



Chronic Musculoskeletal Pain
Prevalence, impact and multidisciplinary treatment in
Iceland

Sigrún Vala Björnsdóttir

Thesis for the degree of Philosophiae Doctor

Supervisor:

Dr. Unnur Anna Valdimarsdóttir

Doctoral committee:

Dr. Jan Triebel, Dr. Patricia Solomon, Dr. Vilhjálmur Rafnsson

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Sigrún Vala Björnsdóttir

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Umsjónarkennari:

Dr. Unnur Anna Valdimarsdóttir

Doktorsnefnd:

Dr. Jan Triebel, Dr. Patricia Solomon, Dr. Vilhjálmur Rafnsson

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Ágrip

Inngangur og markmið: Þrálátir stoðkerfisverkir eru algengt vandamál um allan heim og hafa veruleg áhrif á samfélög. Markmið rannsóknanna var að meta algengi þrálátra stoðkerfisverkja á Íslandi og hugsanleg áhrif á líkamlega og andlega heilsu. Einnig að meta hugsanleg áhrif fjögurra vikna hefðbundinnar þverfræðilegrar verkjameðferðar (TMP) og svipaðs meðferðarúrræðis að viðbætti taugafræðilegri sjúklingafræðslu og gjörhygli (NEM) á heilsutengd lífsgæði (HRQL) og magn verkja, meðal kvenna sem upplifa þráláta stoðkerfisverki.

Aðferðir: Notast var við lýðgrundað slembiúrtak 5.906 Íslendinga á aldrinum 18-79 ára (svarhlutfall = 60,3%) til að meta algengi þrálátra stoðkerfisverkja á Íslandi í desember 2007. Mat á algengi var viktað með tilliti til kyns, aldurs og búsetu til að endurspeglar stöðuna í þjóðfélaginu. Fjölpátta leiðrétt lógistísk aðhvarfsgreining var notuð til að meta tengsl milli þrálátra verkja annars vegar og hömlunnar í daglegum athöfnum og ýmissa einkenna hins vegar. Í íhlutunarrannsókninni var notast við gögn frá íslenskri endurhæfingarstofnun, Heilsustofnun NLFÍ. Í rannsókninni tóku þátt 122 konur sem fengu TMP meðferðina, 90 konur í NEM meðferðinni og 57 konur á biðlista. HRQL (kvarðinn Heilsutengd lífsgæði) og magn verkja (100 mm sjónkvarði) voru mæld fyrir og eftir meðferð sem og sex mánuðum eftir að meðferð lauk. Til að greina árangur var notast við fervikagreiningu og línulega aðhvarfsgreiningu.

Niðurstöður: Stundaralgengi þrálátra stoðkerfisverkja var 19,9% með áberandi kynjamun (karlar=15,2%; konur=24,7%) og er breytilegt eftir þjóðfélagslegum aðstæðum. Í samanburði við fólk án þrálátra verkja er fólk með þráláta stoðkerfisverki í aukinni áhættu (líkindahlutfall=OR) fyrir líkamlegum (OR karlar=4,0 [95%CI=3,0-5,2]; OR konur=6,8 [95%CI=5,4-8,5]) og andlegum heilsuþrengingum (OR karlar=1,7 [95%CI=1,3-2,3]; OR konur=2,4 [95%CI=1,9-3,0]), að lýsa hömlunum við ýmsar líkamlega krefjandi athafnir daglegs lífs (OR karlar=2,4 [95%CI=1,8-3,2] – 6,9 [95%CI=4,2-11,5]; OR konur=3,2 [95%CI=2,3-4,6] – 7,9 [95%CI=6,3-10,0]) sem og lakari lífsgæðum (OR karlar=1,5 [95%CI=1,0-2,1]; OR konur=1,6 [95%CI=1,2-2,1]). Heilsutengd lífsgæði jukust í kjölfar þverfræðilegra verkjameðferða (TMP=10,5; NEM=9,7 miðað við biðlista=1,3; $p<0,001$) og verkir voru minni (TMP=22mm; NEM=17mm miðað við biðlista=0,6mm; $p<0,001$). Árangur stóðst sjö mánuðum eftir að meðferðin hófst (aukin HRQL [TMP=6,4;

$p < 0,001$ og $NEM = 6,9$; $p < 0,001$]; minni verkir [TMP=11mm; $p < 0,001$ og $NEM = 15mm$; $p < 0,001$]). Lítil munur fannst á milli meðferðanna tveggja. Árangur þátttakenda í TMP stóðst ekki til lengri tíma með tilliti til svefns (2,4; $p = 0,066$) öfugt við árangur þátttakenda í NEM meðferðinni (3,4; $p = 0,013$).

Ályktun: Niðurstöður benda til að þrálátir stoðkerfisverkir séu algengir á Íslandi og að fólk sem þá upplifir búi við lakara heilsufar og skert lífsgæði. Þverfræðileg endurhæfing eykur lífsgæði og minnkar verki meðal kvenna sem upplifa þráláta stoðkerfisverki og þeirra áhrifa gætir enn hálfu ári eftir að meðferð lýkur.

Lykilorð:

Þrálátir stoðkerfisverkir; algengi; þverfræðileg endurhæfing; heilsutengd lífsgæði; gagnreynd meðferð

Abstract

Background and aims: Worldwide chronic musculoskeletal (MSK) pain is a prevalent problem constituting a considerable societal burden. The aim was to investigate the prevalence of chronic MSK pain conditions in Iceland and the potential impact on physical and mental health, and further, to assess the potential influence of a 4-week traditional multidisciplinary pain management program (TMP) and a similar program adding neuroscience patient education and mindfulness based cognitive therapy (NEM) on health-related quality of life (HRQL) and pain intensity among women experiencing chronic MSK pain.

Methods: Using a population-based randomly selected sample of 5,906 Icelanders, aged 18-79 years (response rate of 60.3%), the prevalence of chronic MSK pain conditions in Iceland, in December 2007, was assessed. The prevalence estimations were weighted by gender, age and residential area to properly represent the underlying population. Multivariate logistic regression models were used to assess associations between chronic MSK pain conditions and functional limitations as well as symptoms. To assess the effectiveness of the two programs we used data from an Icelandic rehabilitation center (Heilsustofnun NLFÍ) including 122 women who received TMP, 90 receiving NEM, and 57 waiting list controls. The HRQL (Icelandic Quality of Life Scale) and pain intensity (100 mm Visual Analogue Scale) had been measured before, as well as after the interventions and 6-months after the completion of the interventions. Analysis of variance and linear regression were used for comparisons.

Results: The point prevalence of chronic MSK pain conditions was 19.9% with distinct gender differences (men=15.2%; women=24.7%) and varied considerably with sociodemographic factors. Compared with individuals without chronic MSK pain, those with the condition reported considerably higher odds ratios (OR) of poor physical (OR men=4.0 [95%CI=3.0-5.2]; OR women=6.8 [95%CI=5.4-8.5]) and mental health (OR men=1.7 [95%CI=1.3-2.3]; OR women=2.4 [95%CI=1.9-3.0]) as well as physically demanding daily activities (OR men=2.4 [95%CI=1.8-3.2] – 6.9 [95%CI=4.2-11.5]; OR women=3.2 [95%CI=2.3-4.6] – 7.9 [95%CI=6.3-10.0]), and lower quality of life (OR men=1.5 [95%CI=1.0-2.1]; OR women=1.6 [95%CI=1.2-2.1]). Statistically significant changes were observed immediately after multidisciplinary pain treatment in terms of increased HRQL (TMP=10.5;

NEM=9.7 versus waiting list controls=1.3; $p<0.001$) and reduced pain intensity (TMP=22mm; NEM=17mm versus waiting list controls=0.6mm; $p<0.001$), with sustained improvements 7 months from baseline (increased HRQL [TMP=6.4; $p<0.001$ and NEM=6.9; $p<0.001$]; reduced pain intensity [TMP=11mm; $p<0.001$ and NEM=15mm; $p<0.001$]). Limited differences in treatment effectiveness were noted between the two interventions. The TMP participants did not sustain improvement in sleep domain (2.4; $p=0.066$) whereas the NEM did (3.4; $p=0.013$).

Conclusions: The findings suggest that chronic MSK pain conditions are common in Iceland and are associated with poor health and diminished quality of life. Multidisciplinary interventions improved quality of life and pain intensity among women with chronic MSK pain conditions with lasting effects observed half a year after treatment completion.

Keywords:

Chronic musculoskeletal pain; prevalence; multidisciplinary rehabilitation; health related quality of life; evidence based practice

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This thesis is the product of a small experiment that started in 2000. The chronic pain team at Heilsustofnun NLFÍ in Hveragerði made a crucial decision to start a structured group program for people experiencing chronic musculoskeletal pain. From the beginning we decided to make use of several outcome measures and that's when the data collection started. We also decided to limit hands-on treatment for various reasons but now, 16 years later, it is evident that our decisions were justified. Since the program started as an experiment we really did not know where it would lead, but with time we understood that extensive data existed and it seemed logical to turn it into a research project.

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List of abbreviations

ANOVA	Analysis of variance
BDNF	Brain-derived neurotrophic factor
BMI	Body Mass Index
C-CBP	Current chronic back pain
C-CPD	Current chronic musculoskeletal pain disorder
CI	Confidence interval
DALYs	Disability-adjusted life-years
GDP	Gross domestic products
HRQL	Health-related quality of life
HSD	Honestly significant difference
IASP	International Association for the Study of Pain
ICC	Intra-class correlation coefficient
ICF	International Classification of Functioning, Disability and Health
IHD	Ischemic heart disease
IPAQ	International Physical Activity Questionnaire
IQL	Icelandic Quality of Life Scale
IQOLA	International Quality of Life Assessment
MBCT	Mindfulness-based cognitive therapy
MET	Metabolic equivalent of task
MOS SF-36	Medical Outcome Study-short form
MSK	Musculoskeletal
N-CPD	Non-chronic musculoskeletal pain disorder
NEM	Neuroscience patient education and mindfulness-based cognitive therapy
NRS	Numerical Rating Scale

NSAID	Non-steroid anti-inflammatory drug
OR	Odds ratio
P-CBP	Past chronic back pain
PNE	Pain neurophysiology patient education
PROMIS	Patient-Reported Outcome Measurement Information System
PSS	Perceived Stress Scale
SD	Standard deviation
SWEMWBS	Short Warwick-Edinburgh Mental Well-being Scale
SWL-scale	Satisfaction with Life Scale
TMP	Traditional multidisciplinary pain management program
VAS	Visual Analogue Scale
WHO	World Health Organization

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List of original papers

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals (I-IV):

- I. **Functional limitations and physical symptoms of individuals with chronic pain.** Björnsdóttir SV, Jónsson SH, Valdimarsdóttir UA (2013). *Scand J Rheumatol* 42(1): 59-70
- II. **Mental health indicators and quality of life among individuals with musculoskeletal chronic pain: A nationwide study in Iceland.** Björnsdóttir SV, Jónsson SH, Valdimarsdóttir UA (2014). *Scand J Rheumatol* 43(5): 419-423
- III. **Health-related quality of life improvements among women with chronic pain: comparison of two multidisciplinary interventions.** Björnsdóttir SV, Arnljótsdóttir M, Tómasson G, Triebel J, Valdimarsdóttir UA (2016). *Disabil Rehabil* 38(9): 828-836
- IV. **Long-lasting improvements in health-related quality of life among women with chronic pain, following multidisciplinary rehabilitation.** Björnsdóttir SV, Triebel J, Arnljótsdóttir M, Tómasson G, Valdimarsdóttir UA (2016). Submitted for publication.

All papers are reprinted by kind permission of the publishers. In addition, some unpublished data may be presented. The papers or manuscripts do not appear in the online version of this thesis.

Declaration of contribution

The doctoral student, Sigrún Vala Björnsdóttir, designed the research questions and methods, and ran statistical analyses for studies I and II, drafted the manuscripts and prepared them for publication in close collaboration with supervisor and co-authors. For studies III and IV the doctoral student, in close collaboration with team members at Heilsustofnun NLFÍ, designed the two programs under investigation, planned the data collection, and applied for ethical clearance. Together with her supervisor, co-authors and doctoral committee, the student planned and ran statistical analyses, drafted the manuscripts and prepared them for publication. The doctoral student wrote this thesis with guidance from the thesis supervisor.

1 Introduction

On October 28, 2010, delegates to the International Pain Summit of the International Association for the Study of Pain (IASP) announced a declaration designated to Montréal ("Declaration of Montréal," 2010). The summit declared that "access to pain management is a fundamental human right" and as such the following should be recognized worldwide:

- "The right of all people to have access to pain management without discrimination"
- "The right of people in pain to acknowledgment of their pain and to be informed about how it can be assessed and managed"
- "The right of all people with pain to have access to appropriate assessment and treatment of the pain by adequately trained health care professionals"

The overarching aim of this thesis has been to elucidate improved understanding of the prevalence of chronic musculoskeletal (MSK) pain in the Icelandic population and associated co-morbidities as well as to test the effectiveness of multidisciplinary interventions. As background to this work, existing knowledge on chronic MSK pain was reviewed, including, but not limited to, prevalence and societal burden, etiologic factors, and pain neurophysiology with reference to the importance of such knowledge in the management of chronic MSK pain; further, the impact chronic MSK pain conditions may have on the individual is discussed. "Up to date" evidence-based pain management, with the aim of introducing appropriate treatment for people with chronic MSK pain as stated in the above declaration is elaborated on.

1.1 Definitions and terminology of pain

Searching the literature for research on chronic MSK pain can be challenging due to a wide range of operational definitions of both pain and chronic pain. However, it was necessary to be sure that the most accepted definitions by experts in the field were used. The IASP has published definitions of both terms and used an expert panel to conclude the most relevant terminology (IASP, 1986). The panel defined pain as:

“...an unpleasant sensory and emotional experience associated with actual or potential damage, or described in terms of such damage, and pain is always subjective. Each individual learns the application to the word through experiences related to injury in early life.”

The panel defined chronic pain as:

“...that pain which persists past the normal time of healing...[or] taken three months as the most convenient point of division between acute and chronic pain.”

Although most researchers hold on to the IASP definition of chronicity, low back pain literature tends to be more specific on duration of pain. Some clinical guidelines specify acute low back pain as lasting up to six weeks, subacute from 7-12 weeks and chronic over 12 weeks (Thorson et al., 2008). However, it has been reported that 84% of people who experience and seek care for low back pain recover within three months and 92% within six months (Shekelle et al., 1995). Most research prior to 2010 followed the American College of Rheumatology's criteria for definition of widespread pain which states that pain should be present on both the left and right sides of the body, both above and below the waist, as well as axial skeletal pain. To be diagnosed with fibromyalgia a person must have had widespread pain for at least three months and would also need to have at least 11 of 18 predefined painful tender points (Wolfe et al., 1990). In 2010, the definition was remodeled, stating that three conditions should be met for diagnosis of fibromyalgia; widespread pain (≥ 7 of 19 painful locations with symptom severity of ≥ 5 on a 0-12 scale); symptoms present at least for three months; and that no other disorder could explain the pain (Wolfe et al., 2010).

For the purpose of this thesis, the IASP definitions of pain and chronicity have generally been adopted. The IASP definition includes any kind of chronic pain whereas the American College of Rheumatology's criteria are limited to widespread chronic pain or fibromyalgia.

1.2 Epidemiology of musculoskeletal pain

The impact of disease categories has been changing during the past few decades with decreases in communicable diseases as opposed to increases in non-communicable diseases. The latest research on global health data (Murray et al., 2015) shows that any low back and neck pain, irrespective of pain duration, moved from the 7th place of leading causes of global disability-

adjusted life-years (DALYs) in 1990 to the 5th place in 2005 and the 4th place in 2013. Similarly, depressive disorders transferred from the 15th place in 1990 to the 11th in 2013. Significant increases were also reported from 2005 to 2013 for osteoarthritis, other MSK disorders, and anxiety. In high income countries globally, the number one cause of DALYs rates in 2013 was any low back and neck pain followed by ischemic heart disease (IHD) whereas depression was number six and other MSK were ranked number 10. In both developed and developing countries IHD was the number one cause of DALYs. Any low back and neck pain was the second cause among the developed countries as opposed to the fourth cause in the developing countries. Depression, on the other hand, was number five among the developed countries but was not among the top ten in the developing countries.

From another report using the same data (Vos et al., 2015) the global prevalence rate of any low back pain increased from 1990 to 2013 by 57%, any neck pain by 54%, anxiety disorders by 42%, major depressive disorders by 53%, and other MSK disorders by 78%. Other studies confirm these findings indicating that approximately half of those who are socially active in the community are at risk of any MSK pain (Bingefors and Isacson, 2004; Hagen et al., 2000).

Various definitions of pain chronicity across studies may partially account for the large variation in reported prevalence of chronic MSK pain. Other factors may relate to inclusion criteria across studies, varying study designs, population sampling procedures and assessment tools, which all may account for challenges in estimating the true prevalence rate.

The observed variation in population prevalence of chronic MSK pain is shown in recent studies and has been reported from 12 to 47.5%. A large-scale study was conducted in 15 European countries and Israel, showing that the prevalence of chronic MSK pain was the lowest in Spain or 12%, 13% in the UK and Ireland, 15% in France, 16% in Denmark, 18% in the Netherlands and 30% in Norway (Breivik et al., 2006). In this study, authors defined chronic MSK pain as pain lasting more than six months, experience of some pain during the last month, several times during the last week, and that pain should have exceeded five of ten on a Numeric Rating Scale (NRS) on the last occasion. Other studies on prevalence in some of the same countries have generally used less strict criteria for chronic MSK pain, showing different results. For example, prevalence of chronic MSK pain has also been reported at 41% in England (Parsons et al., 2007), 19-20% in Denmark

(Eriksen et al., 2003; Sjogren et al., 2009), 31.7% in France (Bouhassira et al., 2008), 44.4% in the Netherlands (Picavet and Schouten, 2003), and 24.4% in Norway (Rustoen et al., 2004). Studies show that in other countries the prevalence of chronic MSK pain has been reported from 17-34.5%. In Canada, reported prevalence is 29% (Moulin et al., 2002), 17-20% in Australia (Blyth et al., 2001), 30.7% in the United States (Johannes et al., 2010), and 34.5% in Hong Kong (Wong and Fielding, 2011).

In Iceland, the prevalence of chronic MSK pain has been assessed in only a few studies showing various results. The variation has been most likely due to several factors including definitions, representativeness of the population and response rate. One study from 1998 reported chronic MSK pain prevalence estimates of 26.9% among women and 12.9% among men (Birgisson et al., 1998) and another study published in 2010 reported a prevalence of 30.6% (Gunnarsdóttir et al., 2010). Yet another study reporting prevalence of chronic MSK pain in Iceland showed an even higher figure of 47.5% (Jónsdóttir et al., 2014). In these studies the response rates were calculated as 53.4%, 46.6% and 36.9%, respectively, and the total sample sizes were 1,282, 599 and 1,586, in that order. Although, the studies all focused on chronic MSK pain, the first one focused on chronic widespread pain while the two latter focused on any chronic MSK pain, which may partially explain the prevalence differences. In addition, some bias may have occurred due to the primary focus on pain in the questionnaires. People receiving the questionnaires but did not have any pain condition may have decided not to answer at all. This may also explain the relatively low response rates in these studies.

Research has shown that prevalence of chronic MSK pain varies not only across populations but also depending on cultural and social status. Most studies show that prevalence of all chronic MSK pain conditions increases with age (Ahacic and Kareholt, 2010; Bingefors and Isacson, 2004; Birgisson et al., 1998; Blyth et al., 2001; Bouhassira et al., 2008; Breivik et al., 2006; Jónsdóttir et al., 2014; Mallen et al., 2005) and show higher prevalence among women than men (Bingefors and Isacson, 2004; Birgisson et al., 1998; Blyth et al., 2001; Bouhassira et al., 2008; Breivik et al., 2006; Jónsdóttir et al., 2014; Mundal et al., 2014a). People with a lower educational level tend to report chronic MSK pain more frequently (Bingefors and Isacson, 2004; Blyth et al., 2001; Jónsdóttir et al., 2014) and also people with a lower income (Bingefors and Isacson, 2004), as well as those having lower social class status (Macfarlane et al., 2009).

Besides affecting people on an individual level, chronic MSK pain burdens societies through its effects on people's well-being (Jónsdóttir et al., 2014; Lee et al., 2008; Mäntyselkä et al., 2003) and restriction in societal participation (Bingefors and Isacson, 2004; Breivik et al., 2006; Steingrimsdóttir et al., 1988). It has further been reported that people with chronic MSK pain tend to use the health care system to a greater extent than people who do not experience chronic MSK pain (Blyth et al., 2004; Eriksen et al., 2004; Hagen et al., 2000).

Burden of disease can also be measured by estimating the cost for societies, both direct and indirect costs. Direct costs in the case of chronic MSK pain can be considered as expenditures on inpatient and outpatient health care contacts, diagnostic testing, pharmaceuticals, orthopedic aids, physical therapy and paid home care. Indirect costs in this case could relate to production losses due to changes in health status. This would include absenteeism, lower productivity while working and early retirement. In Sweden, the direct cost of chronic low back pain specifically has been estimated as 15% as opposed to 85% indirect costs per patient (Ekman et al., 2005). In a more recent Swedish study on the socioeconomic burden of patients with any diagnosis related to chronic MSK pain conditions, the direct cost was estimated as 59% as opposed to the indirect cost of 41%. Translated to yearly costs due to chronic MSK pain conditions in Sweden in 2010 meant 10% of gross domestic products (GDP) (Gustavsson et al., 2012). In Ireland in 2008, the yearly cost for the society due to chronic MSK pain has been estimated at 2.9% of GDP (Raftery et al., 2012). In the United States the costs of chronic MSK pain have been estimated considerably higher than the costs of heart disease, cancer and diabetes combined (Gaskin and Richard, 2012). It is clear that chronic MSK pain is expensive for the individual as well as for any society.

Evidently, chronic MSK pain is not one of the leading "causes" of premature mortality, according to the World Health Organization (WHO) ("World Health Organization," 2015). The greatest impact is, nevertheless, on those living with disability as chronic MSK pain conditions seldom shorten life. Yet, recent studies report increased mortality rates among people with various chronic MSK pain conditions (Dreyer et al., 2010; Torrance et al., 2010), perhaps explained by sociodemographic factors (Torrance et al., 2010), while lifestyle-related influences cannot be excluded.

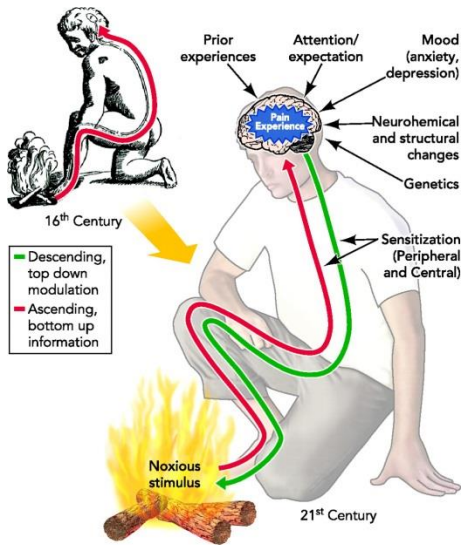
In sum, chronic MSK pain significantly burdens societies due to high prevalence rates across the world and, the negative effects pain has on

people's well-being and restrictions in societal participation. MSK pain, including the chronic phase, is highly ranked globally when measured in DALYs and is costly for the individual as well as for any society.

1.3 Etiology and potential risk factors

Chronic MSK pain conditions generally evolve from tissue origin, although not all MSK pain conditions can be explained by tissue lesions. Therefore, determining the etiology and potential risk factors and treatment methods is complicated. Given the IASP definition of chronic MSK pain as pain that exceeds the normal time of healing, one can consider chronic MSK pain as unexplained even though some tissue lesion initially triggered the condition. For example, it has been reported that up to 50% of people with initial whiplash injury (Carroll et al., 2008; Guez et al., 2002) and up to 25% of those experiencing acute low back pain (Grotle et al., 2005) develop a chronic condition. Chronicity also means that pain spreads to body parts that were not initially injured and people report a variety of somatic and psychological symptoms (Wenzel et al., 2009). Other syndromes present with chronic MSK pain but not necessarily any clear etiological factors and can therefore also be considered unexplained. Among these are fibromyalgia, temporomandibular joint disease, tension-type headache and irritable bowel syndrome. All of the above share a common pathway, namely alterations in the nervous system (Woolf, 2011) which may be one of the most prominent factors contributing to chronicity.

In recent decades, scientists have gained considerable knowledge on pain and pain physiology. Nowadays, it is generally accepted that experiences of pain have direct links to emotions and cognition (Figure 1) (Bingel and Tracey, 2008).



Left: Cartesian view of pain. According to the classical Cartesian view, pain was considered to be a hard-wired system in which noxious input was passively transmitted along sensory channels to the brain. *Right:* 21st century view of pain. Pain is acknowledged to represent a multidimensional experience that is influenced by both bottom-up and top-down modulatory influences.

Courtesy: *Physiology* © *American Physiological Society*.

Figure 1. Pain perception: ancient and current concepts.

As mentioned, recent literature suggests that transition from acute to chronic pain involves alterations in the central nervous system known as “central sensitization” (Figure 2 and Figure 3) (Woolf, 2011). It manifests as heightened sensitivity to injured sites and misinterpretation where touch is signaled as pain (Koneti and Jones, 2013; Woolf, 2011; Zusman, 2002).

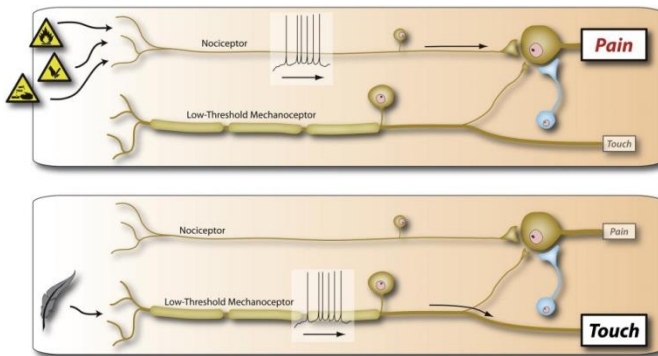


Figure 2. Normal sensation.

The somatosensory system is organized such that the highly specialized primary sensory neurons that encode low intensity stimuli only activate those central pathways that lead to innocuous sensations, while high intensity stimuli that activate nociceptors only activate the central pathways that lead to pain and the two parallel pathways do not functionally intersect. This is mediated by the strong synaptic inputs between the particular sensory inputs and pathways and inhibitory neurons that focus activity to these dedicated circuits.

Courtesy: Pain © Walters Kluwer Health, Inc.

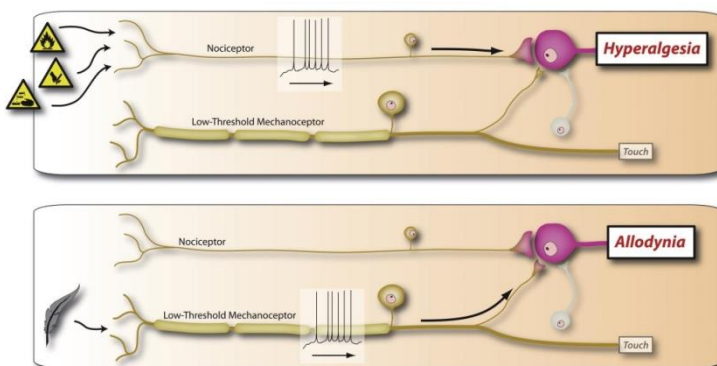


Figure 3. Central sensitization.

With the induction of central sensitization in somatosensory pathways with increases in synaptic efficacy and reductions in inhibition, a central amplification occurs enhancing the pain response to noxious stimuli in amplitude, duration and spatial extent, while the strengthening of normally ineffective synapses recruits subliminal inputs such that inputs in low threshold sensory inputs can now activate the pain circuit. The two parallel sensory pathways converge.

Courtesy: Pain © Walters Kluwer Health, Inc.

Another mechanism involved in central sensitization is loss of inhibition resulting in imbalance between inhibition and facilitation of spinal cord pain pathway neurons (Woolf, 2011; Zusman, 2002). There is also evidence of central and peripheral hypersensitivity in somatic tissues which also means that pain pathways respond abnormally and strongly to stimuli that should normally not evoke pain (Zusman, 2002).

The gate control theory (Melzack and Wall, 1965) explains the neurophysiological basis for the existence of pain and a modified version (Melzack, 1999) involves cognitive functions. Together, these theories form the basis for the importance of a bio-psycho-social approach to the treatment of chronic MSK pain conditions. In the modified version, the scientists proposed that sensory and emotional components of pain are distinctly processed by various brain structures. One component involves sensory-discriminative dimension of pain processing including pain quality, intensity and location. The other component involves the affective-motivational dimension of pain, including emotional processing (Melzack, 1999). Strong association has also been suggested between perceived pain intensity and activation in various brain locations on both hemispheres. Pain intensity processing has been observed in both cortical and subcortical regions of the brain and in areas that were not considered engaged in sensory-discriminative processing in earlier work. Pain intensity related responses have been found, for example, in areas important for motor control, affect, and attention (Coghill et al., 1999). Further, there is a distinct difference in activation patterns in the brain between people with chronic MSK pain and those without. Those with chronic MSK pain also tend to scale induced pain stimuli higher than those without (Burgmer et al., 2009) and those with chronic MSK pain show increased brain activity when pain is verbally described to them (Sitges et al., 2007).

Overall, there are strong indications for hypersensitivity in both the peripheral and central nervous system in people with chronic MSK pain conditions. Neuroplasticity seems to affect pain perception and presents with various somatic-sensory misinterpretation. Recent studies focus on this relationship, indicating that people with chronic MSK pain have altered perceptions with respect to their own body. People with chronic MSK pain tend to have problems discriminating between left and right when presented with pictures of body parts, especially if their own body part is painful (Bray and Moseley, 2011; Schwoebel et al., 2001). Further, people with chronic MSK pain tend to distort affected body parts when asked to draw a picture of the painful area (Moseley, 2008) and are presented with disrupted tactile

perception and motor control (Catley et al., 2013; Luomajoki and Moseley, 2011).

There is evidence that people's experiences of pain can be influenced, including emotions, motivation, attention and cognition (Meeus and Nijs, 2007; Price, 2000; Zusman, 2002). Further, that activity in descending pathways can be modulated by awareness, stress or attention (Meeus and Nijs, 2007; Rygh et al., 2002). It has also been shown that memory and pain share similar pathways (Ji et al., 2003; Rygh et al., 2002) suggesting the existence of cellular pain memory (Rygh et al., 2002). This may explain the signs that people with chronic MSK pain remember their past pain consciously or unconsciously (Rollman et al., 2004). The reported co-occurrence of chronic MSK pain and depression (Ohayon, 2004) may also possibly be explained by common brain activity and neural pathways (Zambito Marsala et al., 2015).

All the above are important when considering potential treatment methods for chronic MSK pain conditions and show the complexity and multidimensional nature of the condition. This relates to the importance of neuroscience patient education, as discussed in sections 1.6 and 1.7.

Risk factors

Perhaps due to the complex neurophysiological mechanism with respect to pain and the evidence for forebrain involvement, researchers have been suggesting that various psycho-social factors may contribute to chronicity (Nicholl et al., 2009). Identified independent risk factors for the onset of chronic MSK pain conditions include, for example, somatization (Gupta et al., 2007; McBeth et al., 2001), health seeking behavior (Gupta et al., 2007; Myrtveit et al., 2015), poor sleep (Gupta et al., 2007), and passive coping strategies (Carroll et al., 2006; Mercado et al., 2005; Myrtveit et al., 2015).

Lifestyle related factors such as smoking (Goldberg et al., 2000; John et al., 2009; Mundal et al., 2014b; Palmer et al., 2003), overweight/obesity (Caldwell et al., 2009; Mundal et al., 2014b; Nilsen et al., 2011), physical inactivity (Holth et al., 2008; Nilsen et al., 2011; Perruchoud et al., 2014; Teichtahl et al., 2015) and poor physical functioning (Caldwell et al., 2009) have also been shown to be associated with chronic MSK pain conditions. Causal relationships remain unclear.

As mentioned, unmodifiable factors such as female gender and higher age are associated with increased risk of chronic MSK pain conditions. Some

evidence exists suggesting that genetic factors may also be involved with chronic MSK pain development (Kato et al., 2006; Schur et al., 2007).

In summary, chronic MSK pain may or may not have an explainable origin, but it is clear that central mechanisms are involved in the development and persistence of the condition. Somatization, poor sleep, health seeking behavior, poor coping skills, smoking, overweight/obesity, physical inactivity, and poor physical functioning have been identified as risk factors for developing chronic MSK pain.

1.4 Physical deconditioning and impact on activities

Numerous physical symptoms have been reported in association with chronic MSK pain contributing to potential physical disability. Besides the obvious symptoms of heightened pain perception, people may also report chronic fatigue (Meeus et al., 2007), which may restrict participation in social life (Lee et al., 2008). In addition, perceived activity decline has been reported in association with disability among people with chronic MSK pain (Friedrich et al., 2009; Verbunt et al., 2005). It has further been suggested that people with chronic MSK pain may tend to fear physical strain believing that physical demands may increase pain or do harm (Friedrich et al., 2009; Nijs et al., 2008). Recent studies indicate that people experiencing chronic low back pain may be exposed to lower levels of physical activity, physical activity avoidance and generally lower levels of physical fitness, compared with healthy controls (Duque et al., 2009; Rudy et al., 2007). Conversely, recent systematic reviews suggest that evidence for such differences is inconclusive (Griffin et al., 2012; Van Weering et al., 2007).

Fear avoidance beliefs and behavior are important factors when considering treatment methods for chronic MSK pain. Research has shown that high levels of fear avoidance are associated with low levels of physical activity and disability among people with chronic MSK pain conditions (Crombez et al., 1999; Feleus et al., 2007; Grotle et al., 2004; Luning Bergsten et al., 2012). The fear-avoidance model of chronic pain (Figure 4) has been used to explain different coping styles when people are expecting or are exposed to pain (Vlaeyen and Linton, 2000). The model suggests two opposing behavioral responses to a painful experience. One leads to confrontation and recovery, whereas the other leads to catastrophic thought processes. The path of confrontation is characterized by the person as looking at the current pain experience as a temporary hindrance instead of a

catastrophic event. In the latter it is proposed that negative affectivity or a threat to health status triggers catastrophic thought processes characterized by the tendency to focus on pain sensation, helplessness and magnification. Consequently, the individual fears movement and therefore avoids pain provocative activities. This will then lead to disuse, physical deconditioning and disability.



Figure 4. Fear-avoidance model of chronic pain.

If pain, possibly caused by an injury, is interpreted as threatening (pain catastrophizing), pain-related fear evolves. This leads to avoidance behaviors, and hypervigilance to bodily sensations followed by disability, disuse and depression. The latter will maintain the pain experiences thereby fueling the vicious circle of increasing fear and avoidance. In non-catastrophizing patients, no pain-related fear and rapid confrontation with daily activities is likely to occur, leading to fast recovery. Pain catastrophizing is assumed to be also influenced by negative affectivity and threatening illness information.

Courtesy: Pain © Walters Kluwer Health, Inc.

A recent systematic review of clinical guidelines for the management of chronic low back pain warrants the path of confrontation by encouraging engagement in physical activity and early mobilization (Pillastrini et al., 2012).

This is supported by clinical guidelines on various other chronic MSK pain conditions (Carville et al., 2008; Fitzcharles et al., 2012; "Scottish Intercollegiate Guidelines Network (SIGN)," 2013). On the other hand, the path of catastrophic thought processes is apparent in research showing that disability is strongly associated with fear of movement and pain catastrophizing (Chou and Shekelle, 2010; Keefe et al., 2000; Picavet et al., 2002; Somers et al., 2009). Further, people with chronic pain engage in low levels of physical activity (Elfving et al., 2007; Lin et al., 2011) and are suspect of having less physical strength which may be associated with fear of movement (George et al., 2008; Trost et al., 2011). Pain-related fear also affects spinal movements with a risk of adopting alternative maladaptive body mechanics (Thomas and France, 2007).

It is well understood, according to the fear avoidance model, that pain recruits cognitive, emotional and behavioral responses which perhaps may aggravate pain sensation and disability. This understanding generally harmonizes well with evidence explaining central sensitization and pain modulation. However, shortcomings in the fear avoidance model have been discussed in review articles (Crombez et al., 2012; Eccleston and Crombez, 2007; Schutze et al., 2010). Proposed adaptations include a motivational (Crombez et al., 2012; Volders et al., 2015) or a mindfulness perspective (Schutze et al., 2010). This is reflected in the latest research on fear avoidance where motivation is included as an important mechanism. For example, recent studies indicate that under experimental conditions among healthy individuals, competing goals (pain versus reward) can attenuate avoidance behavior and further, that competing goals may influence decision making and avoidance with respect to behavior (Claes et al., 2015; Claes et al., 2014). One study explored the association between mindfulness and the major components in the fear-avoidance model. Results indicate that mindfulness plays a significant role in the model with the strongest association between mindfulness and pain catastrophizing (Schutze et al., 2010).

Although it is proposed that the catastrophic path of the fear avoidance model may lead to physical deconditioning and disability, some research has suggested that people with chronic MSK pain show similar daily activity levels as those of healthy counterparts (Spenkelink et al., 2002; Verbunt et al., 2009). Underlying mechanisms may be explained by the bidirectional nature of motivation that may have positive or negative effects. Some people may, for example, be motivated to keep daily activities ongoing by suppressing or ignoring the pain and fail to integrate relaxation or repose into their daily

routine (Hasenbring et al., 2001). There is also some evidence indicating that people with chronic MSK pain adopt different patterns of activity during the day compared with healthy individuals (Griffin et al., 2012). This may perhaps be due to adaptive coping styles (Myrtveit et al., 2015).

Collectively, people with chronic MSK pain are likely to fear and to avoid pain provocative activities which may initiate physical inactivity and declined health status. Therefore, a combination of treatment methods involving both physical and psychological components is essential when considering rehabilitation for chronic MSK pain conditions.

1.5 Mental co-morbidity and psychological impact

It is well documented that people experiencing chronic MSK pain conditions may also experience various psychological difficulties and may, in some cases, show serious symptoms. Poor mental health has been reported by people with new onset chronic MSK pain, explained by pre-morbid psychological factors such as anxiety and depression (Nicholl et al., 2009), which also may contribute to the development from acute to chronic pain (Koleck et al., 2006). However, chronic MSK pain and work related stress have also been reported as strong predictors of depression (Munce et al., 2006).

Depression is one prominent symptom repeatedly reported by people with chronic MSK pain (Demyttenaere et al., 2007; Munce and Stewart, 2007; Tsang et al., 2008). In a cross-national survey on chronic neck and back pain and mental morbidity, authors concluded that people in general populations, experiencing these pain problems, report depression and anxiety independent of cultural or demographical origin (Demyttenaere et al., 2007). From the same data, authors included other chronic pain conditions in their analyses and further suggested an association with depression and/or anxiety (Tsang et al., 2008). Other population-based studies on the association between chronic MSK pain (Miller and Cano, 2009; Munce and Stewart, 2007) or chronic back pain (Currie and Wang, 2004), and depression show similar results. Studies on specific patient groups such as chronic back pain (Glombiewski et al., 2010) and post traumatic chronic pain (Roth et al., 2008) also confirm an association between chronic MSK pain and depression. However, it has been reported that among people with chronic MSK pain the association between pain severity and depression is mediated by pain-related interference with family, work and social activities

(Cannella et al., 2007). Studies show that depression as well as co-morbid depression and chronic MSK pain are more prevalent among women than men (Demyttenaere et al., 2007; Munce and Stewart, 2007; Munce et al., 2006; Tsang et al., 2008). Women also tend to report higher levels of disability than men when depressive symptoms are serious in association with chronic MSK pain (Keogh et al., 2006).

Anxiety is another prominent psychological symptom repeatedly reported by people with chronic MSK pain. In a recent clinical study, the authors reported that approximately 25% of patients with chronic MSK pain also experienced anxiety (Knaster et al., 2012). Other clinical studies further show an association between various chronic pain conditions and anxiety (Keogh et al., 2006; Newcomer et al., 2010; Rode et al., 2006) as well as population-based studies (McWilliams et al., 2003).

Poor quality of sleep has been reported by 67% of patients with chronic MSK pain (Morin et al., 1998). Other clinical studies confirm that patients with chronic MSK pain generally experience lack of sleep compared with healthy individuals (Okura et al., 2008; Van de Water et al., 2011). Distinct gender differences have further been suggested, with the female patients with chronic MSK pain showing less sleep than the males when complaining of poor sleep (Lavigne et al., 2011). Although lack of sleep is evident among people experiencing chronic MSK pain (Ohayon, 2005), there is no indication of whether chronic MSK pain condition is the cause or consequence of sleeping disturbances (Rains and Penzien, 2003). It has been reported, for example, that sleep deprivation may induce increased pain complaints but also awareness of physical symptoms due to fatigue (Busch et al., 2012). It has also been suggested that the association between disability and poor sleep quality is mediated by depression and pain severity in a population of patients with chronic MSK pain (Naughton et al., 2007).

People with chronic MSK pain, furthermore, report diminished quality of life (Becker et al., 1997; Lamé et al., 2005; Laursen et al., 2005; Lin et al., 2010), satisfaction with life (Boonstra et al., 2013; Silvemmark et al., 2008) and well-being (Becker et al., 1997; Lamé et al., 2005; Laursen et al., 2005; Lin et al., 2010).

In sum, people with chronic pain are exposed to various psychological symptoms that may have an impact on daily life and affect quality of life. Therefore, a psychological component is needed for a successful rehabilitation intervention.

1.6 Bio-psycho-social approach to treatment of chronic MSK pain

Given the complex etiology and symptom appearance in chronic MSK pain conditions, a multimodal approach for treatment success and symptom relief is required. In 2001, the World Health Organization (WHO) introduced a model called the International Classification of Functioning, Disability and Health (ICF), as shown in Figure 5. This model is intended to holistically capture a person's life with respect to health or health conditions reflecting functioning and disability. Although the ICF is a classification system it also provides a conceptual basis for describing and measuring health and health conditions. The ICF puts a person in a context reflecting interaction between health condition and personal and environmental factors. The ICF is not based on diagnosis or symptom etiology but rather on the functioning of a person where body functions and structures, daily activities and societal participation are equally important and interact with each other. Disability is described by the ICF as impairments in body functions and/or structures, activity limitations and participation restrictions. Environmental factors, including physical, social and attitudinal factors are either barriers to or facilitators of an individual's functioning ("World Health Organization," 2013). As such the ICF framework is a bio-psycho-social synthesis and integrates the major models of disability, namely the medical model and the social model (Üstün et al., 2003).

The bio-psycho-social model was introduced in 1980 and is characterized by the inclusion of missing dimensions of the biomedical model. It demands that the person be looked at in a holistic way with inclusion of psychological and social influences where people's health is concerned (Engel, 1980).

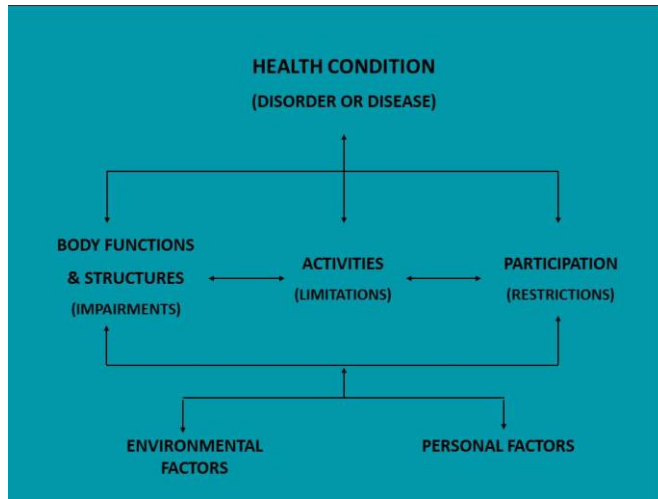


Figure 5. The ICF model.

The International Classification of Functioning, Disability and Health model showing the interaction between ICF components.

Courtesy: World Health Organization

The bio-psycho-social approach and the ICF well capture treatment needs in the case of chronic MSK pain conditions, namely an interdisciplinary approach. There is no single treatment method applicable for a multidimensional condition as chronic MSK pain. This is well shown by initial health care seeking among people at risk of developing chronic MSK pain conditions (Breivik et al., 2006). People tend to seek specialized treatment according to obvious symptoms and may involve various or multiple professionals with inadequate treatment success (Andersson et al., 1999; Breivik et al., 2006). Interdisciplinary bio-psycho-social treatment for chronic MSK pain has been offered for years in various clinical settings, worldwide. Recent studies support the effectiveness of such rehabilitation for people with various chronic MSK pain conditions (Busch et al., 2011; Demoulin et al., 2010; Dysvik et al., 2010; Gagnon et al., 2009; Heiskanen et al., 2012; Kamper et al., 2014, 2015; Meineche-Schmidt et al., 2012; Myhr and Augestad, 2013; Stein and Miculescu, 2013), even when carried out as group therapy (Meineche-Schmidt et al., 2012). There is some evidence that intensive inpatient programs show better results than outpatient programs (Guzman et al., 2001, 2002; Scascighini et al., 2008), although the evidence is inconclusive (Kamper et al., 2014).

Researchers use various comparisons for judging the effectiveness of differing interdisciplinary interventional approaches. Some studies use waiting list controls (Becker et al., 2000; Dysvik et al., 2010) and/or compare with usual care (Becker et al., 2000; Busch et al., 2011; Lang et al., 2003) or compare various treatment methods to interdisciplinary treatment (Busch et al., 2011; Wong et al., 2011). Nevertheless, improvements have consistently been reported following interdisciplinary treatment in terms of increased physical fitness (Demoulin et al., 2010; Gagnon et al., 2009), decreased pain related disability (Dysvik et al., 2010; Gagnon et al., 2009; Kamper et al., 2014, 2015), improved mental well-being (Demoulin et al., 2010; Myhr and Augestad, 2013), improved quality of life (Dysvik et al., 2010; Gagnon et al., 2009; Heiskanen et al., 2012; Meineche-Schmidt et al., 2012), and decreased pain intensity (Demoulin et al., 2010; Dysvik et al., 2010; Gagnon et al., 2009; Kamper et al., 2014, 2015; Myhr and Augestad, 2013). In addition, societal participation has been investigated in follow-up studies on interdisciplinary treatment. A ten year follow-up study shows that an interdisciplinary program for chronic MSK pain is more successful in achieving return to work than behavioral physical therapy, cognitive behavioral therapy and treatment as usual. Consequently, cost-effectiveness is shown in reduced societal expenses in terms of sick leave and disability pension (Busch et al., 2011). A one-year follow-up study further suggests increased social activity and thus less sick leave following interdisciplinary treatment among people with chronic MSK pain (Stein and Miculescu, 2013). In contrast, one most recent systematic review on effectiveness of interdisciplinary treatment for chronic low back pain suggests improved odds of returning to work compared with physical treatment alone, but not more effective than usual care (Kamper et al., 2015). Yet, there is lack of evidence for effectiveness of interdisciplinary treatment for neck and shoulder pain (Karjalainen et al., 2010) and for whiplash associated disorders (Cameron et al., 2008).

Systematic reviews and/or clinical guidelines on treatment for individuals with chronic MSK pain conditions (Scascighini et al., 2008; "Scottish Intercollegiate Guidelines Network (SIGN)," 2013), chronic low back pain (Pillastrini et al., 2012), chronic pelvic pain (Fall et al., 2010), complex regional pain syndrome (Harden et al., 2013) or fibromyalgia syndrome (Carville et al., 2008; Fitzcharles et al., 2012) have recommended interdisciplinary bio-psycho-social rehabilitation programs and some have agreed on the content of such programs. Ideally, an interdisciplinary program should include coordinated intervention covering several domains of the bio-psycho-social model. It should be delivered by skilled clinicians from different

backgrounds. The program should generally include: physical reconditioning; some kind of relaxation techniques; psychological group therapy; patient education related to neurophysiology; physical therapy for pacing strategies; and medical exercise therapy. Pharmacological management is recommended depending on individual needs, such as analgesics and antidepressants (Carville et al., 2008; Pillastrini et al., 2012; Scascighini et al., 2008).

Collectively, based on existing evidence and due to the complex etiology and symptom appearance, clinical guidelines recommend bio-psycho-social interdisciplinary treatment for chronic MSK pain. The effectiveness of such rehabilitation is shown in numerous studies with improvements in disability, mental well-being, quality of life, and pain.

1.7 Evidence for bio-psycho-social treatment components

Despite the evidence strongly indicating that interdisciplinary treatments are effective, it is not clear which treatment components are important, whether all components are equally effective or whether all patients would benefit from all components. A patient-centered approach is generally warranted in guidelines for various chronic MSK pain conditions (Fitzcharles et al., 2012; "Scottish Intercollegiate Guidelines Network (SIGN)," 2013). It is also recognized that clinicians and patients should work together in a problem-solving manner for better results (Eccleston and Crombez, 2007). Patient's expectations, beliefs and preferences should therefore be taken into account when treatment alternatives are considered. Effective treatment results should reflect changeable influences maintaining pain related problems such as acceptance, understanding of mind-body interaction and self-management.

The biological component

The biological component of an interdisciplinary program may consist of many factors including medication, various physical therapies and physical reconditioning.

Medication

Clinical guidelines suggest various medications for various primary symptoms

among people with chronic MSK pain. For example, patients with fibromyalgia may benefit from tramadol or other weak opioids and simple analgesics with positive effects on pain and functioning (Carville et al., 2008). Similar effects on pain and functioning may be achieved with antidepressants such as amitriptyline, fluoxetine, duloxetine, milnacipran, moclobemide and pirlindole (Carville et al., 2008). Other medication such as tropisetron, pramipexole and pregabalin are recommended for pain reduction (Carville et al., 2008). For people with chronic low back pain recommendations suggest that acetaminophen and non-steroid anti-inflammatory drugs (NSAIDs); tramadol and weak opioids; benzodiazepines; muscle relaxants; and tricyclic antidepressants might be effective (Pillastrini et al., 2012). Other guidelines on chronic MSK pain conditions suggest fairly similar pharmacological interventions (Fall et al., 2010; "Scottish Intercollegiate Guidelines Network (SIGN)," 2013). The effectiveness of such medications is shown in many studies but detailed discussion on mechanisms involved is beyond the scope of this thesis.

Physical therapy

Physical therapies are generally included in recommendations for the treatment of chronic MSK pain conditions. Other physical treatments depending on cultural and national preferences in health care education may be recommended. Table 1 summarizes selected systematic reviews that suggest quality of evidence for various treatment methods commonly used by physical therapists for chronic MSK pain conditions. For chronic low back pain, moderate to strong evidence is provided suggesting that spinal manipulations and/or mobilizations are equally effective as other active therapies with reduced pain and disability (Hidalgo et al., 2014; Merezpeza, 2014; Rubinstein et al., 2011). Low quality evidence suggests that exercises, behavior therapy, multidisciplinary treatment and massage are effective when compared with passive controls (Furlan et al., 2015; Van Middelkoop et al., 2011) but traction has no effect on pain and disability (Wegner et al., 2013). For chronic neck pain, moderate to high quality evidence suggests that manual therapy, alone or in combination with exercises, reduces pain and disability compared with other active treatments (Miller et al., 2010), but spinal manipulation is just as effective as other active treatments (Gross et al., 2015). Exercises reduce pain in the short term among people with chronic whiplash associated disorder (Teasell et al., 2010). Transcutaneous electrical nerve stimulation may reduce pain among people with chronic MSK pain but

the evidence is of low quality (Nnoaham and Kumbang, 2008), whereas high quality evidence suggests that pain may be reduced by acupuncture (Hopton and MacPherson, 2010).

Data is scarce on the effectiveness of physical therapy interventions for the treatment of fibromyalgia. Clinical guidelines recommend that physical therapists' intervention should be in the form of counselling for pacing strategies, self-management and individually tailored exercise programs (Carville et al., 2008; Fitzcharles et al., 2012).

Table 1. Evidence synthesis for physical therapy interventions with respect to chronic MSK pain conditions

Source	Primary condition	Evidence classification	Intervention	Outcome	Comparison ^a	Quality of evidence ^b
(Hidalgo et al., 2014)	CLBP	SR	spinal manip	↓ pain ST ↓ disability ST	passive	moderate to strong
			spinal manip/mob + exercise	↓ pain ST/LT ↓ disability ST/LT ↑HRQL ST/LT	= active	moderate
(Rubinstein et al., 2011)	CLBP	SR-Cochrane	spinal manip	↓ pain ST ↓ disability ST	= active	strong
(Merepeza, 2014)	CLBP	SR	spinal manip	↓ pain ST ↓ disability ST	= active	Non-rated
(Van Middelkoop et al., 2011)	CLBP	SR	exercise	↓ pain ST/LT ↓ disability ST/LT	passive	low
			behavior therapy	↓ pain ST	passive	low
			multi-disciplinary treatment	↓ pain ST ↓ disability ST	passive	moderate
(Furlan et al., 2015)	CLBP	SR	massage	↓ pain ST ↓ disability ST	passive	low
			massage	↓ pain ST/LT	active	low
(Wegner et al., 2013)	CLBP	SR-Cochrane	traction	pain NE disability NE	passive	low to moderate
			traction + other physiotherapy	pain NE disability NE	active	low to moderate
(Miller et al., 2010)	CNP	SR	manual therapy + exercise	↓ pain ST	active	high
			manual therapy + exercise	↓ pain ↑HRQL	active	moderate
(Gross et al., 2015)	CNP	SR-Cochrane	spinal manip	↓ pain ST/LT ↓ disability ST/LT ↑HRQL ST/LT	= active	moderate to high
(Teasell et al., 2010)	CWAD	SR	exercise	↓ pain ST	passive	high

Table 1. (continued)

Source	Primary condition	Evidence classification	Intervention	Outcome	Comparison ^a	Quality of evidence ^b
(Nnoaham and Kumbang, 2008)	CP	SR-Cochrane	TENS	↓ pain	passive	low
(Hopton and MacPherson, 2010)	CP	SR of SRs	acupuncture	↓ pain ST/LT	passive	high

^a passive comparison includes inactive controls, waiting list controls, placebo, sham, usual care; active comparison includes any form of treatment

^b authors assessed quality of evidence according to Cochrane standards, Physiotherapy Evidence Database (PEDro) criteria or other quality control assessment tools, as applicable

CLBP=chronic low back pain; CNP=chronic neck pain; CWAD=chronic whiplash associated disorder; CP=chronic pain; SR=systematic review; manip=manipulation; mob=mobilization; TENS=transcutaneous electrical nerve stimulation; ST=short term effectiveness; LT=long term effectiveness; NE=no effect; HRQL=health related quality of life

The observed lack of evidence for the effectiveness of commonly used physical therapy interventions, summarized in Table 1 and in clinical guidelines, for chronic MSK pain conditions may be due to lack of high quality research in the field. The reason may also relate to the fact that most of the methods included in guidelines focus on input and output mechanisms. That is, the treatment is aimed at peripheral elements such as muscles and joints, and motor control. However, in line with new knowledge in pain neurophysiology some promising modern treatment methods have been introduced. One promising treatment method, graded motor imagery (GMI), supposedly targets directly cortical reorganization, i.e. the combination of sensitization and disinhibition (Moseley and Flor, 2012). It is based on the evidence that “danger” has the potential to trigger strong reactions including cognition, perception and action. Therefore, retraining the brain should result in threat reduction, graded exposure and precision. Briefly, this method is based on three components; left/right discrimination, motor imagery and mirror therapy. A recent systematic review suggests effectiveness of GMI and mirror therapy alone for chronic MSK pain conditions (Bowering et al., 2013). The methodological quality was assessed according to Cochrane standards and the evidence was generally judged low.

Another treatment method introduced in a review article allegedly targets central processing mechanisms (Nijs et al., 2014). The method suggests three phases: the first phase constitutes pain neuroscience patient education,

the second phase is based on cognition-targeted neuromuscular training, and the third phase includes cognition-targeted dynamic and functional exercises. A randomized controlled trial is ongoing and results are to be expected in 2017 (Dolphens et al., 2014).

For the management of low back pain, stratified models of care have been introduced. Such models are characterized as having the right treatment, for the right patient at the right time. One model introduces the concept of combining prognostic screening with matched treatment options. The key principle is that clinical decisions are made according to prognostic factors and the patient population is stratified. The treatment for the low risk patients is based on advice, reassurance and medication, but unnecessary treatment and investigation is avoided. The medium risk patients are treated with evidence-based physical therapy. The high risk and more complex patients are treated with psychologically informed physical therapy over a longer period of time. A recent large scale cohort study shows that stratified care for low back pain improves patients' disability without increased health care costs (Foster et al., 2014). Other studies support the effectiveness of this treatment method (Hill et al., 2011; Murphy et al., 2015; Whitehurst et al., 2012). Another model introduces the concept that patients are matched to treatment according to underlying mechanisms that may drive pain or disability. The idea is that the management of low back pain is targeted with cognitive functional therapy. The model addresses fear avoidance, pain provocative functional behavior and activity avoidance. A recent randomized controlled trial shows superior results using this method over manual therapy and exercises for chronic low back pain (Vibe Fersum et al., 2013).

Physical activity

Physical activity is recommended in clinical guidelines for chronic MSK pain conditions (Cameron et al., 2008; Carville et al., 2008; Fitzcharles et al., 2012; "Low back pain in adults: Early management," 2009; "Scottish Intercollegiate Guidelines Network (SIGN)," 2013) and may include body awareness training (Busch et al., 2011; Caby et al., 2010; Stein and Miculescu, 2013) in addition to general and/or specific physical reconditioning (Busch et al., 2011; Caby et al., 2010; Cassidy et al., 2012; Demoulin et al., 2010; Gagnon et al., 2009; Lang et al., 2003; Skouen et al., 2006; Stein and Miculescu, 2013). Generally, the physical activity component in interdisciplinary treatment is led by physical therapists and/or recreational therapists.

Physical activity is recommended for apparently healthy individuals (Garber et al., 2011) and even so for all individuals living with chronic conditions or disability (Pedersen and Saltin, 2006). The American College of Sports Medicine recommends a minimum of 150 minutes per week of moderate-intensity aerobic training, 75 minutes per week of vigorous aerobic training, or a combination of the two. In addition, individuals should engage in strengthening, flexibility and neuro-motor exercises 2-3 times a week. It is further recommended that individuals avoid prolonged sedentary tasks even though extensive physical activity is practiced (Garber et al., 2011). These recommendations are evidence based and those who follow these recommendations enhance healthy living and prevent the adverse effects of a sedentary lifestyle. Mounting evidence supports the importance of a healthy lifestyle, including advice on physical activity among people with various chronic MSK pain conditions (Hayden et al., 2005; Liddle et al., 2007; Pedersen and Saltin, 2006).

It is evident that physical fitness programs are included in interdisciplinary treatment for improving fitness and functioning, regardless of the kind of exercises chosen (Hooten et al., 2012; Valkeinen et al., 2008). The question remains as to what extent physical exercises and what kind can improve chronic MSK pain conditions specifically. Table 2 summarizes selected systematic reviews on various exercise methods as treatment for chronic MSK pain conditions. For fibromyalgia, systematic reviews consistently conclude from low quality evidence that physical activity and/or various forms of strengthening and aerobic exercises improve pain and disability compared with no treatment (Bidonde et al., 2014; Busch et al., 2007; Busch et al., 2013; Lima et al., 2013) or is equal to other forms of treatment (Bidonde et al., 2014; Busch et al., 2013). Strong to moderate quality evidence suggests that movement therapies such as Qigong, Tai Chi and Yoga are more effective than no treatment for fibromyalgia (Lauche et al., 2015; Mist et al., 2013). For chronic neck pain, strong evidence suggests that exercises are more effective than no treatment (Bertozzi et al., 2013; Cheng et al., 2015). For chronic low back pain, strong evidence suggests that exercises facilitating motor control improve pain and disability compared with no treatment (Bystrom et al., 2013; Smith et al., 2014; Wells et al., 2014) and are generally equal to (Sharma and Haider, 2013; Smith et al., 2014; Wells et al., 2013, 2014) or more effective than (Bystrom et al., 2013; Scharrer et al., 2012) other forms of active treatment, although the strength of evidence varies. With respect to other forms of land-based or aquatic exercises, evidence suggests that improvements are more than if no treatment is

offered or equal to active treatment (Lawford et al., 2016; Meng and Yue, 2015; Slade and Keating, 2007; Waller et al., 2009). The quality of the evidence varies, but low quality evidence suggests that, with the exception of one systematic review (Searle et al., 2015), improvements are superior to active treatment (Hayden et al., 2005; Hendrick et al., 2010; Waller et al., 2009).

Table 2. Evidence synthesis for physical activities as treatment, with respect to chronic MSK pain conditions

Source	Primary symptoms	Evidence classification	Intervention	Outcome	Comparison ^a	Quality of evidence ^b
(Bidonde et al., 2014)	FM	SR-Cochrane	aquatic exercise	↓ pain ↓ disability ↓ stiffness ↑ strength	passive	low to moderate
			aquatic exercise	↓ pain ↓ disability ↓ stiffness	= active	very low to low
(Lima et al., 2013)	FM	SR	aquatic physical therapy	↓ symptoms ↓ disability ↑ HRQL	passive	low
(Busch et al., 2013)	FM	SR-Cochrane	resistance exercise	↓ pain ↓ disability ↑ strength	passive	low
			resistance exercise	↑ pain ↓ disability	= active	low
(Nelson, 2015)	FM	SR	strengthening exercise	↓ pain ↑ strength	active	non-graded
(Busch et al., 2007)	FM	SR-Cochrane	aerobic exercise	↓ pain ↑ HRQL	passive	moderate
(Lauche et al., 2015)	FM	SR of SRs	Qigong	↓ disability ↓ symptoms	passive	strong to moderate
			Tai Chi	↓ disability ↑ sleep quality	passive	strong to moderate
			yoga	↓ pain ↑ HRQL ↓ disability	passive	strong to moderate
(Mist et al., 2013)	FM	SR	Qigong	↓ symptoms ↓ disability	passive	strong to moderate
			Tai Chi	↓ symptoms ↓ disability	passive	strong to moderate
(Chan et al., 2012)	FM	SR	Qigong	↑ HRQL	passive	low
(Cheng et al., 2015)	CNP	SR	exercise	↓ pain ↑ HRQL ↓ disability	passive	strong
(Bertozi et al., 2013)	CNP	SR	exercise	↓ pain ↓ disability	passive	strong to moderate
(Bystrom et al., 2013)	CLBP	SR	motor control exercise	↓ pain ↓ disability	passive	strong to moderate
				↓ pain ↓ disability	active	strong to moderate

Table 2. (continued)

Source	Primary symptoms	Evidence classification	Intervention	Outcome	Comparison ^a	Quality of evidence ^b
(Hayden et al., 2005)	CLBP	SR-Cochrane	exercise	↓ pain ↓ disability	active	low
(Searle et al., 2015)	CLBP	SR	exercise	↓ pain	active	strong to moderate
(Slade and Keating, 2007)	CLBP	SR	movement facilitation exercise	↓ pain ↓ disability	passive	strong
				↓ pain ↓ disability	= active	strong
(Smith et al., 2014)	CLBP	SR	stabilization exercise	↓ pain ↓ disability	passive	strong to moderate
				↓ pain ↓ disability	= active	strong to moderate
(Scharrer et al., 2012)	CLBP	SR	Medical exercise therapy	↓ pain ↓ disability	active	strong
(Waller et al., 2009)	CLBP	SR	aquatic exercise	↓ pain ↓ disability	passive	low
				↓ pain ↓ disability	active	low
(Meng and Yue, 2015)	CLBP	SR	aerobic exercise	↓ pain ↓ disability	passive	strong
(Hendrick et al., 2010)	CLBP	SR	walking	↓ pain	active	low
(Lawford et al., 2016)	CLBP	SR	walking	↓ pain ↓ disability ↑HRQL	= active	low
(Wells et al., 2014)	CLBP	SR	Pilates	↓ pain ↓ disability	passive	strong to moderate
				↓ pain ↓ disability	= active	strong to moderate
(Wells et al., 2013)	CLBP	SR of SRs	Pilates	↓ pain ↓ disability	= active or inconclusive	low
(Sharma and Haider, 2013)	CLBP	SR	yoga	↓ pain ↓ disability	passive	non-graded
(Hall et al., 2009)	arthritis	SR	Tai Chi	↓ pain ↓ disability ↑HRQL	passive	low
(Bussing et al., 2012)	CP	SR	yoga	↓ pain ↓ disability	passive	strong to moderate

^a passive comparison includes inactive controls, waiting list controls, placebo, sham, usual care; active comparison includes any form of treatment and exercise methods other than the one investigated. ^b authors assessed quality of evidence according to Cochrane standards, Physiotherapy Evidence Database (PEDro) criteria or other valid and reliable quality control assessment tools, as applicable. FM=fibromyalgia; CNP=chronic neck pain; CLBP=chronic low back pain; CP=chronic pain; SR=systematic review; HRQL=health related quality of life.

Exercise and regular physical activity are considered as prevention for the development of chronic MSK pain and have been shown to activate the central neurons (Sluka et al., 2013). There is compelling evidence suggesting that regular exercise may alter structures in the central nervous system leading to long-term pain reduction (Erickson et al., 2011). Whichever the kind of exercise people with chronic MSK pain choose to practice, it is recommended to: “start low and go slow”, that is, to gradually progress from low intensity exercise to more vigorous as symptoms decline (Hooten et al., 2012; Nelson, 2015; Valkeinen et al., 2008).

In sum, high quality evidence supporting input/output-based physical therapy modalities in the treatment of chronic MSK pain is lacking. The role of physical therapists in interdisciplinary treatment, therefore, must be considered. Based on the evidence, there are mainly two courses of treatment interventions feasible: one is that physical therapists take the role as advisors encouraging evidence-based physical activity and patient education; whereas the other is to actively treat patients according to new evidence of targeting central mechanisms, including physical activity and neuroscience patient education.

The psycho-social component

A recent systematic review on guidelines for the management of chronic back pain concludes that a psychological intervention should be included in the management of chronic back pain. Given the current level of evidence it is not possible to recommend one treatment method over another (Reese and Mittag, 2013). This notion is supported by a recent randomized controlled trial suggesting that cognitive behavior therapy versus acceptance and commitment therapy are equally effective treatments of chronic MSK pain conditions (Wetherell et al., 2011). It is evident that some interdisciplinary programs encompass cognitive behavioral therapy (Busch et al., 2011; Dysvik et al., 2010; Lang et al., 2003; Stein and Miculescu, 2013; Turner-Stokes et al., 2003), while others include mindfulness-based cognitive therapy (Meineche-Schmidt et al., 2012) or psychological counselling (Caby et al., 2010; Gagnon et al., 2009).

Relaxation techniques

Relaxation techniques aim to modify the physiological response system to pain, by reducing muscular tension. In theory, it is assumed that a pain-

tension cycle is responsible for symptoms and that interrupting the cycle by relaxation may be effective (Henschke et al., 2010). Limited evidence has been reported that progressive relaxation is effective for short term pain relief and improved disability in people with chronic low back pain but is not effective for depression (Henschke et al., 2010). Evidence for effectiveness is lacking for fibromyalgia and chronic fatigue syndrome (Meeus et al., 2015). Despite lack of evidence, guidelines suggest that progressive relaxation should be considered for the treatment of patients with chronic MSK pain ("Scottish Intercollegiate Guidelines Network (SIGN)," 2013).

Cognitive behavioral therapy

Cognitive behavioral therapies (Beck et al., 1979) are based on the concept that symptoms and dysfunctional behavior may be mediated through cognition; hence the therapy aims at modifying dysfunctional thinking and beliefs to improve symptoms (Butler et al., 2006). The treatment aims at helping people to decrease maladaptive behaviors and increase adaptive behaviors by identifying and correcting maladaptive thoughts and beliefs about pain and its potential consequences, thereby increasing self-efficacy (Ehde et al., 2014; Williams et al., 2012). Cognitive behavioral therapy is frequently recommended and has been shown to improve coping with pain and to reduce depressed mood as well as less healthcare-seeking behavior among people with fibromyalgia (Bernardy et al., 2010). In patients with orofacial pain, cognitive behavioral therapy has been shown to be effective in terms of improvements in pain reduction, depression, activity interference and disability, on a long-term basis (Aggarwal et al., 2011). The efficacy of cognitive behavior therapy has been shown in patients with chronic low back pain, in reducing pain intensity and pain-related interference, depression, disability and to improve health-related quality of life (Hoffman et al., 2007). Overall, a recent Cochrane systematic review suggests that cognitive behavioral therapy is effective for chronic MSK pain (Williams et al., 2012).

Mindfulness-based therapies

Mindfulness-based therapies have become increasingly popular interventions for chronic MSK pain and other long-term conditions. Mindfulness-based cognitive therapy (MBCT) (Segal et al., 2012) was developed by integrating some aspects of cognitive behavioral therapy and mindfulness-based stress reduction (Kabat-Zinn, 2005). MBCT was initially developed as treatment for

depression and mindfulness-based stress reduction for stress; however, both therapies have been used as treatment options for people with chronic MSK pain conditions (Carlson, 2012). MBCT accentuates the finding that people become aware of and differently relate to their own thoughts, emotions and bodily sensations. The aim is to develop skills that allow disengagement from habitual dysfunctional ruminative thought patterns. People are trained to focus on acceptance, awareness and to be “right here and right now”. It is suspected that participants foster greater willingness to accept each situation as it appears to them and what sometimes may appear as aversive experiences (Larouche et al., 2014; Segal et al., 2012). Likewise, acceptance and commitment therapy is meant to encourage people to reevaluate the relationship with their own experiences and to learn to distinguish between themselves and their thoughts (Veehof et al., 2011).

Mindfulness-based interventions are effective in diminishing symptoms among people with fibromyalgia by reducing perceived stress (Cash et al., 2015), reducing symptom severity (Cash et al., 2015; Grossman et al., 2007), improving well-being and quality of life (Grossman et al., 2007), improving coping with pain (Grossman et al., 2007), and alleviating depressive symptoms (Sephton et al., 2007), although results may be controversial (Schmidt et al., 2011). Among people with chronic MSK pain conditions, mindfulness-based interventions alleviate disability and decrease emotional distress (McCracken et al., 2007; Rosenzweig et al., 2010; Vowles et al., 2009), and reduce pain intensity (Garland et al., 2012; Reiner et al., 2013; Rosenzweig et al., 2010; Wong et al., 2011). People with chronic low back pain report improved physical disability, sleep, attention, and quality of life, as well as improved pain and pain acceptance following mindfulness-based intervention (Esmer et al., 2010; Morone et al., 2008a; Morone et al., 2008b; Morone et al., 2009). However, a recent systematic review of the literature suggests that evidence for effectiveness of mindfulness-based interventions for low back pain is inconclusive (Cramer et al., 2012). On the other hand, mindfulness-based interventions have been shown to be effective for various other symptoms often accompanying chronic MSK pain such as chronic insomnia (Ong et al., 2014) and irritable bowel syndrome (Garland et al., 2012).

Mechanisms and conclusion

It appears that cognitive behavior therapy results in improvements that are correlated with increased activation within the prefrontal cortex area,

suggesting executive control modulating dysfunctional activity in the brain (Ehde et al., 2014; Jensen et al., 2012). Similar mechanisms are warranted for mindfulness-based therapies (Chiesa and Serretti, 2010; Day et al., 2014; Hofmann et al., 2010; Kerr et al., 2013; Santarnecchi et al., 2014). It is therefore proposed that these psychologically based interventions are an important adjunct to chronic MSK pain management and that they harmonize well with our present knowledge on pain neuro-physiology and neuroplasticity.

The educational component

Most clinical guidelines agree that return to former daily activities and to physical activity is one central goal in patient education in rehabilitation (Reese and Mittag, 2013). As knowledge on pain neurophysiology has evolved during recent decades, so has the content of patient educational programs for people with chronic MSK pain.

Back School based patient education

The Back School education for prevention and as a treatment for low back pain was initially developed in Sweden in 1969. The concept was that low back pain was the result of mechanical stress. It was considered important to educate people on the anatomy and physiology of spinal structures and to teach load reducing methods in material handling. The main ingredients in Back Schools were therefore ergonomic counselling and information on ways to avoid back pain and mechanical stress (Forsell, 1981). In the early days of Back School education a prospective study showed lessened disability and pain compared with exercises only (Klaber Moffett et al., 1986). Some programs emphasized exercises in addition to education and results from such studies show, for example, significant reduction in recurrence and sick leave (Lonn et al., 1999). Systematic reviews at that time showed that Back School education had some effects in pain reduction and functional improvement (Heymans et al., 2004, 2005; Maier-Riehle and Harter, 2001), but more as part of more comprehensive rehabilitation programs (Di Fabio, 1995). Back School education changed with augmented knowledge in the years to come. This would mainly be related to the addition of cognitive concepts such as fear-avoidance and catastrophizing, and as such develop towards a bio-psycho-social approach (Brox et al., 2008a, 2008b). Furthermore, the advice to stay active has also been included and shown to

be effective (Liddle et al., 2007).

Pain neurophysiology patient education

With new evidence on the etiology and mechanisms of chronic MSK pain, patient education has evolved and advances are shown in recent literature. Pain neurophysiology education (PNE) is now recognized as an important piece of the puzzle and dates back to 2002 (Moseley, 2002). It is supposed to help people to re-conceptualize their pain experiences as less threatening (Moseley et al., 2004; Robinson et al., 2015; Van Oosterwijck et al., 2011). PNE, in combination with manual therapy and specific exercises (Moseley, 2002) or motor control exercises (Moseley, 2003) has been shown to be effective as compared with usual care in terms of pain intensity and disability. PNE further helps people to reverse maladaptive attitudes and beliefs about pain, reduces catastrophizing and improves physical performance (Moseley et al., 2004). In a recent systematic review, the authors concluded that PNE is a promising adjunct to chronic low back pain management and it is suggested that this approach has a positive effect on pain and disability related to physical, psychological and social functioning (Clarke et al., 2011). PNE has been shown to be effective in various chronic MSK pain conditions and is therefore not limited to low back pain. It has been shown, for example, that PNE improves health status and endogenous pain inhibition in fibromyalgia (Van Oosterwijck et al., 2013). PNE improves pain behavior and pain-free movement performance in people with chronic whiplash associated disorder (Van Oosterwijck et al., 2011). PNE improves pain beliefs among people with chronic fatigue syndrome (Meeus et al., 2010). PNE has positive effects on disability, catastrophizing, physical performance, and pain among people with chronic MSK pain conditions (Louw et al., 2011).

In sum, patient education has developed through the years with new knowledge on pain neurophysiology. Educating the patient on underlying mechanisms and strategies to overcome pain-related fear is essential in chronic MSK pain management.

Collaborative care

There is increasing interest and demands in the application of collaborative care in various health care settings (Ehde et al., 2014). It is proposed that collaboration in health care delivery encompasses a model of care management as well as system support with the aim of educating the patient

and integrating multiple health professionals (Katon et al., 1999). For successful collaborative treatment, a team approach is used and one major element in such models is to include dedicated staff to coordinate, support and educate the individual. The team should utilize reliable and systematic follow-ups and consistently use evidence-based treatment practices (Hooten et al., 2013). Collaborative practice is both team-based and patient centered, maximizing the strengths and skills of each partner to increase the quality of patient care (Hoffman et al., 2008). WHO now recognizes the importance of collaborative health care services, which is shown by the emphasis on inter-professional education within schools of health sciences for enhanced health care services. WHO defines collaborative practice as health care provided by multiple health professionals from different backgrounds. Together they offer comprehensive services by integrating the patients, their families, caregivers and communities to provide high quality health care services across clinical settings ("World Health Organization," 2010).

In relation to collaborative care, various terminology and definitions are reflected in the literature but most use the terms "multimodal", "inter-disciplinary", "multidisciplinary" and "inter-professional" interchangeably. Team-based health care can be considered as care that is delivered by small work groups created for a patient or a group of patients. The team shares a collective identity and the responsibility for patient care and should be recognized by others and by themselves ("Interprofessional Education Collaborative Expert Panel," 2011). The terms "multidisciplinary" and "inter-disciplinary" indicate that professionals from different disciplines are involved with the task in hand or a given activity but may perhaps not interact. On the other hand, the term "inter-professional" indicates that teamwork between professionals from different disciplines is interactive and that they rely on each other to accomplish a shared goal (Atwal and Caldwell, 2006). For the purpose of this thesis the terms "multimodal", "multidisciplinary", "inter-disciplinary" and "inter-professional" are used interchangeably. They all refer to integrative cooperation between various health care professionals from different fields of practice, for patient-centered health care delivery, working with a common purpose, mutual respect and commitment.

Successful team-work is utterly important in interdisciplinary rehabilitation for a multidimensional condition like chronic MSK pain. A bio-psycho-social health care team could be composed of various combinations of physicians, physical therapists, chiropractors, dieticians, pharmacists, recreational therapists, vocational counsellors, psychologists, psychiatric nurses, psychiatrists, physiatrists, or pain management physicians (Cassidy et al.,

2007). The inclusion of a professional would depend on several factors in addition to individual patient needs. For example, the team may depend on institutional human resources, budget, cultural preferences and local health care policy.

It should be kept in mind that the bio-psycho-social concept is a reminder to all health care providers to consider each patient's health status holistically. The patient may or may not need care from a large team of health care professionals but it is perhaps not for any one professional to decide, particularly in a multidimensional condition like chronic MSK pain.

1.8 Study motivation

It is clear that extensive research exists on the burden of illness of chronic MSK pain worldwide and some on the Icelandic population as well. There are a few factors that may influence the prevalence rate and impact of chronic MSK pain in Iceland specifically. Iceland has for the last six years been ranked as the most peaceful country in the world with low rates of criminality, domestic and international conflicts ("Global Peace Index," 2016). Thus, Iceland is considered a safe place to live in and the threat of violence is low. Iceland is ranked the third happiest country in the world (Helliwell et al., 2016), twelfth with respect to GDP per capita in 2015 ("GDP Per Capita Ranking 2015," 2016) and is the fifth in the number of providing skilled health professionals ("World Health Statistics 2016," 2016). Therefore, Icelanders live in a safe place, with good access to health care services, the standard of living is generally high and people seem to be happy. On the other hand, Icelanders live under the threat of natural disasters including earthquakes, volcanic eruptions, violent winds, snow storms and avalanches. Furthermore, Icelanders work long hours, longer than any other Nordic country. The average annual hours worked per worker in Iceland from 2000 to 2015 is 1,928, whereas the next most industrious country, Finland, worked 1,683 hours, and the Norwegians worked the lowest number of hours per year, or 1,421 ("Average annual hours actually worked per worker," 2016). Thus, it is not clear if chronic MSK pain has a similar prevalence and burden of illness in Iceland as in other countries with apparently a similar culture. Research on the situation in Iceland specifically is therefore essential.

According to the Icelandic Act on patients' rights no. 74 from 1997 and last updated the 1st of January 2015, each citizen has the right to the best health care services available at the time. Patients are responsible for their

own health in accordance with their own condition. It is further stated that patients are to be active participants in their own treatment, which they have agreed to ("Act on patients' rights no. 74 from 1997," 2015). This legislation is in line with the Montréal Declaration that pain management is a fundamental human right. It is therefore clear that health care authorities have the obligation to provide high quality pain management services for anyone in need.

In Iceland, interdisciplinary pain management programs are provided in a few rehabilitation facilities. A search of the international literature uncovered only one journal article on the effectiveness of chronic MSK pain management in Iceland (Olason, 2004). The data provided for this study was collected in 1997-1999 from an inpatient interdisciplinary pain management program offered at the Reykjalundur Rehabilitation Clinic in Iceland. It was concluded that patients significantly improved anxiety/depression and reduced pain intensity following the 7-week program and that improvements were sustained one year later. There was no control group in this study but there are signs that controlled research may be in the pipeline and perhaps in the process of publication ("Reykjalundur," 2009).

To the best of our knowledge, no interdisciplinary pain management programs exist within the primary health care in Iceland. Thus, Icelanders with chronic MSK pain conditions are probably arbitrarily assigned to single-disciplinary treatments, and perhaps at a later stage, to interdisciplinary pain management programs in rehabilitation facilities.

Our study was driven by this observed lack of research in the field in Iceland. The research for this thesis was divided into two parts: firstly, a nationwide population-based study, and secondly, single center effectiveness study. We anticipate that our study results will, on the one hand, shed light on the prevalence of chronic MSK pain conditions in Icelandic society together with the impact chronic MSK pain may have on physical activities, daily life and mental co-morbidity. On the other hand, we expect to provide data on the effectiveness of specialized interdisciplinary pain management programs in Iceland.

In line with the above, we believe that the research presented here is an important contribution to the literature and to the Icelandic community. It may influence health care authorities to consider the importance of well-established pain management at all stages within the health care system. It may further influence authorities responsible for educating health care

professionals to reinforce interdisciplinary health care education in the field of chronic MSK pain management.

2 Aims

Even though research on chronic MSK pain conditions has received considerable attention in the peer reviewed literature, not much is known about the condition – neither about public health relevance nor the effectiveness of treatments - in Iceland. Therefore, our overall objective of the studies that constitute the foundation of this thesis was to shed light on, and to bridge the apparent knowledge gap with respect to, chronic MSK pain and pain management among the Icelandic people. For this purpose, we used two sets of data, a population based data set and a clinical data set.

2.1 Specific aims of study I

The aim of study I was to investigate the point prevalence of self-reported chronic MSK pain, among adult men and women of all ages, in Iceland. The aim was further to investigate functional limitations among people experiencing chronic MSK pain conditions. The specific hypothesis was that individuals with chronic MSK pain experience physical symptoms and limitations in daily life to a greater extent than people without the condition.

2.2 Specific aims of study II

The aim of study II was to investigate mental health indicators, including depressive symptoms, sleep disruption, stress, well-being and quality of life, among individuals with self-reported chronic MSK pain. Our hypothesis was that people with chronic MSK pain are subject to a higher risk of mental health symptoms in comparison to people without this condition.

2.3 Specific aims of study III

The aim of study III was to compare the effectiveness of two multidisciplinary bio-psycho-social rehabilitation interventions for chronic MSK pain as compared with waiting list controls. One intervention was a traditional multidisciplinary pain management program (TMP) including exercises, traditional Back School and relaxation techniques. The other intervention added neuroscience patient education and mindfulness-based cognitive therapy (NEM), including neuroscience patient education with reference to behavioral patterns and catastrophic thought processes. Our hypothesis was

that both 4-week interventions would result in improvement in health-related quality of life (HRQL) and diminished pain intensity in comparison to waiting list controls receiving no treatment. We proposed that both intervention groups would show improvements while significantly greater improvement would be achieved among individuals receiving the NEM intervention.

2.4 Specific aims of study IV

This study is a follow-up of study III with the primary aim to assess the 6-months' effectiveness of the two multidisciplinary bio-psycho-social rehabilitation interventions for chronic MSK pain, TMP versus NEM. In this study, the primary endpoint was the change in quality of life and pain intensity measures from baseline to 6-months after the intervention ended, in total seven months. We hypothesized that both groups would experience improved HRQL and reduced pain intensity, expecting that significantly greater improvement would be observed among those receiving the NEM intervention. A secondary aim of this study was to compare the baseline characteristics of those who are lost to follow-up to those who completed treatment and provided 6-months of follow-up data. We expected no baseline differences.

3 Materials and methods

3.1 Source of data and study settings

Studies I and II

For the observational studies I and II we used cross-sectional data retrieved from a general health survey; Health and well-being 2007 ("Survey on Health and Well-being among Icelanders 2007," 2007). The survey was conducted in December 2007 by The Public Health Institute in Iceland and used a stratified random sample of 9,807 Icelanders aged 18-79 years. This sample was obtained from the national register of the total population, which is maintained by Statistics Iceland. This health survey used mailed questionnaires. The responders totaled of 5,906 individuals, yielding a response rate of 60.3%. The survey was processed according to a validated methodology with the purpose of maximizing the response rate (Dillman et al., 1991), including adaptations approved in advance by an ethics committee. The stratification of the sample was not reflective of the population, neither in terms of age nor residential area. A higher proportion of individuals in the sample were of higher ages compared with the general population and a higher proportion of individuals were from the countryside areas. In studies I and II we compared two cohorts, people with chronic MSK pain versus those without the condition, across sociodemographic characteristics and various health-related factors.

Studies III and IV

The longitudinal data for these two observational studies was retrieved from the HNLFI Rehabilitation Clinic in Iceland in 2001-2010, using patient records and mailed questionnaires. The rehabilitation clinic serves as an inpatient institution on a national basis and provides various rehabilitation services. The TMP approach was offered from 2001 through 2005. The NEM intervention was introduced in January 2006 with the cessation of the TMP approach. The change was made in order to incorporate mindfulness-based cognitive therapy and neuroscience patient education. In study III we compared potential immediate improvements among three cohorts: NEM intervention participants who received treatment from 2006 to 2009; TMP participants who received treatment from 2001 through 2005; and a reference

cohort of individuals on a waiting list for admission to the rehabilitation clinic. In study IV we compared potential long-term improvements among two cohorts: the NEM intervention versus the TMP intervention. We further compared the baseline characteristics among responders and non-responders at 6-months' follow-up.

3.2 Population

Studies I and II

The questionnaire includes a question on various chronic conditions and diseases. It was initially designed in accordance with methodology recommended by WHO (Buratta et al., 2003) on interviewing processes although adaptations were made to fulfil requirements for a self-administered questionnaire. The question is comprised a total of 20 items including chronic back pain, chronic neck symptoms and fibromyalgia. The question is stated thus:

Have you ever had any of the following diseases or symptoms?

Response options are:

Yes, have now

Have had before, but not right now

No, have never had

Individuals currently having one or more of those three conditions met our criteria for current chronic musculoskeletal pain disorder (C-CPD). The cohort of C-CPD was created by merging answers to those three questions. The reference cohort (non-chronic musculoskeletal pain disorder [N-CPD]) was generated by merging all those who reported no chronic low back pain, no chronic neck symptoms nor fibromyalgia and those who reported they had had one or more of these three conditions earlier in life.

Studies III and IV

The participating individuals in studies III and IV were 234 females who had had chronic MSK pain (IASP, 1986) for at least six months when admitted to the rehabilitation clinic. All participants agreed to join an inpatient group-based program for one month and refrain from other treatment modalities. Intervention group allocation was based on the time of admission, since the

two interventions were not offered simultaneously. Therefore, the group allocation was non-randomized. The reference group was recruited from women on a waiting list for admission to the rehabilitation clinic in 2008. The eligibility criteria were set at any diagnosis relating to chronic musculoskeletal condition and age 18-70 years. Every fifth eligible woman applying for admission received an information letter and was invited to participate.

3.3 Intervention

Studies III and IV

Both interventions were multidisciplinary group-based programs led by an inter-professional team devoted to pain management; physical therapists, a psychologist, a psychiatric nurse, a recreational therapist, a rehabilitation physician, and a medical massage therapist. The team had access to a nutritionist for counselling. Other professionals were involved with various group activities. These highly qualified professionals adhered to the proposed treatment approach. The work was coordinated through weekly meetings during the 4-week interventions.

Physical therapy sessions were focused on assessment and consultancy on physical activities and exercises to optimize health benefits with respect to pain control and movement as treatment (Pedersen and Saltin, 2006; Sundberg et al., 2010).

Physical therapists consulted on self-management strategies, coping and fear-avoidance in relation to physical activity. Patients were specifically instructed on strategies to overcome limitations in a positive manner. Figure 6 shows a graph that physical therapists used in order to explain how one can increase awareness of body signals and to respect those with the aim of increasing activity tolerance with less pain.

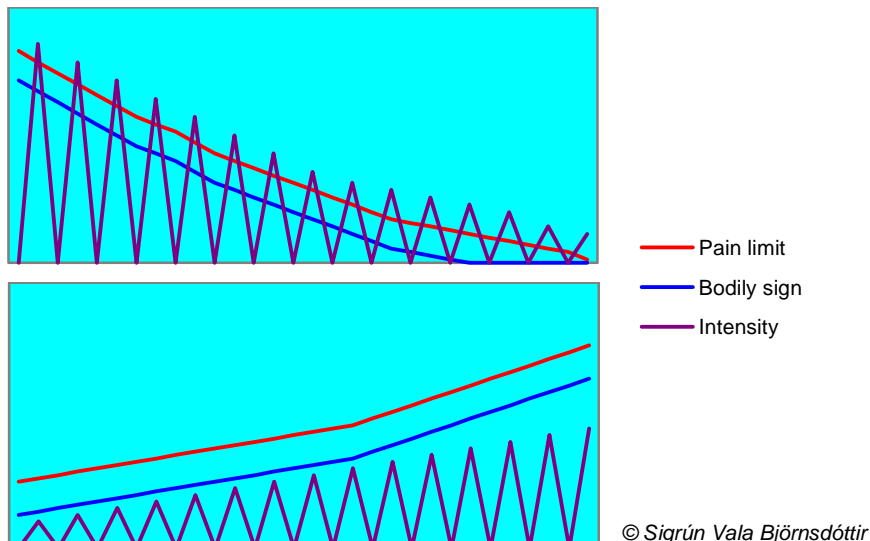


Figure 6. Explaining pain limits and physical activity

Top: The schematic demonstrates physical deconditioning as a result of provoking pain when performing an activity. *Bottom:* Physical reconditioning as a result of “listening to the bodily signs” and to respect the limits by avoiding provoking pain. Bodily signs are explained as those that “tell” the person that pain is emerging. The signs can relate to altered movement patterns, fatigue or whatever each person perceives as a signal that pain may be on the way.

The psychologist and the psychiatric nurse also emphasized fear-avoidance and health promotion by consulting on coping strategies and overcoming limitations in daily life. The physician participated in the initial assessment procedure and patient education and led weekly discussion sessions. Any pharmaceutical adaptations were checked on and prescribed by the physician.

Tai Chi based body awareness sessions were incorporated in both intervention programs. Physical training in the TMP intervention included traditional strength, flexibility and aerobic exercises while the NEM intervention emphasized motor control with reference to neuroscience patient education and mindfulness-based cognitive therapy (Segal et al., 2012). The characteristics of the two intervention programs are listed in Table 1, Paper III.

Traditional Back School versus neuroscience emphasized patient education

The 12 sessions' traditional Back School program included lectures and exercises. The emphasis was on enhancing proper body mechanics through exercises. The Back School program was in line with other programs described earlier (Forssell, 1981; Klaber Moffett et al., 1986; Schenk et al., 1996). The neuroscience patient education (Louw et al., 2011) was included in an extensive program called "Health and Activities" (see Appendix, Paper III) with termination of the former Back School. Throughout this modern educational program the knowledge imparted was referred to behavioral patterns known to accompany chronic MSK pain, including catastrophic thought processes and fear avoidance beliefs and behavior.

Relaxation versus mindfulness-based cognitive therapy

In the TMP intervention, the relaxation sessions were generally led by nurses on call. The methods used were modified versions of the Jacobson's progressive muscle relaxation technique (Weber et al., 2002). The MBCT (Segal et al., 2012) approach used for the NEM intervention included two-hour sessions two times a week during the 4-week period. The MBCT program includes extensive homework for participants.

3.4 Outcome measures

Studies I and II

The survey Health and Well-being in Iceland 2007 was composed of 98 questions which generally were based on recommended guidelines (Buratta et al., 2003) and validated measurements. However, some measures in this questionnaire were uniquely designed for this survey and have not been psychometrically tested. On the other hand, the survey was initially tested on university students and eight persons were selected for cognitive interviewing. These people gave comments that were used to adapt the questionnaire and to ensure suitable wording for the Icelandic population. This survey included extensive data on background and socioeconomic factors such as educational level, financial status and societal participation

among the respondents.

In both studies the research team treated variables for missing values if imputation was likely to positively affect systematic error due to participants' answering styles (Jónsson et al., 2011). Background and potential confounding variables were categorized for facilitating analysis. Age was treated throughout analyses as in the stratified sampling with the same six categories (18-29, 30-39, 40-49, 50-59, 60-69 and 70-79 years). Outcome variables were categorized as binary variables.

Measures for study I

In study I we used a single question measuring physical health which has been used previously (Hays et al., 2009; Vilhjálmsson et al., 1998). This question, in addition to three other physical measures on the Patient-Reported Outcome Measurement Information System (PROMIS), adequately evaluates global physical health (Hays et al., 2009).

The physical functioning domain of the Medical Outcome Study-short form (MOS SF-36) was used to measure daily activities. The MOS SF-36 measures quality of life and is a standardized generic tool (Ware, 2000). The MOS SF-36 has been used to measure quality of life in numerous peer reviewed publications (Garratt et al., 2002) and reliability and validity has been reported extensively (Jenkinson et al., 1994; McHorney et al., 1994; Ware, 2000).

The International Physical Activity Questionnaire (IPAQ) was used to measure physical activity levels (Hagströmer et al., 2006). In this study a self-administered short form version was used as it is generally recommended for population monitoring purposes (Craig et al., 2003) and reliability and validity have been reported (van der Ploeg et al., 2010). All variables were treated in accordance with the IPAQ guidelines from 2005 to calculate energy cost in minutes per week or metabolic equivalent of task (MET) ("International Physical Activity Questionnaire," 2005). The continuous variable was categorized to low, moderate and high intensity of physical activity. Moderate and high categories were merged to analyze those who did not fulfill the recommendations for physical activity in terms of general health benefits (Haskell et al., 2007; Strong et al., 2005). In addition, three questions including; walking, moderate, and vigorous activities were used to analyze those individuals who reported physical activity of less than ten minutes. This

is in accordance with recommendations stating that episodes of at least ten minutes should be counted to achieve health benefits (Haskell et al., 2007).

For analyses of work-related physical demands, we used a question to obtain sedentary as opposed to physically demanding work. We also used questions on active transportation (the usage of one's own physical power) to and from work.

Measures for study II

In this study we used a single question rated on a 4-point scale to measure general mental health and which has been used in previous studies with similar wording (Hays et al., 2009; Vilhjálmsón, 2007; Vilhjálmsón et al., 1998): *In general, how would you rate your mental health?* In this study the response options were 4=very good to 1=bad. This single item measure, together with three other mental measures on PROMIS, assesses global mental health satisfactorily (Hays et al., 2009). The four-item scale yields an internal consistency reliability coefficient of 0.86 and correlates well ($r=0.53$) with the EuroQol EQ-5D preference-based index score, a comprehensive measure on mental health (Hays et al., 2009). The variable was dichotomized as very good/good contrasting with relatively bad/bad.

A single standardized measure of happiness originated from the European Social Survey and is stated as follows: *Taking all things together, how happy would you say you are?* Response options are from extremely unhappy to extremely happy. The reliability and validity of this single item measure on happiness with an 11-point scale has been reported. The test-retest reliability proved to be 0.86 when measured one week apart. The concurrent validity was tested with Pearson's correlations with the Oxford Happiness Inventory ($r=0.56-0.70$) and the Satisfaction with Life Scale (SWL scale; $r=0.45-0.63$) (Abdel-Khalek, 2006). For analyses, answers 1-5 were rated as unhappy and 6-10 as happy.

Self-designed questions related to feeling stressed at work or at home were originally on a five-point scale but were recoded to rather much/much affected or neutral/rather little/little affected, giving responses as feeling affected or not. Questions on mental health affecting daily living were dichotomized; affected the past year versus not affected or affected over a year ago. A question on medication was also on a three-point scale. The answers yes, the past two weeks and yes, over two weeks ago were merged giving the outcome using medication or not. The variable sleeping

disturbances was retrieved from a question on how many hours were spent sleeping per night. The respondent could answer less than 5 hours, around 6 hours, 7, 8, 9, 10 or over ten hours. The transformed variable yielded a normal sleep of 7-8 hours and abnormal sleep of more or less than 7-8 hours.

Measures on quality of life and well-being were generated from the Short Warwick-Edinburgh Mental Well-being Scale (SWEMWBS). The scale measures positive aspects of mental health and well-being and was originally a 14-item scale but following Rasch analysis the short version of 7-items was recommended (Stewart-Brown et al., 2009). The SWEMWBS scale has been proven reliable (intraclass correlation coefficient [ICC] =0.83) in terms of test-retest reliability. The scale has been reported valid in comparison to other well-being scales such as the Scale of Psychological Well-being ($r=0.74$), the Short Depression Happiness Scale ($r=0.73$), the WHO-5 ($r=0.77$) and the SWL scale ($r=0.73$) (Tennant et al., 2007). There are no cut-off points available for this scale since it was not specifically designed to measure high or low positive mental health. The total scores range between seven and 35, with a higher score representing better well-being. The raw scores were transformed to metric scores in accordance with published data from a linear transformation (Stewart-Brown et al., 2009). The mean of the total sample was calculated and the score representing one standard deviation (SD) under the mean was selected as the reference score, yielding approximately 16% of the total sample reporting poor well-being. Our calculations showed a mean score of 25.04 (SD=4.21) yielding <20.83 as a reference score for poor well-being. A dichotomous variable was then created with response options of poor or good well-being. The Cronbach's alpha reliability for the SWEMWBS was 0.86 in our sample.

Measures on quality of life and satisfaction with life were derived from the SWL scale which has been shown to be reliable with a mean Cronbach's alpha coefficient of 0.78 through meta-analysis of sixty-two articles (Vassar, 2008). The convergent validity has been confirmed with comparison to other measures of subjective well-being ($r=0.47-0.75$) (Diener et al., 1985). The total scores of the SWL scale range between 5 and 35, with a score of 20 representing a neutral point where respondents are neither satisfied nor dissatisfied. It has been suggested that scores between 5 and 9 indicate extreme dissatisfaction with life and scores above 30 indicate high satisfaction. It has further been noted that mean scores across samples tend to range between 23 and 28, indicating slightly satisfied to satisfied levels of satisfaction with life (Pavot and Diener, 1993). We used the same procedure for the SWL scale as for SWEMWBS to determine a reference score. Our

analyses reveal a mean score of 26.19 (SD=5.62), determining ≤ 20 as a reference score for dissatisfaction with life. A dichotomous variable was created with response options of dissatisfaction versus moderate to high satisfaction with life. The Cronbach's alpha for the SWL scale was 0.91 in our sample.

In this study the level of stress was measured with the four item Perceived Stress Scale (PSS) (Cohen et al., 1983) where the Cronbach's alpha for internal consistency has been reported at 0.67 (Leung et al., 2010). The coefficient alpha reliability of the PSS-10 scale was reported as 0.84-0.86 and two day test-retest reliability 0.85. The correlation with the Stress Measures with Depressive Symptomatology was $r=0.65-0.76$ (Cohen et al., 1983). The 4-item PSS scale was created based on psychometric principles as its usage has been recommended on a practical basis such as when included with other measures. Normative data is available from a national area-probability sample from the adult non-institutionalized population of the US, where the mean score for females is 4.7 (+/-3.1) and 4.2 (+/-2.8) for males (Cohen and Williamson, 1988). To calculate the total score, the scaling on two positively stated questions was reversed. The PSS scoring ranges between zero and 16 but it is not a diagnostic tool and no cut-off points are available. Therefore, we used the same method as described for SWEMWBS. Our calculations confirmed a mean score of 4.24 (SD=2.89), indicating ≥ 7 as the reference score for stress. The Cronbach's alpha for the PSS was 0.68 in our sample.

The WHO-5 well-being index has been used to measure levels of depressive symptoms. The scale's internal consistency has been reported as 0.91 tested with Cronbach's alpha statistics, and the scale correlates well with The Patient Health Questionnaire ($r=-0.73$) and The Hospital Anxiety and Depression Scale ($r=-0.76$). The cut-off point for screening or diagnosing major depressive disorder with WHO-5 has been suggested as ≤ 7 with respect to maximal sensitivity and a specificity of at least 75% as well as with the maximal Youden Index (sensitivity + specificity -1). The cut-off points for screening any depressive disorder are recommended as ≤ 9 (maximal sensitivity and a specificity of $\geq 75\%$) and ≤ 7 (maximal Youden Index) (Lowe et al., 2004). However, conventional recommendations state that a score of less than 13 should indicate a need for specific testing for depression ("World Health Organization info package," 1998); therefore, for the purpose of this study the standard cut-off score of less than 13 was used. The total score was calculated and the variable was recoded to obtain a binary variable

yielding potential depression or no depression. The Cronbach's alpha for the WHO-5 well-being index was 0.82 in our sample.

A 4-item questionnaire measuring sleep disruption was designed specifically for this survey. The measure is from a 5-point scale (from never to every night) and the questions are as follows:

How often during the past three months have you experienced:

- a. Difficulties falling asleep?*
- b. Waking up after falling asleep and having difficulties falling asleep again?*
- c. Feeling well rested following a good night's sleep?*
- d. Waking up several times during the night?*

The scaling on the positive question was reversed to obtain a summary score. We selected the score that represents one SD over the mean as the reference score. Our calculations demonstrated a mean score of 10.0 (SD=3.07) yielding >13 as the reference score for sleep disruption. The questionnaire yielded a Cronbach's alpha of 0.73 in our sample.

Measures for studies III and IV

All outcome measures for the intervention groups were assessed at admission, at discharge (after 31 days) and 6 months after discharge. At admission and at discharge the participants were invited to fill in the questionnaires and other forms and return them shortly to staff members. For the follow-up data, participants received a mailed questionnaire six months after discharge and a reminder one week after the initial mailing. Assistance was available when needed. Two sets of questionnaires were mailed to the reference individuals. They were instructed to fill in and return the first questionnaire promptly and the second questionnaire in 31 days. Figure 7 demonstrates the timeline for assessment points.

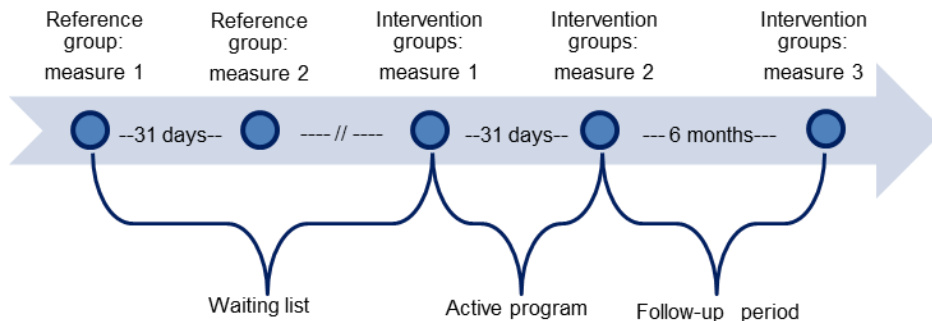


Figure 7. Timeline for assessment points in studies III and IV

Pain intensity was assessed on a commonly used 100mm visual analogue scale (VAS). Test-retest reliability of the VAS scale has been confirmed using five minutes ($r=0.95$; $ICC=0.96$) and 24 hours apart ($r=0.95$) when rating memory from initial marking, and no significant difference was observed when rating pain distant in time (5 min and 24 h) (Revill et al., 1976; Sindhu et al., 2011). Concurrent validity was confirmed by comparison of VAS on paper and a digital version of the VAS scale ($r=0.97$) as well as VAS on paper and NRS ($r=0.84$) when reporting pain before performing a pain inducing task. After performing a pain inducing task the Pearson correlation coefficients were 0.95 and 0.93, respectively. The VAS on paper was considered the most accurate scale of these three but participants consistently scored less pain on the VAS than on the NRS (Sindhu et al., 2011). Good correlation has been reported between VAS and NRS when the scales were completed along with other questions ($r=0.90$) (Downie et al., 1978).

For the purpose of this study The Icelandic Quality of Life (IQL) questionnaire was used (Helgason et al., 1997). It is a generic measure of HRQL including 32 questions addressing 12 domains; general health, concentration, depression, social functioning, financial status, energy, anxiety, physical health, pain, self-control, sleep, and general well-being. The instrument also offers a summary score for HRQL. The mean summary score for each domain is 50 and the standard deviation is 10. Lower scores always indicate poorer HRQL for the domain in question. Psychometric properties have been tested on various patient populations. The coefficient alpha reliability for the total scale has been reported as 0.95 and internal consistency for the subscales ranging from 0.59-0.88. Test-retest reliability

eight weeks apart has been reported as $r=0.76$ for the whole questionnaire (Björnsson et al., 1997). Reliability and validity have been confirmed in other studies (Helgason et al., 2000a; Helgason et al., 2000b). In our sample the Cronbach's alpha for the total questionnaire was 0.93 and 0.94 pre- and post-test, respectively.

We obtained information on employment status, sick leave, disability status and educational level through questionnaires. We used patient records at admission to obtain information on number of diagnoses, analgesic medication, and measurements of height (in cm) and weight (in kilograms). We calculated body mass index (BMI) as $\text{weight (Kg)}/\text{height}^2 \text{ (m}^2\text{)}$. The follow-up data included, in addition, questions relating to physical activity, relaxation and/or meditation practices following discharge.

3.5 Data analysis

Studies I and II

Weighted data analyses were performed in order to adjust the sample's raw data to reflect the Icelandic population. Therefore, population estimates were based on weighted data accounting for overrepresentation of older age groups in the sample and adjusting for uneven response rate by gender. Prevalence estimates were calculated for chronic MSK pain conditions as well as separately for each of the three conditions - chronic low back pain, chronic neck symptoms and fibromyalgia.

For comparisons related to physical symptoms, daily activities and mental health indicators among people with current chronic MSK pain versus those without, logistic regression analyses were utilized to compute odds ratios (OR) with 95% confidence intervals (95% CI). Further, to contrast symptoms of individuals with current chronic back pain (C-CBP) and those who successfully recovered from the condition (P-CBP), we also applied logistic regression. We estimated the odds of symptoms among people with past chronic back pain with those who never had experienced chronic back pain as the reference. We further ran linear regression models, comparing the means of mental health indicators on a continuous scale between people with and without chronic MSK pain conditions. We observed similar results as with logistic regression models (data not shown).

In order to identify the best regression models, including potential confounding variables, we applied backward selection. The variables

included to identify the best regression model were: age, gender and marital status, number of children, residential area, monthly income, educational level, BMI, and smoking. The appointed model incorporated gender, age, monthly income, BMI, smoking and educational level. In addition, the final model included the variable residence for weighting purposes. The variable gender was excluded due to gender stratification in further analyses. Cronbach's alpha statistics were calculated for measurement scales to determine internal consistency for each scale in our sample.

Studies III and IV

For a priori power assessment for sample size estimation, we used the G*Power software version 3.0.10 (Heinrich Heine Universität Düsseldorf, Germany). For a power of 80% to declare a difference between groups and estimated effect size of 0.25 at an alpha-level of 0.05 we calculated that 53 participants in each group were needed to adequately power the study.

To assess group differences in mean changes in pain intensity and HRQL scores we used analysis of variance (ANOVA) contrasting baseline to the end of intervention and paired samples t-tests contrasting baseline to the 6-months' follow-up.

To assess if assumptions of variance homogeneity were violated we calculated F_{\max} ratio, i.e. the ratio of the largest cell variance to the smallest, for all outcome measures. Considering that our sample sizes were relatively equal (the largest to the smallest cell size ratio in study III was 2.1 and 1.3 in study IV, and therefore within a ratio of 4 to 1) we assumed homogeneity of variances if the observed ratio was less than 10 (Tabachnick and Fidell, 2001). To compare any differences between the three groups we used Tukey's HSD (honestly significant difference) post hoc comparisons, where applicable (Daniel, 2005).

For subgroup analyses the summary scores for HRQL were stratified with respect to background variables. Potential differences between TMP and NEM groups in study outcomes were assessed using linear regression models adjusted for age, the variable in question at baseline, medication use, number of diagnosis, and employment status.

Data was analyzed to assess potential baseline differences between respondents and non-respondents at the 6-months' follow-up. To assess differences in proportions, Pearson Chi Squared statistics for categorical variables were used. To assess differences in overall means, as well as

stratified by intervention, independent sample t-tests for continuous variables were used.

We ran backward stepwise logistic regression analyses to predict for potential non-response at 6 months. We used response (yes=1; no=0) as the dependent variable and change scores for all outcome measures as the independent variables. Change scores were calculated as differences in outcome measures from baseline to the end of the intervention period. Included in the models were age, BMI, employment status, medication use, number of diagnoses, and intervention method as covariates. To compare the intervention groups with respect to physical activity and using relaxation techniques and/or meditation after intervention completed, we used Chi Squared statistics.

Results are communicated in terms of changes in mean scores for each outcome measure and a p-value equal or less than 0.05 was considered statistically significant.

In all studies we used the software SPSS-18-20 (PASW statistics 18-20, SPSS Inc, Chicago, IL) for statistical analyses.

3.6 Ethical clearance

Studies I and II

The original study protocol was accepted by the Icelandic Bioethics Committee and received the approval number 07-081-V1. For these specific studies an announcement was sent to the Committee stating the usage of the data and names of the researchers.

Studies III and IV

All participants in the studies signed an informed consent prior to inclusion. The studies were approved by the Icelandic Bioethics Committee with approval no. 07-146-S1 and by the Icelandic Data Protection Authority with approval no. 2007120859.

4 Results

4.1 Studies I and II

The health survey's data includes responses from 5,906 Icelanders; 2,724 men and 3,108 women. The study population consisted of 5,756 individuals when missing values were considered, of whom 1,292 individuals reported current chronic MSK pain condition. Figure 8 shows the study flow chart. The weighted prevalence estimate was calculated as 19.9% in the adult Icelandic population.

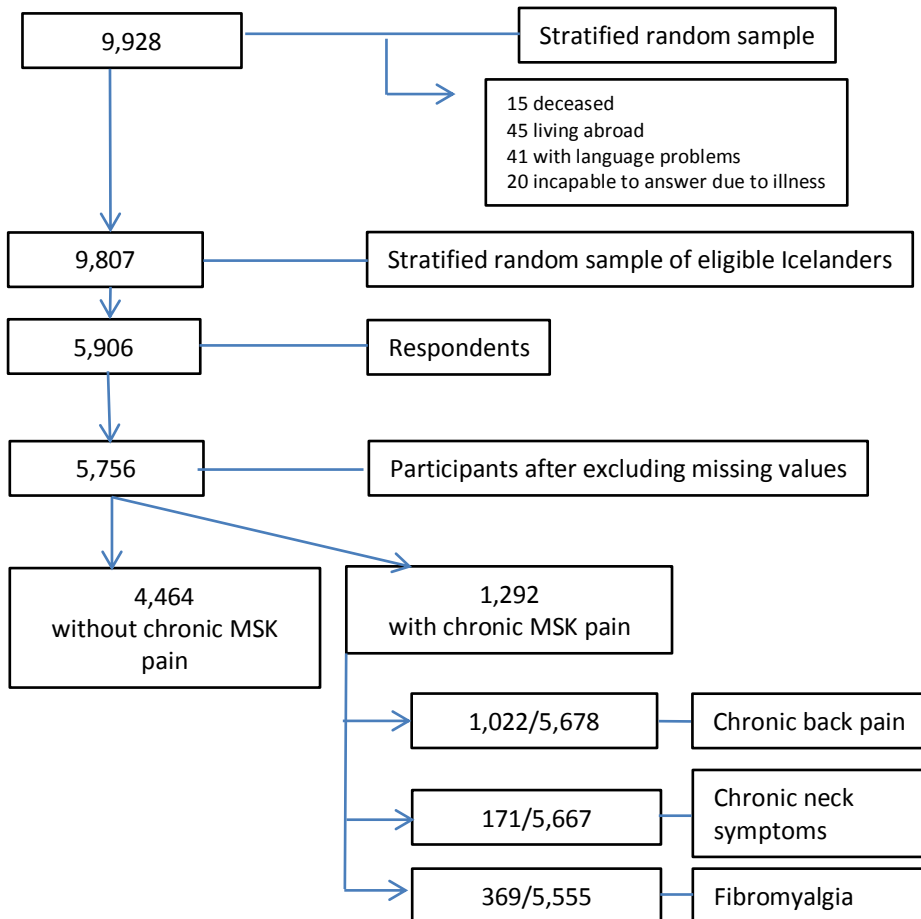


Figure 8. Studies I and II flow chart.

Overall, women had a higher estimated prevalence of all chronic MSK pain conditions; 24.7% versus 15.2% among men. The weighted prevalence of chronic back pain was 16.2% (men=13.6%; women=19.0%), chronic neck symptoms 2.6% (men=1.8%; women=3.4%) and fibromyalgia 5.3% (men=1.6%; women=9.2%). Prevalence of all chronic MSK pain conditions increased with: higher age (18-29 years = 13.4%; 70-79 years = 28.7%), decreased income (\leq 200 thousand IKR=25.3%; \geq 370 thousand IKR=14.1%), less educational level (primary school=26.0%; university =13.6%), obesity and underweight individuals (BMI \geq 30=29.0%; BMI $<$ 18.5=30.2% versus BMI 18.5-29.9=15.8%-18.8%), and smoking (smoking=22.8%; not smoking=16.4%). Higher prevalence was also observed of all chronic MSK pain conditions among home makers, the unemployed and disabled individuals in comparison with individuals actively working, studying or only temporarily on sick leave (Table 1, Paper I).

In general, individuals with C-CPD reported considerably higher odds of physical symptoms that disturb daily life, and women generally higher odds than men (Table 2, Paper I). For example, individuals with chronic MSK pain reported higher odds of poor physical health (OR men=4.0 [95%CI=3.0-5.2]; OR women=6.8 [95%CI=5.4-8.5]), physical mobility limitations (OR men=4.0 [95%CI=2.8-5.6]; OR women=5.1 [95%CI=3.8-6.7]) and insufficient general energy (OR men=2.4 [95%CI=1.8-3.2]; OR women=3.5 [95%CI=2.9-4.4]), compared with those without CPD.

Our results indicate that chronic MSK pain had a considerable impact on daily activities (Table 3, Paper I), increasing with more physically demanding activities (OR men=2.4 [95%CI=1.8-3.2] – 6.9 [95%CI=4.2-11.5] OR women=3.2 [95%CI=2.3-4.6] – 7.9 [95%CI=6.3-10.0]).

The results show that people with C-CPD are equally likely to achieve the recommended physical activity level measured on IPAQ as those without CPD (OR men=1.0 [95%CI=0.8-1.3]; OR women=1.2 (95%CI=1.0-1.5)), although marginal differences were observed among women. Further, no differences were observed in frequency of medium intensity work-out, prolonged sitting or physically demanding work. Women with C-CPD compared with those without are more likely to never work out vigorously (OR=1.5 [95%CI=1.2-1.8]) or walk more than ten minutes at a time (OR=1.3 [95%CI=1.1-1.7]). On the other hand, no such difference was observed among men (OR=1.2 [95%CI=0.9-1.6] and OR=0.8 [95%CI=0.6-1.1], respectively). Both men and women with C-CPD perceived their physical strength (OR men=2.5 [95%CI=1.8-3.5]; OR women=3.9 [95%CI=3.1-5.0])

and endurance (OR men=1.9 [95%CI=1.4-2.6]; OR women=3.0 [95%CI=2.4-3.8]) less than among other people of the same age and gender in comparison with the N-CPD groups (Table 4, Paper 1).

Individuals with chronic MSK pain reported higher odds of poor mental health, (OR men=1.7 [95%CI=1.3-2.3]; OR women=2.4 [95%CI=1.9-3.0]), diminished quality of life (OR men=1.5 [95%CI=1.0-2.1]; OR women=1.6 [95%CI=1.2-2.1]), increased stress (OR men=1.5 [95%CI=1.1-2.1]; OR women=1.7 [95%CI=1.3-2.2]), potential depression (OR men=2.8 [95%CI=2.1-3.7]; OR women=2.4 [95%CI=1.9-3.0]) and sleeping disturbances (OR men=2.2 [95%CI=1.5-3.1]; OR women=2.8 [95%CI=2.2-3.5]) in comparison with individuals without CPD (Table 2, Paper 2).

In general, individuals with chronic MSK pain reported considerably higher odds of poor mental health status such as unhappiness, worries, anxiety, depression, sleep problems and stress that affects daily life, in comparison with people who did not report chronic MSK pain conditions (Table 3).

Table 3. Self-assessed mental health and symptoms in adults with and without current chronic musculoskeletal pain disorder

	Women			Men		
	n/N (%)	OR ^{adj}	95% CI	n/N (%)	OR ^{adj}	95% CI
Feeling unhappy						
N-CPD	166/2136 (7.8)	1		191/2151 (8.9)	1	
C-CPD	108/778 (13.9)	1.6	1.2-2.2	80/460 (17.4)	1.7	1.2-2.4
Excessive worrying affecting daily living, the past year						
N-CPD	479/2151 (22.3)	1		336/2161 (15.5)	1	
C-CPD	242/775 (31.2)	1.7	1.4-2.1	109/453 (24.1)	1.8	1.3-2.4
Anxiety affecting daily living, the past year						
N-CPD	532/2153 (24.7)	1		382/2159 (17.7)	1	
C-CPD	276/776 (35.6)	1.7	1.4-2.1	121/454 (26.7)	1.8	1.3-2.4
Depression affecting daily living, the past year						
N-CPD	430/2038 (21.1)	1		293/2161 (13.6)	1	
C-CPD	226/723 (31.1)	1.7	1.4-2.2	100/451 (22.2)	1.7	1.3-2.3
Sleeping disturbances affecting daily living, the past year						
N-CPD	549/2163 (25.4)	1		375/2162 (17.3)	1	
C-CPD	349/782 (44.6)	2.3	1.9-2.8	141/452 (31.2)	2.0	1.5-2.7
Insufficient or excessive sleep, in general (reference is 7-8 hours)						
N-CPD	607/2143 (28.3)	1		671/2127 (31.5)	1	
C-CPD	312/772 (40.4)	1.7	1.4-2.0	209/457 (45.7)	1.8	1.4-2.3
Using medication due to sleeping disturbances						
N-CPD	710/2114 (33.6)	1		550/2108 (26.1)	1	
C-CPD	439/765 (57.4)	2.3	1.9-2.8	187/440 (42.5)	1.8	1.4-2.4
Feeling lately affected by stress at work (self-designed question)						
N-CPD	1416/1796 (78.8)	1		1462/1879 (77.8)	1	
C-CPD	427/540 (79.1)	1.4	1.0-1.9	283/365 (77.5)	1.6	1.0-2.1
Feeling lately affected by stress in private life (self-designed question)						
N-CPD	1251/2169 (57.7)	1		1122/2138 (52.5)	1	
C-CPD	498/782 (63.7)	1.5	1.3-1.9	255/456 (55.9)	1.3	1.0-1.7

95% CI: 95% confidence interval for Odds Ratio; OR^{adj}: odds ratio adjusting for age, monthly income, body mass index, smoking, educational level and residential area; N-CPD: non-chronic musculoskeletal pain disorder; C-CPD: current chronic musculoskeletal pain disorder

The results have shown that a considerable proportion of individuals reporting N-CPD had recovered from chronic MSK pain condition (n=847) at some point. Considering individuals with current (n=1,022) versus past (n=663) chronic back pain independently, the results indicated a general trend towards higher odds ratios of poor health and limited activities, among individuals with C-CBP, than those individuals who have recovered from chronic back pain, compared with people who never experienced the condition (Table 4).

Table 4. Self-assessed health and activity limitations in people with current chronic back pain, recovered from chronic back pain and without chronic back pain

	<i>Women</i>			<i>Men</i>		
	n/N (%)	OR ^{adj}	95% CI	n/N (%)	OR ^{adj}	95% CI
Poor physical health, in general						
N-CBP	279/1895 (14.7)	1		305/1785 (17.1)	1	
C-CBP	348/603 (57.7)	6.9	5.4-8.8	211/396 (53.3)	4.1	3.1-5.5
P-CBP	86/313 (27.5)	1.8	1.3-2.5	97/332 (29.2)	1.5	1.0-2.0
Poor mental health, in general						
N-CBP	257/1898 (13.5)	1		251/1786 (14.1)	1	
C-CBP	197/603 (32.7)	2.4	1.9-3.1	114/397 (28.7)	1.9	1.4-2.6
P-CBP	62/314 (19.7)	1.7	1.2-2.4	79/335 (23.6)	1.7	1.2-2.5
Lifting or carrying groceries						
N-CBP	233/1877 (12.4)	1		82/1787 (4.6)	1	
C-CBP	324/589 (55.0)	7.0	5.4-9.0	102/391 (26.1)	6.2	4.2-9.3
P-CBP	71/308 (23.1)	1.6	1.1-2.3	39/330 (11.8)	2.7	1.7-4.4
Climbing several flights of stairs						
N-CBP	465/1871 (24.9)	1		340/1786 (19.0)	1	
C-CBP	374/589 (63.5)	4.2	3.3-5.3	180/393 (45.8)	2.8	2.1-3.8
P-CBP	119/311 (38.3)	1.4	1.0-1.9	115/331 (34.7)	1.8	1.3-2.5
Bending, stooping or kneeling						
N-CBP	326/1879 (17.3)	1		276/1787 (15.4)	1	
C-CBP	352/586 (60.1)	5.7	4.5-7.2	222/392 (56.6)	7.3	5.4-9.8
P-CBP	98/310 (31.6)	1.6	1.2-2.2	99/331 (29.9)	2.0	1.5-2.9
Walking over one kilometer						
N-CBP	262/1868 (14.0)	1		201/1788 (11.2)	1	
C-CBP	272/589 (46.2)	4.4	3.5-5.7	142/392 (36.2)	3.2	2.3-4.5
P-CBP	76/310 (24.5)	1.6	1.1-2.3	73/328 (22.3)	1.7	1.2-2.5

95% CI: 95% confidence interval for Odds Ratio; OR^{adj}: odds ratio adjusting for age, monthly income, body mass index, smoking, educational level and residential area; N-CBP: non-chronic back pain; C-CBP: current chronic back pain; P-CBP: past chronic back pain

4.2 Studies III and IV

The initial enrollment in the two programs consisted of 234 women, of whom 212 participated in the studies, aged 23 to 67 years old (mean = 49.6 years). The TMP intervention was received by 122 and 90 participated in the NEM intervention. The follow-up data included responses from 75 TMP and 56 NEM participants, yielding response rates of 61.5% and 62.2%, respectively. The reference group included 57 female participants. The study flow chart is presented in Figure 1, Paper 3.

Demographic characteristics of participants and baseline outcome measures are presented in Table 2, Paper III, and stratified by response 6 months after intervention in Table 1, Paper IV.

Our analyses revealed no significant baseline differences between those who responded at the 6-month follow-up and those who did not (Table 1, Paper IV). This includes all background variables and outcome measures, both overall and stratified by intervention. Nevertheless, marginal differences were detected for the anxiety score among TMP participants where those responding had a mean score of 41.0 ± 9.6 and those not responding a mean of 36.8 ± 12.6 ($p=0.054$). Further, marginal differences were also detected among the NEM participants on pain (VAS) scores where those responding had a mean of 64.1 ± 15.5 versus 70.3 ± 14.0 among those who did not respond ($p=0.060$). Our analyses revealed (data not shown) that neither any background variable nor any outcome measures predicted which individuals would respond at the 6-month follow-up.

In studies III and IV we found the data consistent with homogeneity of variances for all outcome measures. In study III (Table 2, Paper III) the F_{\max} ratios varied between 1.68 (pain on HRQL) and 5.39 (depression on HRQL) and in study IV (data not shown) between 1.00 (energy on HRQL) and 2.07 (depression on HRQL).

Effect of NEM and TMP interventions on HRQL and pain intensity

Table 3, Paper III summarizes the effect of the two interventions on all HRQL domains, the HRQL summary score and pain intensity. Significant improvements were observed on all outcome measures, except for financial status, among women receiving the TMP or NEM interventions compared with the reference group. Comparisons between the two interventions

revealed no significant differences except for the sleep domain of the HRQL. NEM participants improved their sleep to a greater extent than both the TMP and the reference group; 8.0 ± 9.6 versus 4.4 ± 8.8 ($p=0.008$) and 8.0 ± 9.6 versus 1.5 ± 6.0 ($p<0.001$), respectively. Comparisons between the NEM and TMP groups head to head, revealed that NEM participants improved more than the TMP participants in terms of sleep ($p=0.024$ [adjusted]; $p=0.005$ [unadjusted]), whereas the TMP improved more than the NEM in decreased pain intensity (21.8 ± 20.1 mm versus 17.2 ± 20.7 mm [$p=0.013$ adjusted; $p=0.105$ unadjusted]) measured on the VAS scale. The TMP group also improved more than the NEM group in depression scores (10.0 ± 9.2 versus 7.6 ± 7.9 [$p=0.043$ unadjusted]) but following adjustment for potential confounders the observed difference was not significant.

The results showed that improvements sustained significantly on all outcome measures regardless of intervention method, with the exception of the sleep domain ($p=0.066$) on HRQL among the TMP participants. Financial status was not significant, as before (Table 2, Paper IV). Figure 1, Paper IV shows the mean of HRQL summary scores and Figure 2, Paper IV the pain intensity, at three time points, among participants in both TMP and NEM intervention groups and the results are stratified by response at the 6-month follow-up.

Our results indicate that the TMP participants improved in anxiety significantly more, six months after intervention, than the NEM participants (change score for TMP= 7.1 ± 9.9 versus NEM= 3.3 ± 7.9 ; $p=0.038$). However, the improvement may have been influenced by lower anxiety scores at admission among people not responding to the follow-up, especially among the TMP participants (scores among TMP respondents= 41.0 ± 9.6 versus non-respondents= 36.8 ± 12.6 and the NEM= 42.9 ± 10.2 versus 43.8 ± 9.6). More improvement was observed among the NEM participants than those in the TMP group in pain scores measured on IQL (6.3 ± 8.6 versus 3.6 ± 7.1 [$p=0.047$ unadjusted]) but the difference was not significant following adjustment for potential confounding variables. We observed no other differences between the NEM and the TMP intervention groups (Tables 1 and 2; Paper IV).

Subgroup analyses

Our results indicate that women with low HRQL at baseline improved considerably more by the end of intervention (mean change score for TMP =

13.4 and for NEM = 12.9, for those with HRQL summary score ≤ 35 vs. mean for TMP = 6.6 and for NEM = 7.8 for those with HQRL > 35) and that the improvements were sustained (mean change score for TMP = 8.1 and for NEM = 9.1, for those with HRQL summary score ≤ 35 vs. mean change score for TMP = 4.3 and for NEM = 5.7 for those with HQRL > 35). However, we observed that the effect of the treatment interventions was not modified nor by other factors that we tested. The results are presented in Figure 9 and Figure 3, Paper IV.

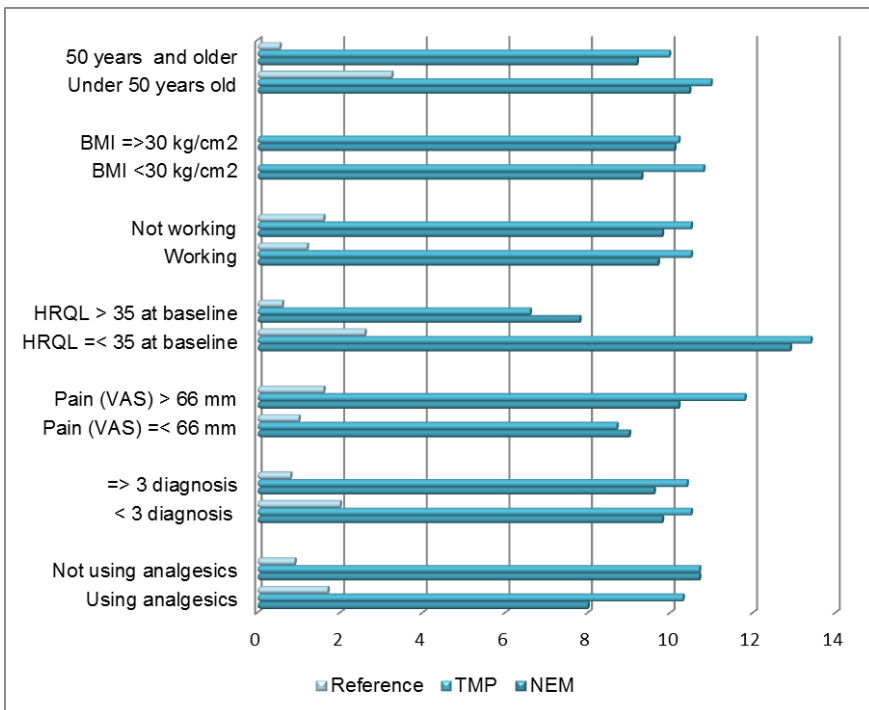


Figure 9. Change in HRQL from baseline to end of intervention

Change scores for health-related quality of life (HRQL) as a result of treatment comparing two interventions and a reference group, stratified by potential confounding factors measured at baseline. BMI: body mass index; VAS: visual analogue scale; TMP: traditional multidisciplinary pain management program; NEM: Neuroscience patient education and mindfulness-based cognitive therapy.

Engagement in physical and mental activities following intervention

Our results indicate that 84% of the TMP participants and 95% of the NEM participants reported that they regularly exercised following completion of the intervention. Around 61% of the TMP participants compared with 71% of the NEM group reported practicing relaxation and/or meditation. The observed differences were non-significant; $p=0.058$ and 0.229 , respectively.

5 Discussion

The findings from our population-based research (studies I and II), using a randomly selected sample of close to 5,700 Icelanders, suggest a prevalence rate of self-reported chronic MSK pain conditions of nearly 20%. Our results are in line with previous findings and suggest that prevalence is higher among women and among individuals with lower socioeconomic status. In support of our hypotheses we found that people with chronic MSK pain conditions, women in particular reported poor physical and mental health and increased impact on daily activities, quality of life and well-being. Men and women with chronic MSK pain reported increased limitations on daily activities, perceived stress, depressive symptoms, sleep disruption, and life dissatisfaction. In addition, distinct gender differences were observed. Women with chronic MSK pain disorder tended to report less physical activity levels than women without the disorder, but no such differences were observed among men. Our results lend support to previous research on chronic MSK pain and various physical and mental health indicators and add to the literature some new perspectives, mainly due to our population-based data. Our research provides an in-depth and realistic picture of the physical and mental health among people with chronic MSK pain conditions and is the first Icelandic research to present in-depth evidence.

The findings from our clinically based data (studies III and IV) suggest that women with chronic MSK pain participating either in a traditional multidisciplinary pain management program or a similar program adding mindfulness-based cognitive therapy and neuroscience patient education show significant immediate improvement in all domains of HRQL (except financial status) and decreased pain intensity in comparison to reference individuals on a waiting list. Further, the improvements were sustained up to 6 months after the interventions were completed, in most aspects of HRQL and pain intensity. Our results indicated that both groups improved significantly from baseline to end of intervention in the sleep domain of HRQL but participants in the NEM program significantly more than the TMP participants. The NEM participants retained significant improvements when measured from baseline to 6 months after intervention was completed, whereas no difference was detected among TMP participants. The findings further suggest that TMP participants showed more immediate improvement

than the NEM in pain intensity but this difference was no longer evident at the 6-month follow-up. Both groups sustained improvement. Thus our results lend support to existing evidence that intensive multidisciplinary bio-psychosocial rehabilitation is effective for women experiencing chronic MSK pain conditions. Moreover, our results suggest sustained effectiveness.

5.1 Studies I and II

The prevalence of chronic MSK pain conditions in population-based studies varies from 12% to 47.5%, depending on research methodology and operational definitions. Our results show that a fifth of Icelandic adults report chronic MSK pain conditions, which is in line with many other international studies (Blyth et al., 2001; Breivik et al., 2006; Eriksen et al., 2003; Rustoen et al., 2004; Sjogren et al., 2009). Considering Iceland only, conflicting results have been reported. Our results showed that prevalence among women was 24.7% and 15.2% among men, which is in line with previous results showing 26.9% and 12.9%, respectively (Birgisson et al., 1998). More recent and conflicting results show overall prevalence of 30.6% (Gunnarsdóttir et al., 2010) and 47.5% (Jónsdóttir et al., 2014), whereas our results showed 19.9%. In comparison with these studies our results are supported by a higher response rate and a larger sample size. Furthermore, our estimates were weighted to represent the true population. However, our data included only three chronic MSK pain conditions, which may underestimate the true prevalence. In agreement with previous research our results indicated increased prevalence with age, lower educational level, and lower income, and showed distinct gender differences with the female responders reporting a higher prevalence (Ahacic and Kareholt, 2010; Bingefors and Isacson, 2004; Birgisson et al., 1998; Blyth et al., 2001; Bouhassira et al., 2008; Breivik et al., 2006; Jónsdóttir et al., 2014; Mallen et al., 2005; Mundal et al., 2014a).

Our results indicated that people with chronic MSK pain conditions more frequently reported physical symptoms that disrupted their daily life than those without the condition. In comparison with older data from Iceland the prevalence of chronic pain in shoulder, neck and back areas may be decreasing; women 62-78% and men 38-58% (Steingrimsdóttir et al., 1988) versus 46-50% and 23-38%, respectively in our sample (data not shown). We further observed that individuals with chronic MSK pain conditions also tended to report mental symptoms that disrupted daily life more frequently

than those without. For example, around 33% of those with chronic MSK pain also reported potential depression as measured by the WHO-5 well-being index, compared with 17% of those without the condition (Table 2, Paper II). Our results showing increased reports of depression among individuals with chronic MSK pain are in line with previous studies (Demyttenaere et al., 2007; Munce and Stewart, 2007; Tsang et al., 2008). In addition, approximately 36% of women and 27% of men with chronic MSK pain reported anxiety to the extent that it affects their daily life, compared with around 25% of women and 18% of men without pain (Table 3). The observed association is supported by other studies (Keogh et al., 2006; Knaster et al., 2012; McWilliams et al., 2003; Newcomer et al., 2010; Rode et al., 2006). In our sample around 45% of women and 31% of men with chronic MSK pain reported sleeping disturbances (Table 3), which is considerably less than the 67% reported in a clinical study (Morin et al., 1998).

Our findings indicated other gender differences with respect to chronic pain conditions. For example, we observed that women but not men with chronic MSK pain conditions tended to skip vigorous work-outs and to take a walk. We propose that women with chronic MSK pain are more exposed than men to fear of movement or to the risk of re-injury, which is in line with other research (Elfving et al., 2007). On the other hand, men and women with chronic MSK pain conditions believe that they have less physical endurance and strength than people without chronic MSK pain. Similar results have been reported in other studies (Friedrich et al., 2009; Verbunt et al., 2003). Our results further indicate that both men and women report activity limitations as a result of health conditions, and women to a greater extent than men. Altogether, our results support existing evidence suggesting that perceived physical decline and limitation of activity is prevalent among people with chronic MSK pain conditions (Verbunt et al., 2005) and the tendency to fear physical strain possibly because it may increase pain (Friedrich et al., 2009; Nijs et al., 2008). We observed that individuals who recover from chronic MSK pain may still experience physical symptoms and limitations in their activity in their daily life. We propose that avoidance behavior may possibly be a remaining symptom that motivates changes in daily life with the purpose of avoiding activities provoking pain (Young et al., 2011).

Our population-based data suggest that people with chronic MSK pain report diminished quality of life, life satisfaction and well-being, and increased stress in comparison with those who report no chronic MSK pain. Most studies on mental morbidity associated with chronic MSK pain use clinical data mainly from pain clinics or rehabilitation centers (Cannella et al., 2007;

Newcomer et al., 2010; Rode et al., 2006; Roth et al., 2008). The results are consistent, indicating mental co-morbidity to chronic MSK pain conditions (Becker et al., 1997; Boonstra et al., 2013; Lamé et al., 2005; Laursen et al., 2005; Lin et al., 2010; Silvemmark et al., 2008).

5.2 Studies III and IV

Our results indicating immediate effectiveness of both TMP and NEM interventions for women with chronic MSK pain, in comparison to reference individuals, are in agreement with other studies (Busch et al., 2011; Demoulin et al., 2010; Dysvik et al., 2010; Gagnon et al., 2009; Heiskanen et al., 2012; Kamper et al., 2014, 2015; Meineche-Schmidt et al., 2012; Myhr and Augestad, 2013; Stein and Miclescu, 2013). Our follow-up data further indicated sustained improvements, a result which also is supported by other studies (Gagnon et al., 2009; Lang et al., 2003; Meineche-Schmidt et al., 2012; Pieber et al., 2014; Spinhoven et al., 2004; Stein and Miclescu, 2013; Tavafian et al., 2014; Vowles and McCracken, 2010; Vowles et al., 2011; Wong et al., 2011). Although both intervention groups reported decreased pain intensity, the TMP participants showed more immediate improvements than the NEM (change score from baseline to end of intervention = 21.8 versus 17.2 mm). The changes in both groups were greater than were observed in a multidisciplinary Back School program of four weeks where reported changes were 11 mm on the VAS scale (Morone et al., 2011). There was no specific emphasis on pain reduction in either of the two programs, but we expected that the NEM participants would improve more, as in other outcome measures. We have no explanation but conflicting evidence exists on whether pain intensity improves (Reiner et al., 2013) or not (Veehof et al., 2011) as a result of mindfulness-based interventions. However, we propose that a plausible explanation may relate to the complex multidimensional nature of chronic MSK pain (Kerr et al., 2013). An important factor in mindfulness-based intervention is the emphasis on accepting any concurrent experiences, including pain. In addition, participants attend to bodily sensations with the aim of regulating responses to pain (Brown and Jones, 2013). Further, research has shown that people with chronic MSK pain focus their attention on painful areas (Moseley et al., 2005). Participants in our study who received the mindfulness-based intervention had an intensive 4-week course, whereas this kind of intervention is generally offered for 8-week periods. We suggest that our participants had not yet reached the optimum neurological change levels (Kerr et al., 2013) and were still attending to their

pain. Our follow-up data suggest that the TMP participants reported increased pain intensity to a greater extent than the NEM participants 6 months after intervention. We suggest that the NEM participants retained improvement, whereas the TMP did not.

Compared with the TMP approach the NEM intervention included two additional elements, namely, more advanced neuroscience patient education and mindfulness-based cognitive therapy. Both these elements enhance alterations in the nervous system. The primary aim of the mindfulness training is the focus on acceptance, including accepting pain experiences and to change the relationship with catastrophic thoughts and avoidance. The primary aim of neuroscience patient education is to explain possible mechanisms involved. Our results indicate that the two elements combined with a traditional multidisciplinary treatment showed immediate and long-term effectiveness in terms of sleep problems compared with the traditional method alone. These findings are important as prior studies have shown that disrupted sleep is one common complaint among individuals experiencing chronic MSK pain conditions (Breivik et al., 2006; Turk and Cohen, 2010; Wagner et al., 2012) and we have suggested in study II. In support of our immediate and follow-up results, clinical trials have shown that mindfulness based interventions for chronic MSK pain conditions improve HRQL (Buhrman et al., 2013) and sleep disruptions (Cash et al., 2015; Esmer et al., 2010; Garland et al., 2014). It has further been shown that neuroscience patient education improves HRQL in the long run (Van Oosterwijck et al., 2013) and reverses catastrophic thought processes (Louw et al., 2011) in this patient population. There is further evidence suggesting that negative mood (O'Brien et al., 2010) and pain catastrophizing (Buenaver et al., 2012) may have an impact on sleeping disturbances among individuals with chronic MSK pain.

Although our results are supported by other studies, we cannot be sure that some confounding factors, unknown or unmeasured, may account for the observed, although limited, differences between modalities. A randomized controlled trial is needed to determine if one or both new elements are responsible for the potentially superior improvements in sleep disruption in favor of the NEM intervention. However, based on our results and existing evidence we suggest that the sustained improvement in sleep disturbances among the NEM participants may involve multiple factors. One factor may relate to general psychological distress known to contribute to sleep disruption and chronic MSK pain (Sivertsen et al., 2015). As a result of a systematic review and meta-analyses, it has been concluded that

mindfulness-based interventions improve mental health status (Gotink et al., 2015), including depression, anxiety, HRQL, and stress. All these symptoms improved in both intervention groups immediately after intervention and the improvement was still in effect half a year later. Although the NEM participants had more structured and detailed emphasis on cognitive and central changes in their program, we cannot rule out whether elements of these did not also exist in the TMP program. Certainly, the TMP participants learned relaxation techniques, had Back School education and emphasis on incorporating exercises in daily life. All these might have improved self-efficacy and confidence, although we used no measures to identify this. This may, however, explain the observed lack of differences between the two interventions. For example, we observed more improvement among the TMP participants in terms of anxiety. We suggest that differences may also be explained by marginal baseline differences between those who responded and those who did not respond to the follow-up questionnaires.

Enhanced lifestyle changes were emphasized in both intervention groups by using active rehabilitation, counselling and education. Physical and mental health benefits of physical activity have been reported for this patient population (Pedersen and Saltin, 2006; Sundberg et al., 2010). Noteworthy, our results (study I) suggest that people in general do not reach the recommended physical activity levels for health benefits introduced by the World Health Organization. It is important for all people to engage in physical activity, but our data suggest that NEM participants may be more prone to exercise and use meditation or relaxation techniques than the TMP during the follow-up period. Although non-significant group differences were observed we suggest that mindfulness training and neuroscience patient education may complement each other and encourage lifestyle changes. Further research is needed and longer term follow-up may reveal different results.

5.3 Strengths and limitations

The main strength of our survey data relates to the reasonable sample size of a representative sample from an underlying population which we have defined as Icelandic speaking citizens, living in Iceland during the time of data collection. At the time of data collection the total population amounted to 312,872 inhabitants ("Statistics Iceland," 2007). The response rate of this survey was 60.3% which was similar to some other prevalence surveys

(Bingefors and Isacson, 2004; Parsons et al., 2007; Saastamoinen et al., 2009) but higher than in other Icelandic studies (Birgisson et al., 1998; Gunnarsdóttir et al., 2010; Jónsdóttir et al., 2014). More women responded to the questionnaire than men, but all our analyses were gender stratified and we included gender in the weighting process for the prevalence calculations. The questionnaire offered extensive socioeconomic information, enabling us to control our regression models for potential confounding factors such as smoking (Goldberg et al., 2000; John et al., 2009; Palmer et al., 2003), socio-economic factors (Macfarlane et al., 2009) and body mass index (Caldwell et al., 2009). Although the Icelandic population is rather homogenous in terms of ethnicity and culture we conclude that our results can at least represent the situation in other countries with a similar culture. While, the questionnaire includes a range of variables, we recognize the lack of some important measurements on mental co-morbidities such as catastrophizing, fear avoidance and self-efficacy.

Various information biases always constitute a threat to the validity of data in studies relying on self-reports. Reports of chronic MSK pain, physical and mental morbidities are self-reported in these studies, yet in order to distort the reported associations, individuals with chronic MSK pain would need to have a different response pattern compared with those who do not experience the condition. We have no indication for or against this claim, but caution is needed when interpreting the data. The cross-sectional study design is a crucial limitation in these studies which excludes any suggestion on the direction of the associations observed. The aim here was not to establish any causality but namely to investigate physical and mental co-morbidities associated with chronic MSK pain. Furthermore, the questionnaire does not offer information on all conditions related to chronic widespread pain (Wolfe et al., 2010; Wolfe et al., 1990), since it was not explicitly designed for the purpose of our studies. This may have caused underestimation of prevalence rates. We consider the measure of chronic neck symptoms as the weakest variable since the question is ambiguous. The respondents may have understood the item as any chronic symptoms or disorder in the neck area. They may or may not have included chronic pain due to their symptoms such as sore muscles or tension in the neck/shoulder areas, which may possibly bias the results. Authors in other studies frequently refer to neck pain as trouble, problems, discomfort, ache, pain or symptoms in the neck (Johnston et al., 2007; Larsman and Hanse, 2009; Linnman et al., 2009; Szeto et al., 2009; Van den Heuvel et al., 2005). Further, in the questionnaire, there is no

operational definition of the term, chronic or long-lasting, which also may affect the results.

The main strength of our clinical data is the complete set of outcome measures for all participants in both intervention groups at baseline and at discharge. Approximately 62% of the participants responded to all questionnaires six months after the completion of intervention. This response rate is in accordance with some other follow-up studies that have relied on postal responses (Meineche-Schmidt et al., 2012; Van der Maas et al., 2015; Vowles et al., 2011). Some studies report higher response rates (Spinhoven et al., 2004; Stein and Miculescu, 2013). In accordance with our study protocol one reminder was mailed to the participants. We observed marginal baseline differences between those who responded and those who did not respond to the follow-up in terms of anxiety. No other baseline differences were observed, indicating that our data reflect the actual status of participants in the two intervention groups, but interpretation must be cautious.

There were further limitations that need to be respected when results are interpreted. Random assignment to study groups was not possible; consequently, unmeasured confounding factors may have affected the results. Using a waiting list as a control may bias the results even though in our case the participants were on a waiting list for the very same clinic. Cross-contamination should not bias the results since the two intervention groups were not offered treatment simultaneously, although treated at the same clinic. A number of elements were similar in the two programs and they may have been too similar to show distinct differences. For example, the TMP participants did have some behavioral guidance through counselling, patient education and activity recommendations, while the NEM group had a more structured program in behavioral therapy. Although no measure is available for this element we did expect both groups to show behavioral changes. All participants in these studies were women due to the low number of men participating in the programs. Generalizability is therefore limited to women only. Outcome measures are self-reported and, as such, subjective estimates; thus recall biases cannot be excluded. However, we have no reason to assume that participants in the two interventions and on the waiting list would change their answering style between measurement points. Further, the waiting list group received both sets of questionnaires simultaneously but were supposed to answer and return one promptly and the other in one month. There is no certainty that participants waited one month to respond to the second set, but we excluded two participants who mailed the two sets together.

5.4 Implications and future directions

Based on the literature review as presented in the introduction section in this thesis, the research, personal opinions, views and experiences, some relevant implications and future directions are proposed. The aim is to ascertain that people with chronic MSK pain conditions are properly taken care of within the health care system, according to Icelandic law and the Montréal Declaration.

Research

Chronic MSK pain is a transnational and cross-cultural public health threat. Future research needs to focus on monitoring the health of a population, including indicators that may contribute to chronic conditions and in particular those initiating chronic MSK pain. In the population-based studies, emphasis had been placed on the prevalence and the impact chronic MSK pain may have on the individual from various perspectives. The research therefore provides motivation for further Icelandic population-based studies, looking into the impact chronic MSK pain may have on the society and both direct and indirect costs of the condition. It is essential to prevent any chronic condition; therefore research should also be directed towards prevention at all stages. In the clinical research, the emphasis was on the effectiveness of two intensive multidisciplinary rehabilitation interventions for individuals with chronic MSK pain. The research was observational and thus limited. Randomized controlled trials would be essential to reveal which elements in the multidisciplinary interventions are most effective and to determine how much of each element could be enough for treatment success and, additionally to better determine which chronic MSK pain patients would benefit the most from multidisciplinary intervention at each level of health care services. Studies are also needed that can identify those who are most at risk of developing chronic MSK pain conditions.

Clinical practice

Based on the results and the background literature studied for this thesis, it is proposed that no single health care profession has the ultimate solution for people with chronic MSK pain conditions. As revealed in this thesis, multidisciplinary treatment is essential for this multidimensional complex condition. Besides preventing chronicity, health care professionals should cooperate and aim at multidisciplinary treatment options at all levels of the

health care system. In Iceland, there are a number of multidisciplinary treatment options for chronic MSK pain conditions but they all seem to provide services at later stages of the condition. The primary health caregivers, as the patients' first contacts, need to recognize the importance of a bio-psycho-social multidisciplinary assessment team to diagnose the patient and to develop effective treatment. Preferably, the team should meet with the patient and propose a patient-centered treatment plan. The treatment may involve only one health care professional or a team, as applicable, for treatment success. The proposed treatment plan can then be executed by any cooperative professionals providing ambulatory health care services. It is necessary, however, for each provider to understand the importance of a multimodal treatment plan, to participate in a multidisciplinary approach and to emphasize up-to-date evidence-based practices.

Education

For successful multidisciplinary treatment all professionals need to have the proper training for collaborative health care services. Educational institutions providing health care education should aim at inter-professional/multidisciplinary training. In the case of a multidimensional condition like chronic MSK pain a joint inter-professional course may be essential. Such a course should provide knowledge gained from a number of professions. A joint teaching method for basics and theories relevant to all professions could be proposed, with teaching emphasis for each profession as relevant. Inter-professional problem-based learning should then be applied in clinical settings at all levels of the health care system.

Health care policy

Health care authorities need to acknowledge available studies that show the direct and indirect costs of chronic MSK pain conditions. This would encourage health care authorities to initiate proper preventative strategies, as preventing the condition, and not just alleviating it, is essential in every respect. Perhaps the most important factor in preventing the occurrence of chronic MSK pain is to adequately treat individuals with acute MSK pain, followed by identifying those at risk of developing a chronic condition. Information needs to be available to all people experiencing pain on how they can reduce the risk of developing a chronic condition. Health care authorities need to ensure the availability of proper care, information and

encouragement for health promotion and healthy lifestyle choices.

Studies indicate that by providing proper health care for people experiencing chronic MSK pain the total cost would be reduced. It is important for the health care authorities to provide multidisciplinary treatment options at all levels of the health care system, delivered by adequately trained inter-professional health care teams. This can only be achieved by properly involving all relevant health care professionals at all levels of the health care system. It is urgent that health care authorities in Iceland initiate well-established pain management at all stages and provide multidisciplinary services for those in need. Multidisciplinary treatment may not always be indicated, but it is essential that the first contact is capable of assessing the need and to have access to the proper channels as needed.

6 Conclusions

Our population-based findings suggest that the prevalence of chronic MSK pain conditions in Iceland is approximately 20%. In Iceland, chronic MSK pain conditions are more prevalent among women than men, with increased age, increased body mass index, decreased income and with lower socioeconomic status. We found associations between chronic MSK pain conditions and various physical and mental factors. Our findings suggest that people with chronic MSK pain are at increased risk of experiencing limitations in their daily life and are more susceptible to physical and mental symptoms than people without the condition.

Our clinical data suggest that multidisciplinary bio-psycho-social rehabilitation is effective for women with chronic MSK pain conditions and even for six months after intervention ended. Moreover, our results indicate that adding neuroscience patient education and mindfulness-based cognitive therapy to an already effective traditional multidisciplinary pain management program improves sleep to a greater extent and that improvements are sustained for at least half a year.

Although our data are strong and our methods are solid, caution is needed when interpreting our results and causal inferences cannot be drawn from these studies alone. Therefore, more studies in Iceland are needed to confirm our results. We suggest using a longitudinal study design to confirm our population-based results, and randomized clinical trials for replication of our findings observed in our clinical studies.

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Original publications

Paper I

Functional limitations and physical symptoms of individuals with chronic pain

Björnsdóttir SV, Jónsson SH, Valdimarsdóttir UA.

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Functional limitations and physical symptoms of individuals with chronic pain

SV Björnsdóttir^{1,2}, SH Jónsson^{3,4}, UA Valdimarsdóttir^{5,6}

¹Department of Physical Therapy, Faculty of Medicine, University of Iceland, Reykjavik, ²HNLFI Rehabilitation and Health Clinic, Hveragerði, ³Directorate of Health, Reykjavik, ⁴Department of Social Sciences, Faculty of Social and Human Sciences, University of Iceland, Reykjavik, ⁵Centre of Public Health Sciences, Faculty of Medicine, University of Iceland, Reykjavik, Iceland, and ⁶Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA

Objectives: Chronic pain is a debilitating condition that may cause additional symptoms affecting the sufferers' working capacity and quality of life. Studying the prevalence and consequences of chronic pain in various populations remains important for a complete picture of the global burden imposed by chronic pain conditions.

Methods: We investigated the prevalence of self-reported chronic pain conditions in Iceland in addition to symptoms and functional limitations within the group, using a population-based random sample. A questionnaire was mailed to 9807 Icelanders aged 18–79 years and, of these, 5906 participated in the study. Chronic pain was considered manifest in people reporting chronic low back pain, chronic neck symptoms, and/or fibromyalgia. Prevalence calculations were weighted with respect to gender, age, and residential area to represent the underlying population. Associations of chronic pain conditions with symptoms and functional limitations were measured with adjusted logistic regression models, contrasting symptoms in individuals reporting any of the three pain conditions with those who did not.

Results: The population-estimated prevalence of chronic pain condition was 19.9% with distinct gender differences (men = 15.2%, women = 24.7%). Several symptoms and functional limitations in daily life were strongly associated with chronic pain, including deficient energy and muscular discomfort, physical mobility limitations, lifting groceries, climbing stairs, and stooping. Women, but not men, with chronic pain tended to refrain from physical activity.

Conclusions: Chronic pain is a prevalent condition and those who report chronic pain generally suffer from ill health and limitations in their daily life compared to individuals not suffering from the condition.

Paper II

Mental health indicators and quality of life among individuals with musculoskeletal chronic pain: A nationwide study in Iceland

Björnsdóttir SV, Jónsson SH, Valdimarsdóttir UA.
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Mental health indicators and quality of life among individuals with musculoskeletal chronic pain: a nationwide study in Iceland

SV Björnsdóttir¹, SH Jónsson^{2,3}, UA Valdimarsdóttir^{4,5}

¹Department of Physical Therapy, Faculty of Medicine, University of Iceland, Reykjavík, ²Directorate of Health, Reykjavík, ³Department of Social Sciences, Faculty of Social and Human Sciences, University of Iceland, Reykjavík, ⁴Centre of Public Health Sciences, Faculty of Medicine, University of Iceland, Reykjavík, Iceland, and ⁵Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA

Objectives: Musculoskeletal chronic pain is a costly public health threat. The aim of our study was to investigate mental health indicators, including self-reported symptoms of depression, sleep disruption, stress, well-being, and quality of life (QoL), among men and women with musculoskeletal chronic pain in a general population.

Method: This was a cross-sectional study; a postal questionnaire was mailed to a stratified random sample of 9807 eligible Icelanders retrieved from a national registry, of whom 5906 responded (response rate = 60.2%). Chronic pain conditions included reports of current chronic back pain, chronic neck symptoms, and/or fibromyalgia. Gender-stratified associations of chronic pain conditions with mental health indicators were estimated with logistic regression analyses adjusting for age, income, body mass index (BMI), smoking, education, and residence.

Results: We observed higher odds of low satisfaction with life [adjusted odds ratio (OR^{adj}) women 2.0, 95% confidence interval (CI) 1.5–2.6; OR^{adj} men 2.3, 95% CI 1.7–3.1], higher levels of perceived stress (OR^{adj} women 1.7, 95% CI 1.3–2.2; OR^{adj} men = 1.5, 95% CI 1.1–2.1), depressive symptoms (OR^{adj} women 2.4, 95% CI 1.9–3.0; OR^{adj} men 2.8, 95% CI 2.1–3.7), and sleep disruption (OR^{adj} women 2.8, 95% CI 2.2–3.5; OR^{adj} men 2.2, 95% CI 1.5–3.1), and diminished QoL (OR^{adj} women 1.6, 95% CI 1.2–2.1; OR^{adj} men 1.5, 95% CI 1.0–2.1) among individuals with chronic pain compared with those without the condition.

Conclusions: Our data indicate that individuals with musculoskeletal chronic pain have increased risk of poor mental health and diminished QoL. Further studies are needed on treatment and preventative measures of a decline in mental health among individuals with chronic pain.

Paper III

Health-related quality of life improvements among women with chronic pain: Comparison of two multidisciplinary interventions

Björnsdóttir SV, Arnljótsdóttir M, Tómasson G, Triebel J, Valdimarsdóttir UA.

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RESEARCH PAPER

Health-related quality of life improvements among women with chronic pain: comparison of two multidisciplinary interventions

Sigrún Vala Björnsdóttir^{1,2}, Margrét Arnljótsdóttir³, Gunnar Tómasson², Jan Triebel^{3,4}, and Unnur Anna Valdimarsdóttir^{2,5}

¹Department of Physical Therapy, and ²Centre of Public Health Sciences, Faculty of Medicine, University of Iceland, Reykjavík, Iceland, ³HNLFI Rehabilitation Clinic, Hveragerði, Iceland, ⁴Department of Orthopaedic Surgery, Akademiska, University Hospital Uppsala, Sweden, and ⁵Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA

Abstract

Purpose: To measure the effect of 4 weeks traditional multidisciplinary pain management program (TMP) versus neuroscience education and mindfulness-based cognitive therapy (NEM) on quality of life (HRQL) among women with chronic pain. **Method:** This observational longitudinal cohort study conducted in an Icelandic rehabilitation centre included 122 women who received TMP, 90 receiving NEM, and 57 waiting list controls. Pain intensity (visual analogue scale) and HRQL (Icelandic Quality of Life scale) were measured before and after interventions. ANOVA and linear regression were used for comparisons. **Results:** Compared with controls we observed statistically significant changes in pain intensity ($p < 0.001$) and HRQL ($p < 0.001$) among women receiving both interventions, while NEM participants reported significant improvements in sleep (8.0 versus 4.4 in TMP; $p = 0.008$). Head to head comparison between study groups revealed that pain intensity improved more among TMP participants (21.8 versus 17.2 mm; $p = 0.013$ adjusted). Women with low HRQL at baseline improved more than those with higher HRQL (mean TMP = 13.4; NEM = 12.9 if HRQL ≤ 35 versus mean TMP = 6.6 and NEM = 7.8 if HRQL > 35). **Conclusions:** Our non-randomized study suggests that both NEM and TMP programs improve pain and HRQL among women with chronic pain. Sleep quality showed more improvements in NEM while pain intensity in TMP. Longer-term follow-ups are needed to address whether improvements sustain.

Keywords

Chronic pain, health-related quality of life, mindfulness, multidisciplinary rehabilitation, neuroscience patient education

History

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► Implications for Rehabilitation

- Chronic pain is a debilitating condition affecting quality of life and restricting societal participation.
- Intensive multidisciplinary bio-psycho-social rehabilitation is essential for this patient group.
- This study shows improvement in health-related quality of life and pain intensity following such rehabilitation.
- Emphasizing mindfulness based cognitive therapy and neuroscience patient education improves sleep to more extend than more traditional approach.

Paper IV

Long-lasting improvements in health-related quality of life among women with chronic pain, following multidisciplinary rehabilitation

Björnsdóttir SV, Triebel J, Arnljótsdóttir M, Tómasson
G, Valdimarsdóttir UA.

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Long-lasting improvements in health-related quality of life among women with chronic pain, following multidisciplinary rehabilitation

Authors: Sigrún Vala Björnsdóttir; Jan Triebel; Margrét Arnjóltsdóttir; Gunnar Tómasson; Unnur Anna Valdimarsdóttir

Abstract

Purpose: To determine if observed health-related quality of life (HRQL) improvements after 4-weeks traditional multidisciplinary pain management program (TMP) and additional neuroscience patient education and mindfulness-based cognitive therapy (NEM) for chronic pain are sustained at 6-months follow-up.

Method: This observational longitudinal follow-up study was conducted in Iceland and with complete follow up of 75 women (61.5% of group initiating treatment) who received TMP and 56 (62.2%) receiving NEM. Pain intensity (visual analogue scale) and HRQL (Icelandic Quality of Life scale), were measured at baseline and 6-months after interventions. Analysis of variance and linear regression were used for statistical analysis.

Results: Both groups showed sustained improvements from baseline to 6-months follow-up in pain intensity (change score TMP = -10.6 [$p<0.001$]; NEM = -14.5 [$p<0.001$]) and in HRQL (change score TMP = 6.4 [$p<0.001$]; NEM = 6.9 [$p<0.001$]). The sleep domain was not sustained among the TMP participants (change score = 2.4 [$p=0.066$]), whereas all other domains among both groups were sustained. Group comparisons show that the TMP group improved significantly more on anxiety than the NEM group (change score = 7.1 vs 3.3; $p=0.038$ adjusted) which may be due to coincidental non-respondence in TMP group with lower baseline anxiety scores. Significant decline was observed from discharge to 6-months among both groups but the NEM group significantly less in pain intensity (change score TMP=11.6 vs NEM=3.5; $p=0.022$ adjusted). No baseline differences were revealed between responders and non-responders.

Conclusions: These data suggest that improvements observed in 4-weeks multidisciplinary programs for women with chronic pain are sustained for 6-months after treatment.

