. 2007), its effect on the lumbar spine and pelvic girdle complex is not fully understood and multiple mechanisms have been suggested along with specific tailored treatment (Kristiansson 1996; Stuge et al. 2004; O'Sullivan et al. 2007). These findings relating to the first level and simplest form of classification indicates the lack of definition of NSCLBP and the complexity of understanding the mechanisms involved in these disorders. With the acceptance of the biopsychosocial model of chronic pain and the understanding of the interplay between biological and psychosocial factors in the development, expression and maintenance of pain (Hanley 2004), one would expect that a psychological status and screening would be reported were psychotherapy has been advocated. However, we found several RCTs that combined psychological interventions and exercise without reports of the patient’s psychological status when they entered into the study. This is a major limitation given that it only seems to be in a limited group of NSCLBP patients where these factors become the dominant or primary pathological basis for the disorder (O'Sullivan 2005). However when it comes to sick listing and return to work, a growing number of studies have appeared in the literature attempting to identify the best predictors for return to work for patients with musculoskeletal pain (Haldorsen et al. 2002). Psychological trait and state variables have been claimed to give better prediction than conventional medical information alone, especially for sub-acute and chronic pain. Values of up to 80% have been reported predicting return to work after 6 months for models based exclusively on psychological factors (Hasenbring et al. 1994).

Our meta-analysis indicated that there is a statistical significant effect for pain in favour of the intervention where sub-classification strategies had been used both short-term (end of treatment) and long-term (36-52 weeks follow-up). For disability there was also a statistical significant effect short-term (end of treatment) in favour of classification, but the difference did not reach statistical significance (P=0.07) for long-term (36-52 weeks).

For an intervention to be specific it should target the underlying mechanism of the disorder. Of the five papers fulfilling the inclusion criteria and attempting to sub-classify the patients, only one can be said to have used a form of sub-classification strategy aiming to treat different sub-groups with a ‘targeted’ intervention. In Petersen and co-workers study (2002) a McKenzie-based CS was used (McKenzie 1981; Petersen et al. 2002). This system is based on information from history taking, and symptom response to generated loading of the lumbar spine. The system has good inter-tester reliability, but it has a patho-anatomical orientation and lacks clear guidelines for management.

An attempt of sub-classifying according to the underlying mechanism was made by Gudavalli et al. (2006) in their study where they divided patients into sub-groups according to the presence or not of radiculopathy (Gudavalli 2006). The problem with this way of sub-classifying is that it is now fairly well established that radiculopathy is a nerve root problem (Spitzer 1987; O'Sullivan

2005), and therefore do not belong to the group of NSLBP patients. Patients with radiculopathy should be excluded based on the initial exclusion criteria. The intervention of Snook et al. (2002) consisted of instruction in the control and avoidance early morning lumbar flexion compared to sham treatment of six exercises (Snook 2002). Subjects were given a back scratcher and a reacher. After six hours not bending, usual activities were allowed, but extreme bending should be avoided. This may be an attempt to target a mechanism of the disc being more vulnerable and prone to flexion loading and injury in the morning due to increased water content and the changed viscoelastic properties. However, it is well established that CLBP is a multi-dimensional problem consisting of a combination of patho-anatomical, neurophysiological, physical and psychosocial factors (Borkan et al. 2002; McCarthy et al. 2004; Waddell 2004). Thus it is improbable that a general intervention like this could target all these underlying mechanisms and resolve the complexity of a chronic low back problem. A valid classification should identify the underlying mechanism (s) driving the disorder from a biopsychosocial perspective, thus guiding a targeted management intervention, which in turn should predict the outcome of the disorder.

The reviewed literature in our study revealed very little use of sub-classification systems in spite of the fact that several back forums have made calls for research to be based on this for years, and when used it seemed to slightly improve the outcome results for disability and pain. Our data should however be interpreted with caution, as these data are insufficient to definitely quantify the effect of sub-classification strategies in the treatment of NSCLBP. This would possibly require larger numbers of high quality RCTs with similar comparisons. Also some additional factors need to be considered along the results of this meta-analysis. Although we followed the guidelines set by Minozzi et al. (2000) for inclusion of databases as well as the minimal search strategy suggested by van Tulder et al. (2003), we cannot be 100% sure that we included all the evidence on this topic. Limiting the search to English articles could be one factor responsible for this, but for independent reviewers involved this was the only language option shared. Different word combinations used in the search strategy could also have influenced the results of studies retrieved. We choose to rely on the scoring of the included studies from the PEDro database, as this was considered to be the most objective way rather than using the PEDroscale ourselves or using a different scoring system (ie Jadad scale).

5.2 Paper II

Research question: Can clinicians based on all the available information available agree on classification of NSCLBP without use of a standardized examination procedure?

The aim of this study was therefore to examine the inter-tester reliability of clinicians' ability to independently classify a wide range of patients with NSLBP, utilizing an extended mechanism-based classification method lately developed by O'Sullivan.

Validating a classification system requires a whole range of validation processes in order to succeed and be able to give some form of validation of the classification system. A validation model accumulating evidence in the validation process of the OCS has been suggested by Dankaerts et al. (2004). Within this model reliability provides the first essential evidence in this multistep validation process (Dankaerts et al. 2006). The principal finding of our study suggests that therapists with substantial training in the classification system (O'Sullivan 2005) demonstrated fair to excellent agreement (Landis et al. 1977) in primary classification of the disorder as well as in the identification of directional patterns of provocation and the presence of psychosocial factors associated with the disorder, when applied to a wider range of NSCLBP patients. Our findings are in accordance with Dankaerts et al. study (2006), who also found moderate to excellent agreement between raters when examining patients only with motor control impairment. Although the results are comparable, the design was different for the two studies. In the study by Dankaerts et al. (2006) the testers involved in part two of the reliability testing, all watched the same videos and all got the same information. In our study we attempted to imitate normal clinical practice where the different testers examined and interviewed the patients independently. Furthermore, our study added the 6th level for also classifying the contribution of psychosocial factors, whereas Dankaerts el al. focused on classifying the disorder more from a control and directional perspective (Dankaerts et al. 2006).

Most classification systems have been developed using a judgmental approach (McCarthy et al. 2004; Dankaerts et al. 2010). This type of approach is usually based on the synthesis of the current knowledge in the area, linked to observations and insights of clinicians regarding specific subgroups of patients. As a consequence, CS based on this approach present with face validity, but have the potential of being biased by personal opinion.

As in Dankaerts and coworkers study (2006), familiarity with the classification system also influenced the reliability results, demonstrating higher agreement among raters with more familiarity (Dankaerts et al. 2006). These findings are in line with Strender et al. (1997) study, concluding that reliability of clinical tests requires sufficient time for examination and conformity of performance, definitions and evaluations. The protocol of our study followed a similar examination procedure to that of Dankaerts et al. (2006), but the inclusion criteria's in our study involved a more heterogenic sample of patients with NSCLBP.

Eight subjects out of 26 in our study classified with peripherally mediated NSCLBP disorders were also identified as having significant psychosocial factors contributing to their disorder based on the clinical examination. Analysis of the questionnaire data conducted after the raters assessments, confirmed this as these eight patients scored significantly higher on Hopkins Symptoms Check List (HSCL) and the Ørebro questionnaire. Linton and Halden conducted a study in 1998 were they identified potential psychosocial risk factors associated with future sick absenteeism using the Ørebro as screening instrument. The total score appeared to have clinical value because scores were related to outcome, and could be related to cutoff points that correctly identified the prognosis of nearly 80% of the patients (Linton et al. 1998). Psychosocial factors can modulate pain behaviour, which then can increase disability via fear avoidance, as well as promoting pain levels via central mechanisms (Vlaeyen et al. 2000). Dunn et al. also (2005) identified subgroups within the NSCLBP population. High levels of pain and disability were associated with psychosocial factors influence in one group, and the other group with minimal psychosocial factors had lower pain and disability levels.

There are a number of limitations and considerations in relation to the second study as well. Although our inclusion criteria were more open than in the study by Dankaerts et al. (2006) and thereby we hoped for a more heterogenic population, 24 out of the 26 patients were classified as control impairment disorders. One out of the 26 was classified as a pelvic pain disorder and the other as a movement impairment disorder. One could argue that the sample then does not represent the whole variety of NSCLBP and therefore the ability to classify all these different dimensions were not tested sufficiently in this study. However data that we have collected since the, confirms that the control impairment group the most common presentation within the NSCLBP. Out of 113 patients classified with NSCLBP, 101 (89.4%) were classified as LBP control impairment disorders. Range of motion measures showed statistical differences between the two subgroups. The mean total sagittal range of motion for the movement impairment group was 33.7 degrees (SD 11.6), and 50.6 (SD 14.2) degrees for the control impairment group. P <0.05 (95% CI -28.6 to -5.1). The range of motion did not change in these subjects for the control impairment group lending support to subgroup (Fersum et al. 2009). There is growing quantitative evidence to support these groups across a number of studies (Dankaerts et al. 2006; Dankaerts et al. 2009; Dankaerts et al. 2010)

The use of expert clinician as the gold standard to calculate agreement may be another limitation of the study. This method have the potential to be biased, however, in the absence of a true criterion standard for the classifications used in this study method this method reflects current clinical practice (Gracovetsky et al. 1995; Dankaerts et al. 2010).

5.3 Paper III

Research question: What is the efficacy for classification based targeted treatment for patients with non-specific chronic low back pain?

It has been stated that optimal treatment for patients with NSCLBP remains largely enigmatic (Van Tulder 1997), and that caring for chronic LBP, is one of the most difficult and unrewarding problems in clinical medicine (Leclere 1990), as no single treatment has been shown to be clearly effective (Mannion et al. 2001; Assendelft 2004; Hayden et al. 2005; Ostelo 2005). It has been hypothesised that the lack of evidence for managing NSCLBP is a result of the vast majority of RCTs broadly defining heterogeneous populations (Assendelft 2004; Hayden et al. 2005; Ostelo 2005). Further, it has been stated that without sub-classification, research into NSCLBP will be unlikely to provide useful insight (Leboef-Yde 2001).

Despite calls from many international forums on LBP for classification system reflecting a bio-psycho-social model (Borkan et al. 1996; Borkan et al. 1998; Cherkin et al. 2009) very few have been validated and tested in randomized controlled trials for the management of NSCLBP disorders (Fersum et al. 2010). However, the growing evidence that NSCLBP is associated with maladaptive cognitive, movement and lifestyle behaviours that act to promote a vicious cycle of pain, emphasis the need for interventions to address these behaviours in a targeted, functionally specific and patient focussed manner. The aim was to compare the outcome of CB-CFT with current practice (manual therapy and exercise (MT-EX)) in patients with NSCLBP.

Our RCT study revealed that the CB-CFT group showed superior outcomes compared to MT-EX group across every domain measured, post intervention and at 12-months follow-up. Both groups showed significant improvement in short and long term follow-ups, however the CB-CFT group was superior based on clinically meaningful changes as defined by Minimally Important Change (MIC) (Ostelo et al. 2008). The consensus value estimated from the study of Ostelo et al. (2008) have suggested that a MIC should be greater than a 10 point change in the ODI and 1.5 of the PINRS. On this basis, 72% of the CB-CFT group compared to 31.6% of MT-EX group achieved clinically important change in ODI, and 68% of the CB-CFT group compared to 44% of the MT-EX achieved this for a reduction in pain intensity. We believe that these data supports the efficacy of this novel approach to break the vicious pain cycles, change beliefs and behaviours as well as pain experience.

NSCLBP is the second greatest cause for disability in the USA (Dagenais et al. 2008), and in spite of exponentially rising health care costs the disability relating to the disorder is rising. Systematic reviews for the management of NSCLBP highlight the failure of current practice to effectively deal with the disorder, with small effect sizes reported across all interventions (Assendelft 2004; Furlan AD 2005; Hayden et al. 2005; Ostelo 2005; Staal JB 2008). The effect of previous conservative interventions from previous Cochrane reviews reveals similar findings to the MT-EX group in our study, suggesting that the quality of the MT-EX treatment was comparable to previous studies (Assendelft 2004). The proposed reasons for the failure to effectively manage NSCLBP have been two-fold. The first is the lack of a multi-dimensional approach acknowledging the biopsychosocial nature of NSCLBP disorders and facilitating behavioural change in the patient (Leeuw et al. 2007). The second is the failure to deal with patient heterogeneity by identification of valid subgroups and targeting treatment at them (Turk 2005). CB-CFT addresses both of these limitations, by sub-grouping patients based on their movement, cognitive and lifestyle behaviours as well as targeting these behaviours with the aim to break the vicious cycle of pain. The only study that we are aware of that have followed a similar intervention protocol is in a study from Sweden (Asenlof et al. 2005; Asenlof et al. 2009). Our findings are in line with their work, demonstrating clinically significant long tem effects on pain and disability with effect sizes larger than one standard deviation..

Satisfactions rates were high in both groups with 94.1% being completely satisfied in the CB-CFT group and 67.5% in the MT-EX group at 3-months follow up. This gave and odds ratio of 3.27 for the CB-CFT group

(P<0.01), For the 12-months follow up it was 95,8% in the CB-CFT group and 46.2% in the MT-EX group, giving and odds ratio of 5.18 in favor of the CB-CFT (P<0.001). This means that the chance of being completely satisfied was over 3 times higher in the CB-CFT group at 3-months and 5 times higher at 5-months. Guidelines for the management of back pain and chronic disorders urge patient responsibility and self-management (Rosen 1994), where patients must be actively involved in the treatment process and not passive recipients of care (Boreham et al. 1978). The degree of patient satisfaction is seen as a reflection of the quality of care, and as an important outcome in its own right (May 2001). CB-CFT had a strong cognitive focus with an emphasis on communication, reflecting back to patients their vicious cycle of pain and disability based on a comprehensive examination, enhancing their awareness of the pain behaviours by means of verbal, written and visual feedback. On the basis of this communication, a graded program was targeted to challenge provocative pain and avoidance behaviours, in order to allow patients to develop new behaviours that promoted control of pain while enhancing function, in order to break the vicious pain and disability cycle, empowering people to take active control over their disorder and challenging negative beliefs.

Many international low back forums over the last 10 years have proposed a paradigm shift, away from thinking about back pain as a biomedical “injury” model, to viewing LBP as a multifactorial biopsychosocial pain syndrome associated with maladaptive cognitive, pain and physical behaviors (Borkan et al. 2002). These same forums also stated that the future management of chronic low back pain had to involve “a combination of encouraging activity, reassurance, short-term symptom control, and alteration of inappropriate beliefs about the correlations of back pain with impairment and disability.” These aims are underpinned in the CB-CFT intervention. We hypothesise that the reasons for the superior outcomes of CB-CFT lie in this body and mind approach to managing the disorder. This has the potential to promote the top down dampening of the central nervous system (via increased awareness, enhanced control of pain, self empowerment, altered beliefs, reduced fear and anxiety, altered mood and increased functional capacity) as well as a bottom up inhibition of the peripheral nervous system (via enhanced body awareness, body control, relaxation, normalising movement patterns, conditioning and enhanced cardiovascular fitness).

Although it was not a primary aim of the CB-CFT, the results demonstrate a 2.95 times less likelihood of being on sick-leave at the 12-month follow-up compared to the MT-EX group. This is to our knowledge the first study demonstrating effect on returning more patients back to work after treatment given by a physical therapist. We propose that the main reason for this, is that patients were empowered to self manage and control their disorder, increasing their confidence and reducing their fear. This is supported by the greater reduction of fear observed in the CB-CFT compared to the MT-EX group for both physical activity and work. Previously, only studies using cognitive behavioural therapy in intensive multidisciplinary treatment models have shown an effect on sick listing for this patient group (Airaksinen et al. 2006). These models include cognitive, physical and workplace intervention aspect which all seem important concerning returning to work. However, from the systematic review it is only the intensive multidisciplinary treatment models that have effect, often with >100 hours of treatment in the intervention period (Airaksinen et al. 2006). In comparison, the patients involved in our study had between 5-7 hours of treatment during the intervention period. High quality RCT's are still considered a key benchmark for new knowledge in the field of primary care research on LBP (Cherkin et al. 2009). Evidence from RCT that have tested targeted interventions in more homogeneous populations has shown good results (O'Sullivan et al. 1997; Stuge et al. 2004). With the validation process that the OCS have gone through over the last 10 years we wanted to use the RCT methodology to test the efficacy of the CB-CFT. Clinical RCTs are time consuming and an even larger sample size could be warranted. There are also some additional methodological considerations that can have influenced the results. Our patients were recruited from the primary care level. The wide inclusion criteria in the study suggest that we included a common and representative group of patients with chronic localized LBP without objective sign of pathology to the spine. According to the baseline data, the patients recruited to this study were not the most severe chronic patients, but had moderate back pain and functional impairment sufficient to result in sick leave for many patients. Although this intervention has been very successful for the population we tested, further studies are needed to confirm these results also in those with higher levels of pain and disability and in other cultural groups to determine the generalizability of the findings.

6. SUMMARY AND CONCLUSIONS

- It was hypothesized that despite calls for sub-classification of patients within the NSCLBP population from the international research community, there is a lack of validated classification systems using a biopsychosocial construct utilized in RCT.

  In paper I we demonstrated that there is limited to non-existing use of validated classification systems using a biopsychosocial construct utilised in RCT. Even in the simplest form of classification there seems to be a mixture of the understanding and definitions regarding NSCLBP. Targeted classification based treatment did show slightly better results than non-targeted treatments, but the effects sizes were very small.
- In paper II it was further hypothesized that clinicians trained in the use of the OSC could agree on a disorder classification tested out on a broader patient group than previously. This was demonstrated with therapists who had undergone substantial training in the classification system, scoring fair to excellent agreement in the primary classification of the disorder, in the identification of directional patterns of provocation and the presence of psychosocial factors associated with the disorder
- Finally it was hypothesized that a targeted classification based behavioural approach called classification based cognitive functional therapy (CB-CFT) would produce better outcomes than manual therapy and exercise (MT-EX) for patients with NSCLBP. Our findings showed that CB-CFT produced clinically significant outcomes that were superior across all dimensions measured compared to MT-EX. These findings support a change in the management and treatment of these highly complex disorders.
- In conclusion this thesis support the calls for patient centred targeted management approached utilising validated classifications system that are based on a biopsychosocial construct.

7. FURTHER RESEARCH

During the work of this thesis several questions have arisen and should lead to future research:

- Long term follow up on the population of the current study – 3 years
- Comparison of the CB-CFT to other management strategies for NSCLBP i.e. Cognitive Patient Education for Low Back Pain (COPE LBP trial).
- Larger studies enabling better statistical analysis of subgroups with the classification system
- Confirm result in patients with higher levels of pain and disability and in other cultural groups to determine the generalizability of the findings.
- Examine if the results of CB-CFT on sick-leave can be further improved by including an additional workplace intervention.

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