Sonja Broo, Maiju Marjamäki

WHO GETS ADVERSE EVENTS AFTER NAPRAPATHIC MANUAL THERAPY

Bachelor's thesis
Degree programme in Naprapathy, Bachelor of Health Care

2018

South-Eastern Finland
University of Applied Sciences

Tekijät	Tutkinto	Aika
Sonja Broo, Maiju Marjamäki	Naprapaatti	Toukokuu 2018
Opinnäytetyön nimi Who gets adverse events after naprapathic manual therapy		55 sivua 10 liitesivua
Toimeksiantaja Karoliininen instituutti		
Ohjaaja Eva Skillgate, D.N, PhD Petteri Koski, Naprapaatti, D.N Marja Turkki, lehtori		

Tiivistelmä

Manuaalisten terapiahoitojen jälkeen ilmaantuvat sivuvaikutukset ovat erittäin yleisiä. Useimmiten ne ilmaantuvat 24 tunnin sisällä hoidon antamisen jälkeen, ovat lyhytaikaisia, ja intensiteetiltään lievän ja kohtalaisen väliltä. Sivuvaikutuksille altistavia tai suojaavia tekijöitä on tutkittu jonkin verran, mutta nämä tutkimukset ovat osoittautuneet tutkimuskohteiltaan hyvin heterogeenisiksi. Useimmat aikaisemmat tutkimukset eivät ole tutkineet sivuvaikutuksia naprapatian kannalta. Tässä opinnäytetyössä sivuvaikutukset kuvattiin tapahtumina, jotka ilmenivät 24 tuntia annetun hoidon jälkeen ja jotka olivat intensiteetiltään kohtalaisia.

Tämän opinnäytetyön tarkoituksena oli tutkia sivuvaikutusten esiintyvyyttä kahden naprapaattisen manuaalisen hoitokerran jälkeen potilailla, jotka etsivät hoitoa epäspesifiseen niska- tai selkäkipuun tai niska- ja selkäkipuun, kun potilaiden ominaisuudet jaoteltiin alaryhmiin elämäntapojen, kivun ominaisuuksien sekä henkilökohtaisten profiilien mukaan. Tämä opinnäytetyö oli prospektiivinen kohorttitutkimus ja sekundaarianalyysi MINT-trial-nimiseen randomisoituun kontrolloituun tutkimukseen kerätystä materiaalista. Tämän opinnäytetyön tutkimuskohderyhmään valikoituneet (N = 928) vastasivat kerran kyselyyn lähtötilanteestaan ennen hoitoja sekä kyselyyn sivuvaikutuksista ensimmäisen ja toisen hoitokerran jälkeen. Sivuvaikutukset luokiteltiin kohtalaisiksi, kun niiden intensiteetti arvioitiin suuremmaksi kuin kolme numeerisella asteikolla (NRS = 0–10). Binominaalista regressioanalyysia käytettiin tutkimaan lähtötilanteen ominaisuuksien ja sivuvaikutusten esiintymisen yhteyttä.

Suurin osa tutkimukseen osallistuneista (52 %) ei saanut ainuttakaan kohtalaista sivuvaikusta ja toiseksi suurin ryhmä (16 %) sai yhden kohtalaisen sivuvaikutuksen hoidon jälkeen. Naissukupuolisuus tai korkea kivun intensiteetti lähtötilanteessa olivat altistavia tekijöitä sivuvaikutuksille, kun taas fyysinen aktiivisuus oli suojaava tekijä sivuvaikutuksia vastaan.

Tämän tutkimuksen yhteenvetona voidaan todeta, että naissukupuolisuus tai korkea kivun intensiteetti lähtötilanteessa olivat altistavia tekijöitä sivuvaikutuksille, kun taas fyysinen aktiivisuus oli suojaava tekijä sivuvaikutuksia vastaan.

Asiasanat

sivuvaikutukset, naprapatia, manuaalinen terapia, epäspesifi niskakipu, epäspesifi alaselkäkipu

South-Eastern Finland University of Applied Sciences

Author (authors)	Degree	Time
Sonja Broo, Maiju Marjamäki	Bachelor of Naprapathy	May 2018

Thesis title

Who gets adverse events after naprapathic manual therapy

55 pages
10 pages of appendices

Commissioned by

Karolinska Institutet

Supervisor

Eva Skillgate, D.N, PhD
Petteri Koski, Naprapaatti, D.N.
Marja Turkki, senior lecturer

Abstract

Adverse events (AEs) are very common after different manual therapy interventions. They usually occur within 24 h after treatment, are transient and mild to moderate in intensity. Factors exposing to and protective against AEs have previously been studied in some extent, but the studies are quite heterogeneous in regarding the study objectives. Most of the previous studies have not addressed naprapathy. In this thesis, AEs were defined as events occurring 24 h after treatment and being moderate in intensity.

The main purpose of this thesis was to examine the prevalence of AEs after two sessions of naprapathic manual therapy in subgroups of patients with different lifestyle, pain characteristics and personal profiles, seeking care for unspecific neck and/or back pain. This thesis was a prospective cohort study and a secondary analysis of the material collected in a randomized controlled trial called the “MINT-trial”. The population of this thesis (N=928) answered the baseline questionnaire once and AE-questionnaires after the first and the second treatment visits. The outcome AEs were defined as moderate when scored > 3 on an 11-point numeric rating scale (NRS). Binominal regression analyses were used to examine the association between the baseline characteristics and the occurrence of AEs.

Most participants (52 %) did not receive any moderate AEs, with the second major group being those receiving one moderate AE (16 %). Female gender or high pain intensity at baseline were risk factors for experiencing AEs, whereas physical activity was protective against AEs.

As a conclusion female gender and high pain intensity at baseline were risk factors for receiving moderate AEs, whereas physical activity was protective against receiving moderate AEs.

Keywords
adverse events, naprapathy, manual therapy, unspecific neck pain, unspecific low back pain

CONTENTS

APPENDICES

1 INTRODUCTION

Naprapathy has been studied increasingly during the past years. The research is mainly carried out at Karolinska Institutet, Stockholm. The main researcher in this field is Eva Skillgate (D.N., PhD), associate professor and leader of the Musculoskeletal & Sports Injury Epidemiology Center (MUSIC) at the institute. Adverse events (AEs) appearing after manual therapy (MT) has been studied in some degree, but none of the studies have mentioned naprapathy. Most of the studies addressing AEs involved chiropractors. Other included professions were osteopaths and physiotherapists. (Cagnie et al. 2004, 153–154; Rajendran et al. 2015, 640; Rubinstein et al. 2007b, 94; Walker et al. 2013, 1726–1727.)

AEs after naprapathic manual therapy (NMT) have previously been studied by Paanalahti et al. (2014), while Tabell (2015) investigated the role of AEs as prognostic factors. These studies are based on the MINT-trial (see page 33–34). There are some studies addressing predictive factors for AEs (Cagnie et al. 2004, 153–154; Hurwitz et al. 2005, 1480–1481; Senstad et al. 1996; Rajendran et al. 2015, 640; Rubinstein et al. 2007b, 94), but to our knowledge this is the first study that examines factors protective against and exposing to AEs after NMT for patients who have unspecific neck pain (NP) and/or low back pain (LBP).

2 BACKGROUND

2.1 Naprapathy

The word naprapathy comes from the Czech word napravit (fix) and from the Greek word pathos (pain). Naprapathy was derived from the chiropractic approach by Dr. Oakley Smith in the beginning of the 1900s. Based on the “subluxation-theory” used by chiropractors, Oakley developed a new way of thinking that is mainly supported by today’s science. The new approach explains dysfunction and pain e.g. via alterations in different connective tissues and problems in the surrounding soft tissues. (Svenska Naprapatförbundet 2017.)

Naprapathy is a physiatric treatment method specialized in examining, treating and preventing musculoskeletal disorders. Naprapaths are professionals in manual medicine in social healthcare and rehabilitation working multiprofessionally. In naprapathy the skill to examine and treat different mechanical and functional disorders is emphasized. Naprapaths use different clinical examination and treatment methods based on scientific evidence. Maintaining the occupational skills requires continuous following of scientific research and participating in international courses. Naprapaths are educated in college degree level in Finland, Sweden and the USA. In Finland naprapaths are registered professionals by National Supervisory Authority for Welfare and Health (Valvira). (Suomen Naprapaattiyhdistys 2018.)

2.2 Neck pain (NP)

According to the Global Burden of Disease 2010 Study, NP is the fourth leading cause of years lost to disability with annual prevalence rate reaching 30%. It is ranked behind LBP, depression, and other musculoskeletal disorders. (US Burden of Disease Collaborators 2013, 591–608.) Cohen (2015) notes that acute NP will resolve with or without treatment but approximately 50% of NP population will continue to experience notable pain of some degree or frequent pain episodes. It is estimated that about 48.5% of all individuals aged 18-84 are going to experience a clinically important NP during their lifetime (Fejer et al. 2006, 836–845).

Finnish study Terveys 2011 presents the prevalence of NP within Finnish population in 2011. Of all the participants who had experienced NP during the previous 30 day-period, were 41 % of women (as much as BP) and 27 % of men (less than BP, 35 %). The incidence of NP decreased with age for women, but for men there was no age-related connection. Compared to similar study Terveys 2000, the incidence of NP increased for men aged <45 years and women aged <55 years, but decreased in most of the older age groups. (Viikari-Juntura et al. 2012.)

According to Finnish practical guidelines referred in Pohjalainen (2009a, 340–347), NP is classified into different groups according to patient's anamnesis, symptoms and findings:

1. Localized NP (cervigalcia)
2. Radiating NP (cervico brachialgia)
3. Whiplash associated injuries
4. Myelopathy (medulopatia and dural compression)
5. Other NPs (associated to general diseases and tumours, or post-traumatic cervical spine fractures)

The duration of symptoms with the first two neck pain groups are divided into acute (<12 weeks) and chronic (>12 weeks) (Pohjalainen 2009a, 340–347). According to Barnsley et al. (1994) a remarkable proportion of whiplash injury patients develop a chronic state after six months of continuing disabling symptoms and pain (Myrtveit et al. 2013). Spitzer et al. (1995) notify that the Quebec Task Force has suggested the use of the term 'Whiplash Associated Disorders' (WAD) to describe the symptoms of whiplash because they are not always limited to the neck (Lovell & Galasko 2002, 97). Local neck-shoulder pain seems to be the most common symptom with NP patients. It is important to assess differential diagnostic measurements to limit severe diseases such as trauma, rheumatoid arthritis, nerve entrapment, compression of spinal cord, malignity, deep infections and dislocation of arteria carotis or –vertebralis. (Pohjolainen 2009a, 340–347.)

The main risk factors of NP include several physical factors, age and gender (female) and overweight. Smoking seems to be a factor increasing the risk of NP. (Pohjolainen 2009a, 340–347.) Skillgate et al. (2009, 553) found out that smoking is associated with an increased risk of long-term sick leave due to unspecific back or neck pain. Kääriä et al. (2012) state that within working-age population there are some potentially modifiable risk factors for chronic NP. They include workplace bullying, sleep problems, and high BMI in women, while with men, work-related emotional exhaustion plays the biggest role. The importance of pain history, with reference to both neck- and low back pain is accentuated when evaluating the risk for future chronic NP. (Kääriä et al. 2012, 914–919.) The prevention of NP includes maintaining ergonomic posi-

tions at work, but the most effective actions to give positive reactions has been provided with individual training which includes dynamic workout programs, stretching and relaxation techniques. (Pohjolainen 2009a, 340–347.)

2.3 Low back pain (LBP)

LBP seems to be an extensive problem throughout the whole world (Hoy et al. 2012, 2028). Hoy et al. (2012, 2033) estimates the lifetime prevalence of LBP to be 38.9 %, whereas Airaksinen et al. (2006, S208–S209) estimate it to be up to 84 %. The prevalence is higher among females and among those aged 40–69 years, and as well in high-income countries compared to middle- and low-income countries (Hoy et al. 2012, 2033). According to Pohjolainen (2009b, 348–349) the incidence of chronic back pain has declined during a 20-year follow up among Finnish people. The Mini –Suomi study done during 1978–1980 stated that 18 % of men and 16 % of women suffered from chronic back pain, whereas the Terveys 2000 study reported that only 10 % of men and 11 % of women suffered from chronic back pain (Pohjolainen 2009b, 348–349). According to Viikari-Juntura et al. (2012, 92–95) the occurrence of LBP within the past 30 days was 41 % among women and 35 % among men. Among men age was not related to the occurrence of LBP, while the incidence of LBP increased with age among women. Since the year 2000 the incidence of LBP increased among both men and women, mostly in the age group 30–54 years. (Viikari-Juntura et al. 2012, 92–95.) Different conditions of the back are the most common musculoskeletal problems, and the economical burden due to these problems is great (Pohjolainen 2009b, 348-349). After an initial episode of LBP 44–78 % of the population suffers from pain relapses and 26–37 % suffers from relapses of work absence. LBP is disabling in 11–12 % of the population. (Airaksinen et al. 2006, S208–S209.)

Strenuous work, especially repetitive lifting, demanding work positions and vibrations are connected to the frequency of different problems in the back. Smoking, frequent driving and obesity increase the risk of back problems. Psychological factors appear to have an impact on the risk even though the evidence is contradictory. There is not enough convincing evidence of any

specific prevention method against back problems. Enhancing general health seems to be a proper way of preventing different back conditions. Regarding back problems it is furthermore important to do an early assessment, treatment and rehabilitation. In addition, an early activation of the patient and preventing progression of the condition has an important role. (Pohjolainen 2009b, 92–95.)

Pohjolainen (2009b, 92–95) divides acute back pain symptoms in three groups:

1. A possible serious or specific condition, approximately 1–5 % of patients.
2. Sciatica, approximately 5–10 % of the patients. Symptoms in the lower limb implicating dysfunction of the nerve root. These symptoms are usually caused by herniated disc.
3. Unspecific back problems, approximately 80–90 % of patients. Unspecific problems are symptoms in the back area without implications of nerve root damage or serious conditions.

2.4 Characteristics of unspecific neck and back pain patients

Those who seek care for neck or back pain seem to have worse health condition than those who do not seek health care (Côte et al. 2001). Neck and back pain patients visiting chiropractors are more active in daily functioning and report less comorbidities than those who visit medical doctors or physiotherapists, and further those with more severe and complex symptoms rather consult specialized doctors with exception of LBP or fibromyalgia which are usually treated non-pharmacologically. (Côte et al. 2001; Horn et al. 2017, 232.) Freburger et al. (2005, 885, 872) suggest that underuse of the treatment provided by physiotherapists is occurring by those who benefit from it or overuse by those who do not benefit from it, or both.

Patients utilizing the spinal manipulative therapy (SMT) performed by physicians consist mainly of spine problems, of whom LBP without radicular symptoms are 30 % and NP patients 17 % (Schuller et al. 2017, 5). Chiropractors are primarily treating patients with back and neck pain with the distribution of

pain primarily ongoing on the back region (Assendelft et al. 1995; French et al. 2013, 690; Hurwitz et al. 1998, 774).

When spinal pain patients seek care from physicians using SMT, the duration of the spinal pain is mostly long-lasting (> 1 year) with moderate functional disturbance (Schuller et al. 2017, 5-6). In a study examining the LBP patients visiting chiropractors had contrasting results to previous findings. The study showed that > 40 % of patients with LBP had acute episodes and 20 % had chronic episodes which indicate that patients with acute pain episode are more likely to visit a chiropractor. (Hurwitz et al. 1998, 775.) More recent studies show that in Sweden, Denmark and UK the LBP patients seeking care from chiropractors share mostly similar characteristics and course of symptoms. In Sweden, the patients had more longer lasting pain episodes (> 30 days) compared to UK and Denmark, but Denmark had more acute LBP episodes (62 % of patients) compared to UK (49 %). The chronic pain episodes in Denmark consisted only 13 % and in UK 17 % of all patients. (Kongsted et al. 2015, 4–6.)

Neck and back pain patients visiting a physician using SMT had a NRS pain mean score of 6.0 at baseline (Schuller et al. 2017, 5). LBP patients visiting a chiropractor in Northern Europe countries had similar findings but patients in Sweden had lower LBP intensity at baseline of NRS 4.0, while the median score for Denmark was 7.0 and for UK 6.0. In addition the lower LBP intensity at baseline had stronger associations with patient outcomes in Sweden compared to other countries. (Kongsted et al. 2015, 4–6.)

Most encounters between chiropractors and patients (71 %) occur with patients aged 25-64 years-old (French et al. 2013, 689). Hurwitz et al. (1998, 774) supports this finding by claiming that chiropractic patients are mainly middle-aged. According to Freburger et al. (2005, 880) patients visiting a physiotherapist for neck or back pain are more likely to be aged between 35 and 49 than older. In an older study, the chiropractic patients are women with a small majority (Hurwitz et al. 1998, 774). Recent studies support these find-

ings (French et al. 2013, 689; Blum et al. 2008, 178). Patients visiting physicians who use SMT are mostly women (Schuller et al. 2017, 4), and furthermore those visiting a physiotherapist due to neck or back pain are more likely women (Freburger et al. 2005, 880).

There are some differences in health motivations when stratified by gender and geographic regions multi-nationally. The significant differences apply only for European population. More European women prefer chiropractic treatment for prevention care (75 %) about 13 % more than women in Australia or US. The European men prefer to use chiropractic treatment mainly for sick role care with almost 60 % of preference compared to Australia or US (both 34 %). (Blum et al. 2008, 178.) These findings are consistent with the literature and highlight the socio-cultural and ethnic factors for patients' motivations and symptom perceptions for seeking care from MT (Blum et al. 2008, 180). For example, when considering the race factor, the motivation for seeking care for neck and back pain in the US was different between blacks and whites in the early 1990s with black people reporting higher pain and disability but lower use of health care. In modern society the health care utilization for neck and back pain is mainly similar between races. (Carey et al. 2010, 346.) Patients visiting a chiropractor have more likely a higher educational level (French et al. 2013, 689). In addition the patients with a higher level education of more than 4 years utilize physiotherapy 10 % more likely than those with high school education or less (Freburger et al. 2005, 880).

Patients who have visited previously a standard medical care giver or alternative treatment therapist are more likely to visit a manual therapist/physiotherapist/physician using SMT than those who had not previously used any alternative care providers help (Schuller et al. 2017, 5; (Freburger et al. 2005, 880). However, the largest source of referral is not by other therapist/chiropractor but by patient's self-referral (Assendelft et al. 1995), or by another patient in about 52 per 100 encounters (French et al. 2013, 690).

In a multi-national study the patients using chiropractic treatment are mainly those who seek care for wellness, prevention of illness and to reduce the risk of illness or injury without a specific complaint of pain area (42 %). 41 % of patients report the need for self-care and only 17 % are specifically seeking care for illness (sick role). Patients aged ≤ 65 are more likely to be motivated to seek treatment for self-care while patients aged ≥ 66 seek care equally between different motivational aspects of wellness, prevention, risk care, sick role and self care. There is a statistically significant difference between male and female behaviors when seeking the care for health within chiropractic field. Male patients want to reduce the risk of getting an illness or an injury or seek care for specific sickness while women are more likely to seek care for self-care purposes. (Blum et al. 2008, 177–179.) The study by French et al. (2013, 690) promotes the trend for patients seeking care for maintenance and wellness, as well as check-ups.

2.5 Manual Therapy

DeStefano & Greenman (2010) and Farrell & Jensen (1992) define MT as a nonsurgical conservative treatment protocol using the practitioner's hands and/or fingers on the patient's body (Tsertsvadze et al. 2014, 343). The purpose of the manual therapist in patient's rehabilitation is to assess pain and function, detect abnormalities of movements, test anatomical structures of tissues, and contemplate a realistic treatment program. The treatment is optimized to allow full recovery and function. (Maitland 1986 cited in Farrell & Jensen 1992, 843.) MT's are classified into non-thrust and thrust-based techniques. While non-thrust-based techniques apply a low-velocity and low-force procedure that does not involve an audible sound, the thrust-based techniques are applied with a high-velocity and low-amplitude procedure and often accompanied with cavitation sound from one or multiple joints. (Goss et al. 2012, 663.)

The traditional medical medicine, e.g. physiotherapy, orthopedics, and sports medicine, and complementary or alternative medicine, e.g. chiropractics, osteopathy, use MT as a part of their treatment protocols. MT within these fields

consists of different techniques such as manipulation, mobilization, static stretching and muscle energy techniques (MET). Among different health care professionals, the definition and purpose of MT varies, and the key concepts as well as treatment strategies vary. (Tzertsvadze et al. 2014, 345–356.) There are several MT approaches including Cyrlax (Orthopedic Medicine), Mennell, osteopathic, Maitland, Kaltenborn, and McKenzie. (Farell & Jensen 1992, 846–848).

Table 1. Categorization of manual therapy techniques

Manual Therapy Techniques	Definition	Desired Outcome
Joint Biased		
• Manipulation	Passive movement of a joint beyond the normal range of motion	Improved range of motion (ROM) Decreased muscle spasm
• Mobilization	Passive movement of a joint within its normal range of motion	Decreased pain
Soft Tissue Biased		
• Swedish Massage	Stroking and kneading of the skin and underlying soft tissue	Improved circulation Decreased muscle spasm Relaxation
• Deep Tissue Massage	Deep stroking and pressure across the muscles and soft tissue	Re-aligned soft tissue Break adhesions Increased ROM
• Trigger Point Massage	Deep pressure to areas of local tenderness	Releases muscle spasms Removes cellular exudates
• Shiatsu Massage	Varying, rhythmic pressure from the fingers	Improved circulation Decreased muscle spasms Relaxation
• Muscle stretching	Static, dynamic or pre-contraction stretch that increases the length of a musculotendinous unit	Increased ROM Decreased muscle spasm Decreased muscle tension
Nerve Biased		
• Neural Dynamics	Passive, combined movement of the spine and extremities, within their normal range of motion, in ways to elongate or tension specific nerves	Improved range of motion Decreased pain

Table 1 presents the categorization of different MT techniques used in different professions. This table offers a brief definition of the technique in question and the desired outcomes on wanted structures. Joint biased techniques in-

clude manipulation and mobilization, soft tissue biased include different massage and muscle stretching techniques and nerve biased include neural dynamics (Bialosky et al. 2009, 16; Page 2012, 110–112).

Tzersvadze et al. (2014) collected information on clinical practice guidelines from several countries, and found out that in the United States, Great Britain, Canada, and the Netherlands, these guidelines recommend the use of manipulation and mobilization in health care. The guidelines of The European Workgroup recommend the use of spinal manipulation and mobilization for patients concerned with chronic LBP (Airaksinen et al. 2006, 240–244). Furthermore, Finnish guidelines have a strong recommendation for using manipulation therapy for chronic LBP (Jousimaa 2013). The reasons for inconsistent recommendations in different countries are unknown (Coulter et al. 2018, 10).

The MT treatment includes the technique, the provider, the participant, the environment, and the interaction between these different elements. This furthermore contributes to patient outcomes, and the effects of MT are related to multiple mechanisms. (Ernst 2000; Kaptchuk 2002 cited in Bialosky et al. 2011.)

Spinal manual therapy

Manipulation and mobilization therapies seem to present similar results for all of the outcomes at immediate/short/intermediate-term follow-up for neck pain. Multiple cervical manipulation treatments may provide improved functionality and better pain relief than some medications at immediate/intermediate/long-term follow-up. (Gross et al. 2015, 2–3.) Paanalahti et al. (2016), studied the effect of MT including spinal manipulation, mobilization, stretching and massage for patients seeking care for neck and/or back pain, and the results show similar improvements whether spinal manipulation or stretching is excluded separately from the treatment provided. High-level evidence presented by Miller et al. (2010, 315–352) show that with sub-acute and chronic NP, the spinal

MT together with exercise therapy is effective in the short-term but not long-term differences when compared with only exercise therapy.

D'Sylva et al. (2010, 424–429) findings are introduced in this chapter and they suggest that there are no differences between mobilization and manipulation with placebo treatment in subacute or chronic NP when considering pain intensity decrease, improvement of performance or the experienced effectiveness of the treatment. There are some controversial results when compared to physiotherapy, medical treatment or exercise therapy. There seems to be some low-level evidence on the effectiveness of the spinal MT when used on a multiple vertebrae segments with the treatment of acute and subacute whiplash associated disorders (WAD) right after the treatment compared to other treatment modalities or physiotherapy.

The systematic literature studies of manipulation and mobilization for NP have a high standard, but their level of standard is weakened by the absence of blinding process within the original studies. Furthermore, there is no recognition of the possible placebo effect which leads to several methodological faults that might affect the outcomes. The long-term effectiveness has been mainly disregarded, as well as the control to restrict the patients' participation in other treatment modalities during studies. The concept of mobilization varies greatly between the studies. (Coulter et al. 2018; Gross et al. 2015; Gross et al. 2010; D'Sylva et al. 2010; Miller et al. 2010.)

For some individuals, who experience musculoskeletal chronic or subacute LBP, MT has been proven to be partially effective intervention in rehabilitation (Chou & Huffman 2007, 494–499; Furlan et al. 2015, 10–24). Many noninvasive therapies for chronic low back pain seem to be as effective when compared with each other. However, the research on subacute LBP seems to have very little information about the effectiveness of different therapies, even though multiple trials have had mix of both chronic and subacute LBP populations. (Chou & Hoffman, 2007, 494–499.)

Mobilization

There is poor evidence of the beneficial outcomes from cervical mobilization with subacute and chronic NP patients. There is high evidence of short-term effect when combined with exercise therapy in the treatment of chronic mechanical NP, but the evidence lacks on the long-term effectiveness. There are some differences in mobilization techniques and how some may decrease pain more than others. (Farooq et al. 2018, 27–29; Miller et al. 2010, 343–352.) According to Coulter et al. (2018, 5–10), there is medium quality evidence that mobilization affects slightly more positively in regards of reducing pain intensity and disability with chronic LBP when compared to exercise treatment. The difference still is not a statistically significant finding.

Manipulation

Cervical manipulation intervention might decrease acute NP short-term but there is limited research on the subject of its effectiveness when combining manipulation to other active treatment modalities (Gross et al. 2015, 2–3). Manipulation has no long-term effect on chronic NP, and the short-term impact does not differ greatly from the effectiveness of conventional treatment (Gross et al. 2015, 2–3; D'Sylva et al. 2010, 424–429). Manipulation is not more or less effective treatment option than mobilization for acute and chronic NP (Gross et al. 2015, 2–3). Low level evidence on the effectiveness of thoracic manipulation in acute and chronic NP, when the variable for outcomes was the immediate or short-term (2 months) pain relief or decrease. When thoracic manipulation was used together with mobility- and strengthening exercises, the pain decreased more on long-term compared to only exercise intervention. (Gross et al. 2010, 323–327; Cross et al. 2011, 635–637.)

Manipulation is not an effective treatment modality with acute LBP. The effect is same as when treated with conventional medical care. (Rubinstein et al. 2012.) In long term and chronic LBP, the spinal manipulation is an effective treatment modality. It is as equal as the standard medical care, exercise ther-

apy or physiotherapy for the pain reduction and functional improvement. (Rubinstein et al. 2011.) New evidence suggests that there is small to moderate effectiveness on behalf of manipulation for chronic LBP patients when the pain has lasted ≥ 3 months. The effectiveness increases in time after 3-6 months of pain duration. Manipulation has therefore reduced the amount of disability on moderate based evidence. There still seems to be lacking evidence about the effectiveness of manipulation when compared to intervention groups of no treatment or sham. (Coulter et al. 2018, 5–10.)

Massage

The more instances of massages and the longer lasting treatments the patients receive, the better outcome there is on NP reduction on short-term. The benefits diminished after the treatments stopped and were no longer statistically relevant. (Cook et al. 2015, 6–9.) Ezzo et al. (2007) suggest that while the evidence of the effectiveness of massage is not high-quality and there are no recommendations to use it as an intervention with NP patients, it is still used commonly as an independent or combined with other treatment modalities. Furlan et al. (2015, 10–24) propose that the effectiveness of massage for LBP is somewhat effective. Improvements for subacute and chronic LBP are only to be seen in the short-term follow-up, and this is mostly functional improvement compared to inactive individuals. It seems that especially rehabilitative active training combined with massage reduces pain. The evidence suggests that acute LBP is not cured with massage. The studies of the impact of massage are extremely heterogenic, and the massage interventions varied noticeably from their type, intensity and duration. (Furlan et al. 2015, 10–24.)

Muscle stretching

NP can be reduced as well as the neck function be increased within office workers who have moderate to severe NP by stretching the neck and shoulder region in a four-week period on a frequent basis. These findings support previous findings that the frequency of exercises ≥ 3 times/week correlates with

the improvement of the life quality and neck functions. (Tunwattanapong et al. 2016, 66–69.) A novel exploratory meta-analysis shows clinically meaningful improvements within pain score when certain intervention options are included in the rehabilitation among others, and when treating chronic LBP, stretching seems to present the largest improvements for pain outcomes compared to all exercise therapies (Hayden et al. 2005). For people experiencing LBP due to increased anterior pelvic tilt and rotation modified by over active erector spinae muscles, stretching exercise is less effective than motor control exercises, indicating that compensatory pelvic posture and muscle activity is rather altered by motor control than increased muscle stiffness (Park et al. 2016, 580–582). Assisted stretching in water is a beneficial additional pain- and disability reducer along the land based stretching when treating people with chronic LBP but more cost effective when combined with basic stretching. (Keane, 2017.)

The physiology behind MT

Regardless of the clinical evidence, the detailed mechanisms of how MT works on pain are unknown (Bialosky et al. 2011, 1). The clinical effectiveness of non-pharmacologic therapies for acute LBP has limited evidence. The reason for this is the substantial natural improvement of the pain in most patients. (Pengel et al. 2002 cited in Chou & Hoffman 2007, 500.) The only evidence based non-pharmacological therapies that target the acute LBP with good evidence for moderate benefits are superficial heat and with fair evidence for small to moderate benefits is spinal manipulation. Several other noninvasive therapy modalities (back school, interferential therapy, low-level laser therapy, lumbar supports, TENS, traction and ultrasonography) have not been proven to be effective neither with acute, subacute or chronic LBP. (Chou & Hoffman 2007, 494–499.)

2.6 Adverse events after manual therapy

Adverse events (AEs) are defined as any unfavorable and unintended sign (including abnormal laboratory findings), symptom or disease temporally as-

sociated with the use of a medical product, procedure or treatment that may or may not be considered to be related with the product, procedure or treatment. (European Medicines Agency 2002, 5; National Institute of Health (NIH) 2006, 1.) Based on this definition Pohlman et al. (2014, 452) created a definition of AEs suitable for MT: *"Any unfavorable sign, symptom, or disease temporally associated with the treatment, whether or not caused by the treatment."*

Even though the term AE is internationally defined and accepted, the literature still uses various terms to describe the phenomenon in question: adverse reactions, symptomatic reactions, side effects, unpleasant reactions (Eriksen et al. 2011, 2), harm, adverse effects and complications (Carlesso et al. 2010, 456).

The occurrence of AEs is quite common. According to Paanalahti et al. (2014, 5–7) 37 % of patients that had at least three visits reported AEs after every visit, while 51 % had AEs after any of the visits. In their study only 13 % of patients reported no AEs after any of the visits. Similar results were presented by Rubinstein et al. (2007a, 413) who reported that 56 % of the study population had at least one AE after any of the first three treatments and Cagnie et al. (2004, 152) who observed that 60.9 % of the study participants reported at least one AE. Senstad et al. (1997, 435, 436–438) reported at least one experienced AE by 55 % of the study participants at some time during the course of maximum six treatments. Of the 4712 treatments in their study, 1174 (25%) resulted in at least one type of AE. However, Hurwitz et al. (2005, 1480–1481) presented that only 30.4 % of the study participants reported AEs. In their study the total number of reported AEs after chiropractic treatment was 212. Walker et al. (2013, 1726–1727) examined the frequency and severity of AEs occurring after short-term usual chiropractic care of the spine compared to a sham treatment group. They noticed that at least one AE after any of the treatments was reported by 42 % of the usual care group compared to 33 % of the sham group. The total sum of reported AEs was 198, of which 106 was reported in the usual care group compared to 92 in the sham group. However,

according to Walker et al. (2013, 1726–1727), the risk ratio (RR) was not significant for experiencing an AE.

Most of the study participants experiencing AEs reported more than one AE: Of the participants experiencing at least one AE, 62.9 % reported two or more AEs (Cagnie et al. 2004, 152), while Walker et al. (2013, 1726–1727) reported the corresponding numbers to be 71 % in the sham group and 77 % in the usual care group. However, Senstad et al. (1997, 435, 436–438) observed that two or more AEs were reported after 251 (5 %) treatments.

Rubinstein et al. (2007a, 413) concluded that musculoskeletal (72 %) or pain (75 %) related AEs were the most common reported AEs in their study. The most common AEs reported by Paanalahti et al. (2014, 5–7) were soreness in muscles, accompanied by increased pain, stiffness and tiredness. One or all of these AEs were furthermore reported as common by Cagnie et al. (2004, 152), Hurwitz et al. (2005, 1480–1481), Leboeuf-Yde et al. (1997), Walker et al. (2013, 1726–1727) and Senstad et al. (1997, 435, 436–438). Other common AEs reported were headache (Cagnie et al. 2004, 152; Hurwitz et al. 2005, 1480–1481; Leboeuf-Yde et al. 1997; Walker et al. 2013, 1726–1727; Senstad et al. 1997, 435, 436–438), worsening of complaints (Cagnie et al. 2004, 152), radiating pain or discomfort (Cagnie et al. 2004, 152; Hurwitz et al. 2005, 1480–1481; Walker et al. 2013, 1726–1727; Senstad et al. 1997, 435, 436–438), local discomfort in the treated area (Leboeuf-Yde et al. 1997; Senstad et al. 1997, 435, 436–438) and pain in other than the treated area (Leboeuf-Yde et al. 1997).

AEs regarded as uncommon accounted for less than 8 % (Rubinstein et al. 2007a, 413) or less than 5 % (Leboeuf-Yde et al. 1997; Walker et al. 2013, 1726–1727; Senstad et al. 1997, 435, 436–438) of the reported AEs. However, Rubinstein et al. (2007a, 413) highlighted that at least one of these uncommon reactions were reported by 19 % of the study participants. The more uncommon AEs reported in the studies were muscle spasm (Cagnie et al. 2004, 152; Walker et al. 2013, 1726–1727), dizziness, nausea (Cagnie et al.

2004, 152; Hurwitz et al. 2005, 1480–1481; Leboeuf-Yde et al. 1997; Rubinstein et al. 2007a, 413; Walker et al. 2013, 1726–1727; Senstad et al. 1997, 435, 436–438), tiredness or fatigue (Rubinstein et al. 2007a, 413; Walker et al. 2013, 1726–1727) and ringing in the ears (Hurwitz et al. 2005, 1480–1481; Rubinstein et al. 2007a, 413). Hurwitz et al. (2005, 1480–1481) have reported imbalance, weakness in one or more extremities, depression or anxiety, vomiting, blurred or impaired vision and confusion or disorientation, while sleeplessness and joint swelling were reported by Walker et al. (2013, 1726–1727) and hot skin by Senstad et al. (1997, 435, 436–438). No serious AEs were reported in any of the studies (Paanalahti et al. 2014, 5–7; Hurwitz et al. 2005, 1480–1481; Rubinstein et al. 2007a, 413; Senstad et al. 1997, 435, 436–438).

Most AEs typically occur shortly after treatment (Leboeuf-Yde et al. 1997; Senstad et al. 1997, 435, 436–438). Cagnie et al. (2004, 152) and Senstad et al. (1997, 435, 436–438) stated that most of the AEs (60.54 % vs. 64 %) started within 4 hours post manipulation, while Hurwitz et al. (2005, 1480–1481) and Walker et al. (2013, 1726–1727) indicated that most of the reported AEs started within 24 hours post treatment. Rubinstein et al. (2007a, 413) reported that 90 % of the study participants informed that the AE started within two days of the treatment session.

The occurred AEs seem to disappear shortly after treatment or the occurrence of the AE (Leboeuf-Yde et al. 1997; Senstad et al. 1997, 435, 436–438). According to Cagnie et al. (2004, 152), Hurwitz et al. (2005, 1480–1481), Walker et al. (2013, 1726–1727) and Senstad et al. (1997, 435, 436–438) the occurred AEs disappeared 24 hours post treatment or occurrence of the event in question. In the study made by Cagnie et al. (2004, 152) only 19.37 % of the reported AEs lasted more than 48 hours post treatment. Senstad et al. (1997, 435, 436–438) presented that among the different types of reactions, radiating discomfort lasted the longest followed by local discomfort.

AEs seemed to be more common after the first visit or in the early stages of the treatment series (Rubinstein et al. 2007a, 413; Paanalahti et al. 2014, 5–7;

Leboeuf-Yde et al. 1997; Senstad et al. 1996). In their study Rubinstein et al. (2007a, 413) reported 571 experienced AEs after the first visit compared to 166 AEs after the third visit. The number of experienced AEs seemed to be higher after the first treatment visit compared to later visits during the treatment process (Rubinstein et al. 2007a, 413).

The intensity of the reported AEs was mostly regarded as mild or moderate (Cagnie et al. 2004, 152; Rubinstein et al. 2007a, 413; Senstad et al. 1997, 435, 436–438). In the study of Rubinstein et al. (2007a, 413) 13 % of the study participants reported an AE considered severe in intensity after any of the first three treatments, of which 64 % reported only one AE regarded severe in intensity. When considering AEs that occurred after the first and second visit, 14 % and 15 % of the reported AEs respectively were regarded as severe in intensity. Similar results were presented by Senstad et al. (1997, 435, 436–438) who stated that 14 % of the reported AEs were described as definitely unpleasant and 1 % as unbearable. Walker et al. (2013, 1726–1727) reported the most common intensity of AEs as moderate (50 %) in the sham group and moderate (37 %) or severe (37 %) in the usual care group. The number of AEs considered as severe didn't differ between the two treatment groups. A positive association was found between severity and duration of AEs by Senstad et al. (1997, 435, 436–438).

Rubinstein et al. (2007a, 413), Hurwitz et al. (2005, 1480–1481) and Senstad et al. (1997, 435, 436–438) indicated that AEs didn't have a major effect on the study participants' ability to perform their daily activities, while Cagnie et al. (2004, 152) noticed that 26.6 % of the study population reported a negative impact on the ability to perform their daily activities with the corresponding number being 11 % in the study by Senstad et al. (1997, 435, 436–438).
Of the specific AEs, only tiredness were most often reported as mild, while other AEs were most often considered moderate in intensity. Radiating discomfort was most often reported as severe in intensity. Reports of unbearable discomfort came most often from women. (Senstad et al. 1997, 435, 436–438.)

2.6.1 Predictors of adverse events

Studies addressing predictive factors for AEs approached the subject from different perspectives. The predictive factors for AEs could roughly be divided into different categories, such as personal, lifestyle, pain or problem related and treatment related factors. When considering personal factors, Cagnie et al. (2004, 153–154), Hurwitz et al. (2005, 1480–1481), Senstad et al. (1996) and Paanalahti et al. (2014, 5–7) stated that women were more likely to report AEs when compared to men. Rajendran et al. (2015, 640) discovered a small or medium correlation was reported between HVLATT (high velocity low amplitude thrust technique) and female gender. In addition Senstad et al. (1996) noted that when compared to AEs reported by men, women reported different types of AEs, while Cagnie et al. (2004, 153–154) stated that women complained significantly more headache, fatigue and local discomfort. Age was found as predictive by Cagnie et al. (2004, 153–154), Hurwitz et al. (2005, 1480–1481) and Rajendran et al. (2015, 640). Cagnie et al. (2004, 153–154) reported that for every one year of increase in age there was a 2.4 % decrease in the risk of headache after spinal manipulation, while Rajendran et al. (2015, 640) found small or medium correlation between HVLATT and age. Hurwitz et al. (2005, 1480–1481) stated that AEs were more likely reported in the age group 30–39 years old when compared to other age groups. It must however be noted that in their study Rajendran et al. (2015, 640) argued that HVLATT, gender and age didn't function as predictive factors when considered AEs reported 24 hours post treatment. Rubinstein et al. (2007b, 94) proposed a moderate association between working status (e.g. sick leave) and AEs.

When factors related to lifestyle were observed Cagnie et al. (2004, 153–154) discovered that smokers reported significantly more headache after spinal manipulation when compared to non-smokers, while Rajendran et al. (2015, 640) stated that previous smokers seemed a bit more likely to report an AE 24 hours post treatment.

Many studies addressed pain or problem related factors as predictors for AEs. The duration of pain in the previous year (Rubinstein et al. 2007b, 97–99) and the use of regular medication (Cagnie et al. 2004, 153–154) had a significant association to new or increased headache after chiropractic or spinal manipulative treatment. Hurwitz et al. (2005, 1480–1481) reported that study participants with mild or no headaches were much less likely to report headache as an AE after treatment, compared to those with moderate or severe headaches. Similar results were discovered by Cagnie et al. (2004, 153–154) who noted that patients with migraine had significantly more headaches than migraine-free patients.

According to Rubinstein et al. (2007b, 97–99) increased neck pain was weakly associated with neck disability at baseline and moderately associated with intermittent neck pain in the previous year, while headache at baseline was protective against increased neck pain. AEs associated with chiropractic care were more likely reported by study participants with a history of trauma to the neck, pain less than one year, worsening of pain since the onset, pain rated eight or more on a scale from 0–10, Neck Disability Index (NDI) score 16 or more, moderate or severe headache, nausea over the previous month and disbelief towards the treatment. Study participants with higher NDI scores (moderate or severe neck disability) were more likely to report one of the more rare but possibly more severe neurologic AEs (i.e. dizziness, nausea, blurred or impaired vision, weakness in the extremities and confusion) than those with lower NDI scores. (Hurwitz et al. 2005, 1480–1481.) Hurwitz et al. (2005, 1480–1481) highlighted that same or even stronger associations was noted between the predictors discovered in their study and AEs occurring within 24 h post treatment and rated two or more in severity. Visiting a general practitioner six months prior to the chiropractic treatment series was reported as a protective factor against AEs by Rubinstein et al. (2007b, 97–99).

Factors related to treatment were addressed in the literature. Hurwitz et al. (2005, 1480–1481) discovered that study participants randomized to the manipulation group were more likely to report an AE than those randomized to

the mobilization group. Those in the manipulation group tended to report more AEs with an onset 24 hours post treatment and AEs with a higher severity level than those in the mobilization group. However, Paanalahti et al. (2014, 5–7) found no differences between the three treatment arms used in the study (see page 33–34) concerning the occurrence of AEs. According to Senstad et al. (1996) AEs occurred more frequently after thoracic spine manipulation. This is opposed by Cagnie et al. (2004, 153–154) who discovered that manipulation of the cervical spine only caused significantly more headache and fatigue than lumbar and thoracic spine manipulations. The less commonly reported AEs (dizziness and nausea) were significantly more present after cervical manipulation (Cagnie et al. 2004, 153–154). When comparing upper cervical manipulations with lower cervical manipulations Cagnie et al. (2004, 153–154) noticed that upper cervical manipulations caused significantly more headaches compared to lower cervical manipulations. Senstad et al. (1996) reported that AEs occurred more often when many spinal regions were treated, while Cagnie et al. (2004, 153–154) found no association between the number of manipulations performed and the occurrence of AEs. Considering different manipulation techniques, Rubinstein et al. (2007b, 97–99) reported that the use of rotation in manipulation was associated with the occurrence of AEs.

2.6.2 Serious adverse events

The European Commission (2011, 3) defines serious AEs as *"Any untoward medical occurrence or effect that at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect."* Since there are no widely accepted definition for serious AEs in rehabilitation terminology, Hebert et al. (2012, 678) adapted the definition as: *"An untoward occurrence that results in death or is life threatening, requires hospital admission, or results in significant or permanent disability."*

According to Carnes et al. (2010a, 361) and Rubinstein (2008, 462–463) serious AEs following MT seems to be rare. Dabbs & Lauretti (1995) used com-

parative estimates and suggested that the use of NSAIDs is associated with a greater risk of serious complications when compared to cervical manipulation for comparative conditions. Cassidy et al. (2008, S178–S179) found no increased risk of vertebrobasilar artery stroke when visiting a chiropractor compared to a primary care physician (PCP), and similar results were discovered when carotid artery stroke was considered (Cassidy et al. 2017, 842–843). It is however difficult to make any precise and conclusive estimates of the incidence of serious AEs since the studies investigating these are very heterogeneous in reporting (varying units and estimates etc.) and the quality varies greatly with many studies being of poor quality (Nielsen et al. 2017, 14). Based on the conclusions of the included studies in their review Nielsen et al. (2017, 13) made estimates of the incidence of some serious AEs, which are presented in table 2.

Table 2. Estimates of the incidences of serious AEs (some scaled for comparability) adapted from Nielsen et al. (2017, 13)

AE	Estimate of incidence
Death	1 in >3 330 000-3 730 000 manipulations
Stroke	1 in 20 000-2 000 000 manipulations
Vertebrobasilar accident (VBA)	1 in 228 050-1 000 000 manipulations
Cerebrovascular accident (CVA)	1 in 228 050-3 850 000 manipulations
Lumbar disc herniation (LDH)	1 in 8 369 129 manipulations[1]
Cauda equina syndrome (CES)	1 CES in >1 000 000-128 000 000 manipulations
CES or LDH	1 in >1 000 000-3 720 000 manipulations
"Serious AEs"	1 in 1 000 000-250 000 000 manipulations
"Serious complication"	1 in 20 000-2 000 000 manipulations

[1] Only one estimate was available

Studies focusing on serious AEs after MT/spinal manipulation seem mostly to be case studies or reports, case series, literature reviews, trials and commentaries (Chung et al. 2013, 674; Hebert et al. 2012, 678). According to Stevinson et al. (2001, 108–109) and Ernst (2002, 377) serious AEs after MT might be underreported and the number of case reports published is not a sufficient indicator of their incidence. Both authors argued this statement by the fact that many of the in different occasions shared (surveys, polls) serious AE cases are not reported in the literature.

Some authors suggest that there is a causal (Ernst 2002, 377) or independent (Smith et al. 2003, 1424–1426) association between serious AEs and MT, specifically cervical manipulation. Ernst (2002, 377) explains the causal relationship between serious AEs and cervical manipulation by that in most cases the symptoms of serious AEs occurred quickly after or during the therapy session, while Smith et al. (2003, 1424–1426) concluded in their nested case-control study that spinal manipulation was independently associated with dissection in the vertebral arteries. On the other hand, Haldeman et al. (2002, 1098–1102) stated that stroke should be considered as a random and unpredictable complication that can occur after any neck movement including spinal manipulation. This conclusion was explained by the fact that serious AEs could occur at any point of the treatment series, after using a variety of different manipulation techniques and at a range of immediately to 11 days post manipulation.

The most common serious AEs after cervical spinal manipulation reported in different studies were stroke following arterial dissection (most commonly of the vertebral arteries) (Ernst 2002, 376–377; Haldeman et al. 2002, 1098–1102; Stevinson et al. 2001, 108–109; Gouveia et al. 2009, E407–E408). Existing vertebral artery stenosis or occlusion was reported (Haldeman et al. 2002, 1098–1102; Gouveia et al. 2009, E407–E408), as were stroke in carotid territory and acute subdural hematoma (Stevinson et al. 2001, 108–109; Gouveia et al. 2009, E407–E408). Gouveia et al. (2009, E407–E408) reported also cases of transitory ischemic accidents, spinal fluid leak (intracranial hypotension) and spinal epidural hematoma.

The two most commonly reported serious AEs after lumbopelvic spinal manipulative therapy was cauda equina syndrome (Gouveia et al. 2009, E407–E408; Hebert et al. 2012, 679; Oppenheim et al. 2005, 660–661; Assendelft et al. 1996) and lumbar disc herniation (Gouveia et al. 2009, E407–E408; Hebert et al. 2012, 679). Other serious AEs found after lumbopelvic manipulation were fractures, hematoma or hemorrhagic cyst, neurologic or vascular com-

promise, traumas in the soft tissue, abscess formation in muscles, a disruption in fracture healing and rupture in the esophagus (Hebert et al. 2012, 679).

Serious AEs reported after MT in all back regions are myelopathies and other spinal cord injuries, radiculopathies (Gouveia et al. 2009, E407–E408; Oppenheim et al. 2005, 660–661; Stevinson et al. 2001, 108–109), herniated discs, diaphragmatic palsy and vertebral fractures (Gouveia et al. 2009, E407–E408).

In most cases serious AEs occurred within 24 hours post treatment, but the time of onset varied widely (Haldeman et al. 2002, 1098–1102; Hebert et al. 2012, 679). The outcome of serious AEs varied from excellent to permanent neurologic deficits and death (Ernst 2002, 376–377; Gouveia et al. 2009, E407–E408; Oppenheim et al. 2005, 660–661; Hebert et al 2012, 680).

According to Cassidy et al. (2008, S178–S179, S182), Cassidy et al. (2017, 845–847) and Rothwell et al. (2001, 1054–1056) there was an association between both vertebrobasilar artery and carotid artery stroke and visits to a chiropractor in individuals younger than 45 years old. The most common cervical manipulation technique causing serious AEs included rotation (Haldeman et al. 2002, 1098–1102; Assendelft et al. 1996).

2.6.3 Patients' and therapists' experience of adverse events

Both Carlesso et al. (2011, 442–444) and Rajendran et al. (2012, 305, 307–310) studied the way patients define AEs associated with MT. According to Carlesso et al. (2011, 442–444) 9 out of 12 study participants had according to the patients' own description had mild to moderate AEs with earlier or present treatment. The participants in the study by Rajendran et al. (2012, 305, 307–310) reported one or more different kinds of responses to treatment, such as pain and stiffness, change in mobility or functioning, emotional responses that were abrupt or strong, tiredness and feeling relaxed. The treatment response was more probable regarded as adverse if the response was unexpected. Carlesso et al. (2011, 442–444) could establish four most central as-

pects when discussing what kind of responses to MT are considered as AEs and what are not: Functional impact of the response, post treatment pain or symptom response, timing and duration of the response and ruling out possible other causes for the experienced response.

The responses' impact on function was considered as the most important factor in determining if a response to MT is adverse or not, especially if it affected the patients' ability to work or perform daily activities (Carlesso et al. 2011, 442–444; Rajendran et al. 2012, 305, 307–310). The relation between pain and function was furthermore noted. Patients were asked to grade the severity of impact on function resulting in mild impact considered as no impact on function, moderate impact as a need to modify activities performed and major impact as a loss of function or ability to perform intended activities. (Carlesso et al. 2011, 442–444.)

In the study made by Carlesso et al. (2011, 442–444) it seemed to be difficult for patients to determine if increased pain or symptom severity should be considered as adverse or not, and changes in pain location or quality were seen as more adverse, while the patients in the study by Rajendran et al. (2012, 305, 307–310) reported pain arising from treatment as unsettling, while other patients considered an absence of discomfort after treatment as an indication of non-successful treatment. Both studies pointed out that changes in symptoms and development of any symptoms patients related to neurological function was seen as adverse (Carlesso et al. 2011, 442–444; Rajendran et al. 2012, 305, 307–310). Patients in the study by Carlesso et al. (2011, 442–444) rated increasing of pain on a numeric rating scale (NRS 0–10) as follows: Mild increase 0,5–2 points, moderate increase 1–2 points and major increase 3 or more points on the NRS.

When regarding the timing and duration of the treatment response, patients experienced a relation between time of onset and duration of the AE with the onset of the symptoms considered as the most important factor in defining if a response was adverse or not. An AE with short duration lasted until immedi-

ately post treatment and up to 48 h, medium duration AEs lasted from less than 24 h to 5 days and long duration AEs lasted from less than 48 h to the next treatment visit or even longer. If the possible response to MT didn't appear immediately after the treatment, patients often considered other factors to be the cause of their post treatment symptoms. (Carlesso et al. 2011, 442–444.)

Both Carlesso et al. (2011, 442–444) and Rajendran et al. (2012, 305, 307–310) reported factors that were seen to form the big picture in how patients define AEs. They were responses occurring after manual treatment and their relationship (intensity, nature and duration of the response) to the treated condition, the patients' own beliefs, attitudes and expectations of MT and the patients' willingness to take personal responsibility in the self-management of their condition. These factors are correlated with the elements brought to the treatment by the patient (acute vs. chronic pain etc.) and the factors the patient receives before treatment (information about the treatment and possible responses to the treatment) (Carlesso et al. 2011, 442–444). According to Rajendran et al. (2012, 305, 307–310) the patients' expectations of treatment were strongly affected by past experiences of treatment. Those who had had previous treatment usually expected some kind of response to MT and considered the possible response as acceptable, while those with no or less experience of treatment considered information of possible responses to treatment as very important. The patients' beliefs and expectations of treatment are to some extent modifiable during the treatment process, and so is the way a patient define an AE (Carlesso et al. 2011, 442–444; Rajendran et al. 2012, 305, 307–310). Treatment responses that could be described as negative were not always regarded as AEs, but rather as a necessary part of the global treatment experience (Rajendran et al. 2012, 305, 307–310).

Therapists' experience

Carnes et al. (2010b, 2–5) aimed to discover a consensus definition of AEs and to identify and describe AEs in MT by using an expert panel consisting of

multiple professions such as physiotherapists, chiropractors, researchers and general practitioners. The process consisted of three rounds with different themes. The study resulted in a practical definition of AEs after MT.

The aim of round one was to describe the consistence of minor, moderate and major AEs. Minor AEs was ranked 1–2 and described as mild, not serious, no impact on function, transient and reversible, short term and not necessary to modify treatment. The study participants had difficulties in reaching a consensus on the description of moderate AEs. Moderate AEs were ranked as 3–4 and described as events not fitting the description of mild and major AEs. They could occur either during or post treatment. Major AEs were ranked as 5–6 and described as severe and unacceptable and they demanded further treatment. (Carnes et al. 2010b, 2–5.)

Round two aimed to categorize potential AEs as minor, moderate, major or not adverse AEs. The definition of minor, moderate and major AEs accomplished in round one was used as reference. The expert panel reached a consensus on AEs considered as major (coma, dislocation, fracture and loss of bladder and bowel control), but for the rest of the presented possible AEs there was little consensus. There was overlapping in the expert panels' classification of AEs to major and moderate as well as to minor and not adverse AEs. The conclusion of round two was that in order to be properly able to classify AEs to not adverse, minor, moderate or major AEs it is necessary to have knowledge of the history about the occurring AEs. Duration and severity of the event were considered as vital information for the classification. (Carnes et al. 2010b, 2–5.)

The purpose of round three was to examine the severity and duration of AEs. Minor or not adverse AEs were considered as mild in severity and short in duration (hours). Moderate AEs were considered as mild to moderate in severity and medium or long in duration (days to weeks). Major AEs were regarded as moderate or major in severity and medium or long in duration (days to weeks). (Carnes et al. 2010b, 2–5.)

2.7 The aim of the thesis and research questions

The main goal is to examine who gets AEs after naprapathic manual therapy for unspecific neck and /or back pain.

Research question:

1. What is the prevalence of AEs after two sessions of naprapathic manual therapy, in subgroups of patients with different lifestyle, pain characteristics and personal profiles, seeking care for unspecific neck and/or back pain?

3 MATERIALS AND METHODS

3.1 Study Design

Our study design method is a prospective cohort study. This design is exposure oriented which means that the chosen cohort groups' exposure status is defined according to the relations between different exposures in the beginning of the follow-up. The nature of this study is longitudinal in which the information is collected prospectively of the outcome incidence to further examine the possible relationships between the exposure and the outcome. (Sarna 2012.) The risk for the outcomes, in this case AEs, runs throughout the whole period of time that this study was conducted, from the first visit until filling in the second AE questionnaire in the beginning of third visit (Rothman 2012, 85–86). This study is a secondary analysis that applies the data collected by others from a primary study i.e. the MINT-trial (Hirsijärvi et al. 2009, 186–190). AEs were in this thesis defined as events occurring 24 h after treatment and moderate in intensity.

The Stockholm Manual Intervention Trial (MINT-trial), originally published in the journal BMC Musculoskeletal Disorders, was carried out at the educational clinic of the Scandinavian College of Naprapathic Manual Medicine in Stockholm, Sweden. The MINT-trial is a 3-arm randomized controlled trial (RCT) with the main goal to examine the effect of three different combinations of MT on back and/or neck pain patients. The secondary goal was to investigate the

prevalence and severity of AEs after NMT for neck and/or back pain. The study participants were randomized into three different treatment arms: 1) MT including spinal manipulation and mobilization, muscle stretching and massage, 2) MT excluding spinal manipulation and 3) MT excluding muscle stretching. There were a maximum of six treatment visits within six weeks per participant. (Paanalahti et. al. 2014 and 2016.)

3.2 Ethics

The Ethical review board in Stockholm, Sweden (2009/1848-31/2) approved this study. All study participants agreed on informed consent including consent for publication of the results. All data analyses for the study were performed at the Institute of Environmental Medicine, Karolinska Institutet, Stockholm.

3.3 Inclusion and exclusion criteria

The inclusion criteria for the participants were: 1) 18-65 years old, 2) pain in back and/or neck and 3) had not visited the educational clinic during the previous month.

The exclusion criteria were: 1) not mastering the Swedish language properly, 2) scored <2 in two pain questions in the baseline questionnaire (pain at the present moment and worst pain during previous four weeks) regarding neck and/or back on a numeric rating scale (NRS) = 0-10, 3) pregnancy, 4) current or previous cancer, 5) received treatment from chiropractor, naprapath, osteopath or physiotherapist for current pain during the last month, 6) current pain has lasted less than one week, 7) demanding or refusing spinal manipulation or muscle stretching, 8) having contraindication(s) towards spinal manipulation according to the Swedish Board of Social Welfare (Key 2004, 64–68), 9) no indication for manipulation in the pain area, 10) red flags (e.g. previous trauma, infectious or rheumatic illnesses, drug addiction, abundant and rapid decrease in weight etc.), 11) a specific diagnose (e.g. ankylosing spondylitis, spinal stenosis, rheumatoid arthritis) and 12) sick leave because of planned or completed surgery for neck and/or back.

Inclusion criteria for this study

In addition to above mentioned inclusion criteria in the MINT-trial, we added two more to our study: 1) at least two treatment visits during trial and 2) filling of the AE-questionnaire (Appendix 2) after treatments.

3.4 Exposure and outcome

The exposures in this thesis are the patient characteristics collected in the baseline questionnaire (Appendix 1). We divided the characteristics in three domains that are lifestyle factors, pain related factors and personal factors.

The lifestyle domain consists of smoking habits (non-smokers or daily smokers), BMI (> 25 or ≤ 25) and physical activity (inactive or active, participants were considered active if they had exercised on a high exertion level at least two times per week or on a medium exertion level at least two times per week or on a low exertion level at least three times per week in addition to exercising at least once per week on a high exertion level or on a low exertion level at least three times per week in addition to exercising at least once per week on medium exertion level), the pain domain consists of pain duration (acute/subacute or chronic), intensity (low or high, the pain intensity was considered high when ranked 6-10 on an 11-point NRS) and area (back or neck or back and neck), and pain related disability (low or high), the personal factor domain consists of age (> 30 or ≤ 30), gender (male or female) and educational level (low or high, the educational level was considered high when years of education were 13 years or more i.e. University/College education or higher). The outcome is the AEs that possibly occur after NMT, information about these were collected with the AE-questionnaire (Appendix 2). The intensity of the AE was regarded moderate when scored > 3 on an 11-point NRS.

3.5 Statistical analysis

Binomial regression analysis was used to examine the associations between the exposures and the outcome. Prevalence risk ratio (PRR) with 95% confi-

dence intervals (95% CI) was calculated by comparing the prevalence of AEs between patients with and without the characteristics in the three domains in the same model, as well as all characteristics together in one final model. The results are an association, PRR, between the exposure (characteristics) and outcome (AEs) and it reveals if the characteristic is protective against or exposing to AEs. The values in the three domains were adapted from the baseline questionnaire data. The statistical analysis was performed with Stata version 12.0.

4 RESULTS

Figure 1 shows a flow chart describing the inclusion process of the study population. The final study population (N = 928) was formed after those who did not receive treatment during first visit (n = 78) and those who did not answer the first and/or second AE questionnaire (n = 51) were excluded.

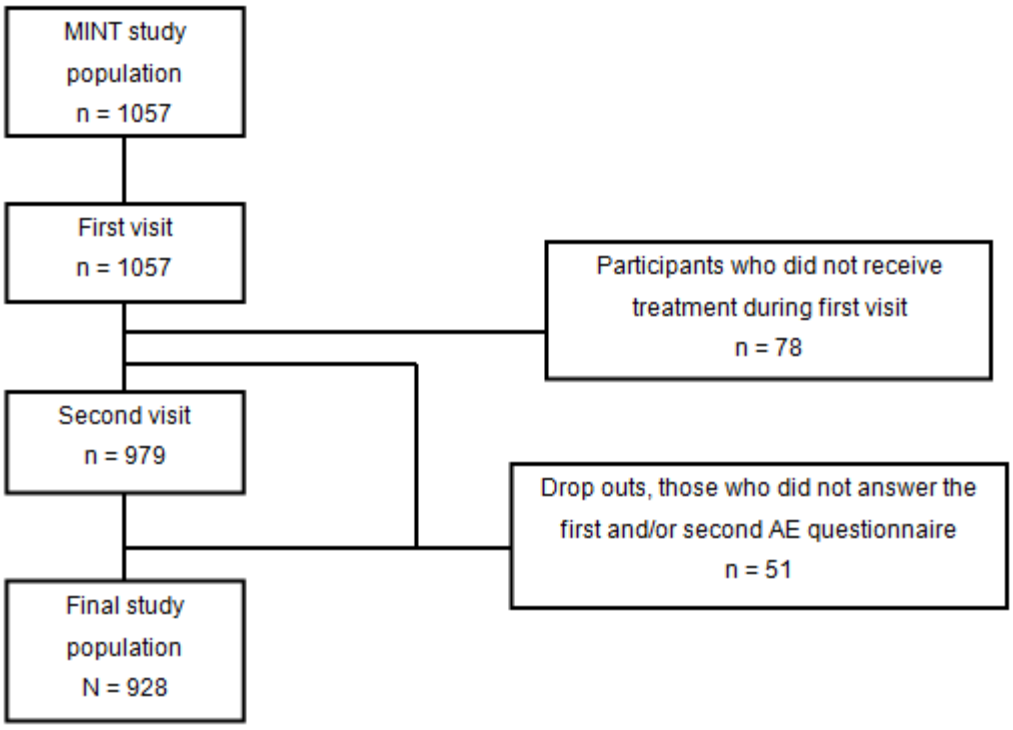

Figure 1. Flow chart of the study population

Table 3 presents the baseline characteristics of the whole study population (N = 928) stratified by gender. The mean age of the study population is 36 (SD 12) and the majority were women (70 %). High educated participants covered 61 % of the population. Physically active patients covered 72 % of all, and mean BMI (Body Mass Index) was 24.0 (SD 3.6) with normal weight persons exceeding 66 %.

Table 3. Baseline characteristics of the study population (N=928), stratification by gender

	All N=928	**Females** n=649 (70 %)	**Males** n=279 (30 %)
Mean age (SD)[1]	36 (12)	35 (12)	36 (11)
Painful area, no. (%)			
Neck	505 (55)	375 (58)	130 (46)
Back	308 (33)	190 (29)	118 (42)
Neck/back	115 (12)	84 (13)	31 (11)
Educational level, no. (%)			
Low (1-12 years)	361 (39)	242 (37)	119 (43)
High (13- years)	567 (61)	407 (63)	160 (57)
Daily smoking, no. (%)	134 (14)	97 (15)	37 (13)
BMI, no. (%)[2]			
Mean (SD)[1]	24.0 (3.6)	23.5 (3.6)	25.2 (3.5)
≤25	617 (66)	464 (71)	153 (55)
>25	305 (33)	182 (28)	123 (44)
Physical activity (PA), no. (%)			
Active	671 (72)	468 (72)	203 (73)
Inactive	257 (28)	181 (28)	76 (27)
Similar previous complaints, no. (%)	716 (77)	511 (79)	205 (73)
Duration of pain, no. (%)			
Acute/subacute (≤ 3 months)	593 (64)	417 (64)	176 (63)
Chronic (> 3 months)	335 (36)	232 (36)	103 (37)
Pain intensity at baseline, no. (%)			
Low (NRS = 0-10, ≤ 5)	388 (42)	254 (39)	134 (48)
High (NRS = 0-10, > 5)	540 (58)	395 (61)	145 (52)
Disability at baseline, no. (%)			
Low (NRS = 0-10, ≤ 2)	469 (51)	327 (50)	142 (51)
High (NRS = 0-10, > 2)	459 (49)	322 (50)	137 (49)
General health, no. (%)			
Good or better	875 (94)	614 (95)	261 (94)
Fair	51 (6)	33 (5)	18 (6)
Poor	2 (0)	2 (0)	0 (0)
RCT group, no. (%)			
Naprapathic manual therapy	313 (34)	208 (32)	105 (38)
NMT - no manipulation	312 (34)	224 (35)	88 (31)
NMT - no stretching	303 (32)	217 (33)	86 (31)

[1]SD = standard deviation
[2]BMI = Body mass index
Six BMI-values missing due to missing baseline data, three males and three females

Daily smokers were a minority group, comprising 14 % of the patients. The most painful area among the patients was neck with 55 % of all, and second was back with 33 % of the patients. The incidence of acute or subacute pain within study population was 64 %, and the pain intensity at baseline was high with the majority of patients (58 %), women covering 61 %, and men covering 52 % within groups characterized by gender. The disability at baseline was reported almost equally, with low disability covering 51 % of the patients.

In Table 4 the number of moderate AEs experienced after two treatment visits for all patients, and stratified by gender, is presented. The majority of the study population (52 %) did not receive any moderate AEs, most of them being male participants. The second major group received one moderate AE (16 %). According to the results, women receive higher number of moderate AEs than men. In this study there were no severe AEs reported.

Table 4. Number of moderate AEs experienced after two treatment visits, for all patients and stratified by gender

AEs, no.	Persons, no. (%)	Females, no. (%)	Males, no. (%)
0	483 (52)	299 (46)	184 (66)
1	146 (16)	117 (18)	29 (10)
2	114 (12)	91 (14)	23 (8)
3	66 (7)	44 (7)	22 (8)
4	41 (4)	34 (5)	7 (3)
5	42 (5)	31 (5)	11 (4)
6	15 (2)	13 (2)	2 (1)
7	14 (2)	13 (2)	1 (0)
8	6 (1)	6 (1)	0 (0)
9	1 (0)	1 (0)	0 (0)
Total	928	649	279

Table 5 presents how the different characteristics within the three domains affect the risk of reporting at least one moderate AE after MT. Within the domain of lifestyle factors the results showed that physically active persons receive less moderate AEs than inactive persons (PRR 0.85, 95 % CI 0.74–0.97). Smoking or BMI does not affect the risk. In the domain of pain related factors only the intensity of pain and pain area had significance in the risk of receiving AEs.

Table 5. Comparison of the prevalence of characteristics between patients with at least one moderate adverse event and those with no moderate AE, presented as prevalence risk ratios (PRR) and 95 % confidence intervals (95 % CI)

Domain 1 - Lifestyle factors	**No.**	**PRR**	**95 % CI**
Smoking			
Non-smokers	794	1.0	
Daily smoking	134	1.09	0.92–1.31
BMI			
> 25	305	1.0	
≤ 25	617	0.95	0.83–1.09
PA			
Inactive	257	1.0	
Active	671	0.85	0.74–0.97
Domain 2 - Pain related factors			
Pain intensity			
Low	388	1.0	
High	540	1.31	1.12–1.53
Disability			
Low	469	1.0	
High	459	1.05	0.91–1.21
Pain duration			
Acute/subacute	593	1.0	
Chronic	335	1.05	0.92–1.21
Pain area			
Back	505	1.0	
Neck	308	1.18	1.01–1.38
Back and neck	115	1.07	0.85–1.34
Domain 3 - Personal factors			
Age			
> 30	598	1.0	
≤ 30	410	1.03	0.90–1.17
Gender			
Males	279	1.0	
Females	649	1.59	1.33–1.90
Educational level			
Low	361	1.0	
High	562	0.87	0.76–0.99

Patients with high pain intensity at baseline had a higher risk of receiving moderate AEs than patients with low intensity (PRR 1.31, 95 % CI 1.12–1.53) and as well those with only neck pain at baseline compared to those with only back pain and both back and neck pain (PRR 1.18, 95 % CI 1.01–1 .38). In

the domain of personal factors females have a higher risk of receiving moderate AEs compared to male patients (PRR 1.59, 95 % CI 1.33–1.90), and patients with a high education had less risk of moderate AEs (PRR 0.87, 95 % CI 0.76–0.99).

Table 6. Comparison of the prevalence of all characteristics in the same model between patients with at least one moderate adverse event and those with no moderate AE, presented as prevalence risk ratios (PRR) and 95 % confidence intervals (95 % CI)

Subgroups		No.	PRR	95 % CI
Smoking				
	Non-smokers	794	1.0	
	Daily smoking	134	1.04	0.87–1.24
BMI				
	> 25	305	1.0	
	≤ 25	617	0.90	0.78–1.03
PA				
	Inactive	257	1.0	
	Active	671	0.87	0.76–1.00
Pain intensity				
	Low	388	1.0	
	High	540	1.24	1.06–1.44
Disability				
	Low	469	1.0	
	High	459	1.05	0.91–1.21
Pain duration				
	Acute/subacute	593	1.0	
	Chronic	335	1.05	0.92–1.21
Pain area				
	Back	505	1.0	
	Neck	308	1.12	0.96–1.30
	Back and neck	115	1.01	0.81–1.28
Age				
	> 30	598	1.0	
	≤ 30	410	1.05	0.92–1.21
Gender				
	Males	279	1.0	
	Females	649	1.57	1.31–1.88
Educational level				
	Low	361	1.0	
	High	562	0.92	0.81–1.06

The comparison of subgroups with all characteristics in the same statistical model, adjusted for each other is presented in Table 6. In this fully adjusted

model, the results changed into high educational level (PRR 0.92, 95 % CI 0.81–1.06) not being a protective factor against receiving moderate AEs anymore. In addition, neck pain (PRR 1.12, 95 % CI 0.96–1.30) was no longer a risk factor for receiving moderate AEs. The risks didn't change much for the other factors, resulting in physical activity remaining a protective factor against moderate AEs (PRR 0.87, 95 % CI 0.76–1.00), and high pain intensity at baseline and female gender having higher risk for receiving moderate AEs (PRR 1.24, 95 % CI 1.06–1.44 and PRR 1.57, 95 % CI 1.31–1.88).

5 DISCUSSION

5.1 Main findings and relation to other studies

According to the findings of this prospective cohort study the majority of the study population (52 %) did not experience any moderate AEs, while the second major group (16 %) experienced one moderate AE after two treatment sessions. This result is not directly applicable to results of previous studies, since we examined the occurrence of only moderate AEs. Previous studies (Cagnie et al. 2004, 152; Rubinstein et al. 2007a, 413; Senstad et al. 1997, 435, 436–438) have suggested that AEs are most commonly mild or moderate in intensity.

The results regarding the number of AEs reported in this study are quite in line with previous studies that have reported the occurrence of at least one AE with the percentage varying from 30 to 61 (Rubinstein et al. 2007a, 413; Cagnie et al. 2004, 152; Senstad et al. 1997, 435, 436–438; Hurwitz et al. 2005, 1480–1481; Walker et al. 2013, 1726–1727). When considering the number of AEs reported per participant there are somewhat contradictory results. In our study, reporting of one moderate AE was second most common after reporting no moderate AEs. In the studies by Cagnie et al. (2004, 152) and Walker et al. (2013, 1726–1727) most of the participants experiencing at least one AE reported two or more AEs. However, Senstad et al. (1997, 435, 436–438) observed that two or more AEs were reported after only 5 % of treatments.

This thesis suggests that female gender and high pain intensity at baseline are risk factors for receiving moderate AEs, whereas physical activity seems to be a protective factor. Similar results regarding female gender were discovered by Cagnie et al. (2004, 153–154), Hurwitz et al. (2005, 1480–1481) and Senstad et al. (1996), who stated that women were more likely to report AEs when compared to men. Why women report more AEs compared to men is unclear. One study stated that women reported different types of AEs and more AEs with high intensity when compared to men. (Senstad et al. 1997, 436–438.)

High pain intensity at baseline was reported as a predictive factor for AEs by Hurwitz et al. (2005, 1480–1481) and Rubinstein et al. (2007b, 97–99). This finding could be explained by the treatment induced cellular level changes occurring in the treated tissues (Bialosky et al. 2011, 16). It could be assumed that when treating a patient with an intense pain level might not resolve the pain immediately, still leaving the patient with some pain after treatment, which could further be interpreted as an AE by the patient. It would furthermore seem logical that treating an area with pain might leave some soreness to the area in question.

None of the studies we explored to this thesis had examined the effect of physical activity on experiencing AEs after MT. Physical activity being a protective factor against AEs could be explained by more physically active persons being more adapted to feelings of soreness or pain in muscles and joints. The “no pain no gain” way of thinking among physically active people in the modern society might affect the results because the feeling of pain is more acceptable and encouraged. This observation is supported by the finding of Rajendran et al. (2012, 305, 307–310) who presented that some patients described AEs as a necessary part of the global treatment experience.

Other factors not found significant in this study but reported as predictive for experiencing AEs by other studies were age (Cagnie et al. 2004, 153–154;

Hurwitz et al. 2005, 1480–1481; Rajendran et al. 2015, 640), smoking (Cagnie et al. 2004, 153–154; Rajendran et al. 2015, 640), neck disability and duration of pain in the previous year (Rubinstein et al. 2007b, 97–99; Hurwitz et al. 2005, 1480–1481). In addition this study examined characteristics such as BMI, pain area and educational level. The authors of this thesis did not find any previous studies addressing these factors similarly as was done in this thesis. Rubinstein et al. (2007b, 97–99) and Hurwitz et al. (2005, 1480–1481) addressed disability in the form of neck disability and therefore their findings can't be directly compared with the results of this thesis. Rubinstein et al. (2007b, 97–99) found a moderate association between increased neck pain after treatment and intermittent neck pain in the previous year. The result is however not directly comparable with the findings of this thesis, since this thesis did not focus on the occurrence of and factors protective against and exposing to specific AEs.

The result of this thesis could have been different if the AEs reported in the question ”other AEs” in the AE-questionnaire would have been included to the analysis. However, the number of different AEs reported in the question “other AEs” is small and heterogeneous, and there doesn't seem to be any serious AEs. The AE-questionnaire (Appendix 2) used in this study is based on previous studies (Paanalahti et al. 2014, 4), and it includes a variety of AEs of which most were reported being common AEs after MT also in other studies (Cagnie et al. 2004, 152; Hurwitz et al. 2005, 1480–1481; Leboeuf-Yde et al. 1997; Walker et al. 2013, 1726–1727; Senstad et al. 1997, 435, 436–438). Only nausea and dizziness were reported as more uncommon AEs occurring after MT (Cagnie et al. 2004, 152; Hurwitz et al. 2005, 1480–1481; Leboeuf-Yde et al. 1997; Rubinstein et al. 2007a, 413; Walker et al. 2013, 1726–1727; Senstad et al. 1997, 435, 436–438). Since the AEs reported in the question ”other AEs” were rare, it is justifiable that these AEs were not included in the questionnaire as individual questions.

There are relatively few studies investigating the impact of different characteristics on the occurrence of AEs. This subject has mainly been studied via pro-

spective surveys with quite heterogeneous study objectives, and only one prospective cohort study made of this subject was found. The existing studies investigated the prevalence of AEs after chiropractic and osteopathic treatment and physiotherapy. There was only one RCT; this study was the only one including NMT. Therefore, to the knowledge of the authors of this thesis there are no previous studies examining who gets AEs and the prevalence of AEs after two sessions of NMT, in subgroups of patients with different lifestyle, pain characteristics and personal profiles, seeking care for unspecific neck and/or back pain. It may be difficult to generalize these results to other MT-professions, since the use or indication of different techniques may vary.

The findings regarding protective and exposing factors to AEs after MT are somewhat heterogeneous. More high quality research is needed to provide better understanding and consensus of this subject. As reported in previous studies female gender is the only factor that has been proven to be predictive of receiving AEs.

5.2 Methodological considerations

The design of this thesis was prospective cohort study. The advantage of prospective cohort studies is the low probability of selection bias and recall bias. Cohort studies offer the best knowledge about the causation between exposure and outcome, and the most straightforward measurement of the risk of developing the outcome. The disadvantages include possible lost to follow-up, time enquired and study costs. (Beaglehole et al. 1993, 36–39.) Since the purpose of this thesis was to investigate who gets at least one moderate AE after two treatments of NMT, the authors of this thesis considers this as the most suitable design.

This study had a participation rate of 88 %. It is considered a methodological strength due to the low risk of selection bias, thus increasing the internal validity of this thesis. Selection bias is considered as a systematic error that originates from the study selection procedures and factors that have an impact on the participation to the study. Selection bias should be considered when the

association between exposure and outcome is different among participants and non participants. The problem with selection bias is that since the association between exposure and outcome is unknown among non participants, the presence of selection bias must often be inferred. (Rothman 2012, 126–128.) Do those who had two treatments and had filled in the AE questionnaire differ from those who had two treatments and had not filled in the AE questionnaire? Probably, since those lost to follow up could have had more AEs and be less satisfied with the treatment. This could have influenced the results in such a way that the most severe AEs were not reported, and the associations may be underestimated if this moreover is related to exposure levels. Therefore the level of exposure were compared between those lost to follow up and those not lost to follow up. Since the exposure status were similar in these groups, it is not likely that a selection bias influenced the results of this thesis.

Another possible weakness in this thesis is the misclassification bias leading to a systematic error. The misclassification bias occurs when the categorization of information is misinterpreted and placed in wrong categories. (Rothman 2012, 133–136). In this study there may be some misclassification of exposure, but there's no reason to believe that these potential misclassifications should be related to the outcome, and that a differential misclassification of the outcome shall be present.

Different results might have been seen if we had categorized AEs in another way. Although the AE-questionnaire used in this study was adapted from questionnaires used in previous studies it has not been validated and there is no widely accepted way of interpreting and measuring the occurrence or number of AEs. Therefore this might have lead to misclassification of outcomes in this thesis. In this thesis AEs were classified only according to the intensity of the AE and thus the duration of the AE was not considered. Senstad et al. (1997, 435, 436–438) found a positive association between severity and duration of AEs, and therefore it could be regarded as a possible reason for misclassification. The outcome of this thesis was the prevalence of AEs within different subgroups of patients with the occurrence of at least one moderate

AE used as reference. The subgroups in domain three was tested (gender, age and educational level) with those who had 0–1 moderate AEs compared to those who had two moderate AEs and to those who had three moderate AEs. This comparison showed that the number of moderate AEs had no effect on the outcome.

An important threat to the validity of the study is the risk of confounding from factors not included in the statistical models, such as similar previous complaints, general health and treatment group. It must however be noted that Paanalahti et al. (2014, 5) found no difference in occurrence of AEs between the three treatment groups.

This study examined the occurrence of at least one moderate AE after the first two treatment visits. This aspect is justified by the information presented in previous studies which suggested that AEs seemed to be more common after the first visit or in the early stages of the treatment series (Rubinstein et al. 2007a, 413; Paanalahti et al. 2014, 5–7; Leboeuf-Yde et al. 1997; Senstad et al. 1996).

The treatments were done by student therapists who have less experience in the clinical field. This can have an effect on the results and lead to patients receiving multiple and more severe AEs, but this seems not to be the case. In our study most of the participants had zero or mild AEs. Since the NMT-treatment is dependent on the technique used, the provider, the participant, the environment, and the interaction between these elements, the experience of the treatment is always different (Ernst 2000; Kaptchuk 2002 cited in Bialosky et al. 2011, 1). Therefore the effect of the treatment is related to multiple mechanisms and the patient outcomes can vary. Could it be that the naprapathy students assigned to treat the participants might have different ways of handling patients than experienced therapists? They could possibly use much softer approach and handling towards the patients due to the fact that they might not be as confident with their skills as already graduated naprapaths who have experience in the field. This could have affected the

outcome and generated more moderate AEs or no AEs at all, since the majority of AEs fitted in this category.

The techniques used in this study were mobilization, manipulation, massage and stretching, and the use of these techniques is performed according to the patient's symptoms. Every student treated every patient differently, according to baseline pain intensity or duration, pain area etc. and utilized different techniques in different ways. It could be assumed that this might affect the outcomes since the treatments are not standardized to be exactly the same. However, this is not a threat to the validity of the study since the main aim was not to report of the occurrence of AEs, but to identify what subgroups of patients has the highest prevalence of AEs.

The results of this thesis can well be utilized in clinical practice when informing patients about the occurrence of possible AEs after treatment. They in addition help therapists to foresee which of their patients might experience AEs after treatment.

6 CONCLUSIONS

Physical activity was protective against experiencing moderate AEs when compared to physically inactive participants. Female gender and high pain intensity at baseline had a higher risk of receiving moderate AEs than male participants and those with low pain intensity at baseline.

7 ACKNOWLEDGEMENTS

The authors of this thesis would like to thank the main supervisor Eva Skillgate (D.N., PhD) at Karolinska Institutet for the co-operation and all the guidance, advice, support and comments regarding this thesis. Thank you for this unique opportunity to learn the basics of scientific research. This thesis was financially supported by Kymin Osakeyhtiön 100-vuotissäätiö. The authors of this thesis would like to thank the foundation for the assistance.

REFERENCES

Airaksinen, O., Brox, J., Cedraschi, C., Hildebrandt, J., Klaber-Moffett. J., Kovacs, F., Mannion, A.F., Reis, S., Staal, J.B., Ursin, H., Zanoli, G. 2006. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. *European Spine Journal* 15, S192–S300.

Assendelft, W., Pfeifle, C. & Bouter, L. 1995. Chiropractic in The Netherlands: a survey of Dutch chiropractors. *Journal of Manipulative and Physiological therapeutics* 18, 129–134.

Assendelft, W.J., Bouter, L.M. & Knipschild, P.G. 1996. Complications of spinal manipulation: A comprehensive review of the literature. *The Journal of Family Practice* 5, 475–480.

Beaglehole, R, Bonita, R. & Kjellström, T. 1993. Basic epidemiology. Ebook. Geneva: WHO. Available at: https://kaakkuri.finna.fi [accessed 17.4.2018], 36–39.

Bialosky, J., Bishop, M., Price, D., Robinson, M., & George, S. 2009. The Mechanisms of Manual Therapy in the Treatment of Musculoskeletal Pain: A Comprehensive Model. *Manual Therapy* 14, 531–538.

Bialosky, J., Bishop, M., George, S. & Robinson, M. 2011. Placebo response to manual therapy: something out of nothing? 19, *Journal of Manual and Manipulative Therapy* 19, 1–9.

Blum, C., Globe, G., Terre, L., Mirtz, T.A., Greene, L. & Globe, D. 2008. Multinational survey of chiropractic patients: reasons for seeking care. *The Journal of Chiropractic Education* 53, 175–184.

Cagnie, B., Vinck, E., Beernaert, A. & Cambier, D. 2004. How common are side effects of spinal manipulation and can these side effects be predicted? *Manual Therapy* 9, 151–156.

Carlesso, L.C., Macdermid, J.C. & Santaguida, L.P. 2010. Standardization of Adverse Event Terminology and Reporting in Orthopaedic Physical Therapy: Application to the Cervical Spine. *Journal of Orthopaedic & Sports Physical Therapy* 8, 455–463.

Carlesso, L.C., Cairney, J., Dolovich, L. & Hoogenes, J. 2011. Defining adverse events in manual therapy: An exploratory qualitative analysis of the patient perspective. *Manual Therapy* 16, 440–446.

Carnes, D., Mars, T.S., Mullinger, B., Froud, R. & Underwood, M. 2010a. Adverse events and manual therapy: A systematic review. *Manual Therapy* 15, 355–363.

Carnes, D., Mullinger, B. & Underwood, M. 2010b. Defining adverse events in manual therapies: A modified Delphi consensus study. *Manual Therapy* 15, 2–6.

Cassidy, J.D., Boyle, E., Côté, P., He, Y., Hogg-Johnson, S., Silver, F.L. & Bondy, S.J. 2008. Risk of Vertebrobasilar Stroke and Chiropractic Care - Results of a Population-Based Case-Control and Case-Crossover Study. *Spine* 4S, S176–S183.

Cassidy, J.D., Boyle, E., Côte, P., Hogg-Johnson, S., Bondy, S.J. & Haldeman, S. 2017. Risk of Carotid Stroke after Chiropractic Care: A Population-Based Case-Crossover Study. *Journal of Stroke and Cerebrovascular Diseases* 4, 842–850.

Carey, T., Freburger, J.K., Holmes, M., Jackman, A., Knauer, S., Wallace, A. & Dartery, J. 2010. Race, Care Seeking, and Utilization for Chronic Back and Neck Pain: Population Perspectives. *The Journal of Pain* 11, 343–350.

Chou, R. & Huffman, L. 2007. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Annals of Internal Medicine* 147, 492–504.

Chung, C.L.R, Côté, P., Stern, P. & L'Espérance, G. 2013. The Association between Cervical Spine Manipulation and Carotid Artery Dissection: A Systematic Review of the Literature. *Journal of Manipulative and Physiological Therapeutics* 9, 672–676.

Cohen, S. P. 2015. Epidemiology, Diagnosis, and Treatment of Neck Pain. *Mayo Clinic Proceedings* 90, 284–299.

Cook, A., Wellman, R., Cherkin, D., Kahn, J. & Sherman, K. 2015. Randomized clinical assessing whether additional massage treatments for chronic neck pain improve 12- and 26- week outcomes. *The Spine Journal* 15, 2206–2215.

Côte, P., Cassidy, J.D. & Carroll, L. 2001. The treatment of neck and low back pain: Who seeks care? Who goes where? *Medical Care* 39, 956–967.

Coulter, D., Crawford, C., Hurwitz, E., Vernon, H., Khorsan, R., Booth, M. & Herman, P. 2018. Manipulation and mobilization for treating chronic low back pain: a systematic review and meta-analysis. *The Spine Journal*, 1–10.

Cross, K.M., Kuenze, C., Grindstaff, T., & Hertel, J. 2011. Thoracic spine thrust manipulation improves pain, range of motion, and self-reported function in patients with mechanical neck pain: a systematic review. *Journal of Orthopaedic & Sports Physical Therapy* 41, 633–642.

Dabbs, V. & Lauretti, W.J. 1995. A risk assessment of cervical manipulation vs. NSAIDs for the treatment of neck pain. *Journal of Manipulative and Physiological Therapeutics* 8, 530–536.

D'Sylva, J., Miller, J., Gross, A., Burnie, S.J., Goldsmith, C.H., Graham, N., Haines, T., Brønfort, G. & Hoving, J.L. 2010. Manual therapy with or without physical medicine modalities for neck pain: a systematic rewiev. *Manual Therapy 15*, 415–433.

Eriksen, K., Rochester, R.P. & Hurwitz, E.L. 2011. Symptomatic reactions, clinical outcomes and patient satisfaction associated with upper cervical chiropractic care: A prospective, multicenter, cohort study. *BMC Musculoskeletal Disorders* 12, 1–13.

Ernst, E. 2002. Manipulation of the cervical spine: a systematic review of case reports of serious adverse events, 1995-2001. *Medical Journal of Australia* 176, 376–380.

European Commission. 2011. Information from European Union institutions, bodies, offices and agencies. *Official Journal of the European Union* C 172/1. Updated 11.6.2011. PDF document. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2011_c172_01/2011_c172_01_en.pdf [accessed 9.1.2018].

European Medicines Agency. 2002. Guideline for Good Clinical Practice. PDF document. Available at: http://www.edctp.org/fileadmin/documents/EMEA_ICH-GCP_Guidelines_July_2002.pdf [accessed 24.10.2017].

Ezzo, J., Haraldsson, B., Gross, A., Myers, C., Morien, A., Goldsmith, C., Bronfort, G. & Peloso, P. 2007. Massage for mechanical neck disorders: a systematic review. *Spine* 32, 353–362.

Farooq, M.N., Mohseni-Bandpei, M.A., Gilani, S.A., Ashfaq, M. & Mahmood, Q. 2018. The effects of neck mobilization in patients with chronic neck pain: A randomized controlled trial. *Journal of Bodywork and Movement Therapies* 22, 24–31.

Farrell, J. & Jensen, G. 1992. Manual therapy: a critical assessment of role in the profession of physical therapy. *Physical Therapy* 72, 843–852.

Fejer, R., Kyvik, K.O. & Hartvigsen, J. 2006. The prevalence of neck pain in the world population: systematic critical review of the literature. *Eur Spine J.* 15, 834–848.

Freburger, J., Carey, T. & Holmes, G. 2005. Management of back and neck pain: who seeks care from physical therapists? *Physical Therapy* 85, 872–886.

French, S., Charity, M., Fordsike, K., Gunn, J., Polus, B., Walker, B., Chondros, P. & Britt, H. 2013. Chiropractic Observation and Analysis Study (COAST): providing an understanding of current chiropractic practice. *The Medical Journal of Australia* 19, 687–691.

Furlan, A., Giraldo, M., Baskwill, A. & Imamura, M. 2015. Massage for low back pain. *Cochrane Database of Systematic Reviews* 9, 1–136.

Goss, D., Thomas, J., Walkowskia, S., Clarka, S., Licciardone, J., Yueg, G. & Clarka, B. 2012. Non-thrust manual therapy reduces erector spinae short-latency stretch reflex asymmetries in patients with chronic low back pain. *Journal of Electromyography and Kinesiology* 22, 663–669.

Gouveia, L.O., Castanho, P. & Ferreira, J.J. 2009. Safety of Chiropractic Interventions: A Systematic Review. *Spine* 11, E405–E413.

Gross, A., Miller, J., D'Sylva, J., Burnie, S.J., Goldsmith, C.H., Graham, N., Haines, T., Brønfort, G. & Hoving, J.L. 2010. Manipulation or mobilisation for neck pain: a Cochrane Review. *Manual Therapy* 15, 315–333.

Gross, A., Langevin, P., Burnie, S., Bédard-Brochu, M., Empey, B., Dugas, E., Faber-Dobrescu, M., Andres, C., Graham, N., Goldsmith, C., Brønfort, G., Hoving, J. & LeBlanc, F. 2015. Manipulation and mobilisation for neck pain contrasted against an inactive control or another active treatment. Cochrane Database Systematic Reviews 9, 1–165.

Haldeman, S., Kohlbeck, F.J. & McGregor, M. 2002. Stroke, cerebral artery dissection, and cervical spine manipulation therapy. *Journal of Neurology* 249, 1098–1104.

Hayden, J.A., van Tulder, M.W. & Tomlinson G. 2005. Systematic review: strategies for using exercise therapy to improve outcomes in chronic low back pain. *Annals of internal medicine* 142, 776–785.

Hebert, J.J., Stomski, N.J., French, S.D. & Rubinstein, S.M. 2012. Serious Adverse Events and Spinal Manipulative Therapy of the Low Back Region: A Systematic Review of Cases. *Journal of Manipulative and Physiological Therapeutics* 9, 677–691.

Hirsijärvi, S., Remes, P. & Sajavaara, P. 2009. Tutki ja kirjoita. 15th-16th edition. Helsinki: Tammi, 186–190.

Horn, M., George, S. & Fritz, J. 2017. Influence of initial provider on health care utilization in patients seeking care for neck pain. Mayo Clinic Proceedings: Innovations, Quality & Outcomes 1, 226–233.

Hoy, D., Bain, C., Williams, G., March, L., Brooks, P., Blyth, F., Woolf, A., Vos, T. & Buchbinder, R. 2012. A systematic review of the global prevalence of low back pain. *Arthritis & Rheumatism* 64, 2028–2037.

Hurwitz, E., Coulter, I., Adams, A., Genovese, B. & Shekelle, P. 1998. Use of Chiropractic Services from 1985 through 1991 in the United States and Canada. *American Journal of Public Health* 88, 771–776.

Hurwitz, E.L., Morgenstern, H., Vassilaki, M. & Chiang, L-M. 2005. Frequency and Clinical Predictors of Adverse Events to Chiropractic Care in the UCLA Neck Pain Study. *Spine* 13, 1477–1484.

Jousimaa, J. 2013. Spinal manipulative therapy for chronic low-back pain. Käypä hoito – general guidelines. WWW document. Available at: http://www.kaypahoito.fi/web/kh/suositukset/suositus?id=evd07198 [accessed 14.12.2017]

Keane, L.G. 2017. Comparing Aqua Stretch with supervised land based stretching for chronic lower back pain. *Journal of Bodywork and Movement Therapies* 21, 297–305.

Key, W. 2004. Författningshandbok för personal inom hälso- och sjukvården. Stockholm: Liber, 64–68.

Kääriä, S., Laaksonen, M., Rahkonen, O., Lahelma, E. & Leino-Arjas, P. 2012. Risk factors of chronic neck pain: A prospective study among middle-aged employees. *EJP* 16, 911–920.

Leboeuf-Yde, C., Hennius, B., Rudberg, E., Leufvenmark, P. & Thunman, M. 1997. Side effects of chiropractic treatment: a prospective study. *Journal of Manipulative and Physiological Therapeutics* 8, 511–515.

Lovell, M.E. & Galasko C.S.B. 2002. Whiplash disorders—a review. *Injury, Int. J. Care Injured 33*, 97–101.

Miller, J., Gross, A., D'Sylva, J., Burnie, S.J., Goldsmith, C.H., Graham, N., Haines, T., Brønfort, G. & Hoving, J.L. 2010. Manual therapy and exercise for neck pain: A systemativ review. *Manual Therapy* 15, 334–354.

Myrtveit, S.M., Wilhelmsen, I., Petrie K.J., Skogen J.C. & Sivertsen, B. 2013. What characterizes individuals developing chronic whiplash?: The Nord-Trondelag Health Study (HUNT). *Journal of Psychosomatic Research* 74, 393–400.

National Institute of Health (NIH). 2006. Common Terminology Criteria for Adverse Events v3.0 (CTCAE). PDF document. Available at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcaev3.pdf [accessed 24.10.2017].

Nielsen, S.M., Tarp, S., Christensen, R., Bliddal, H., Klokker, L. & Henriksen, M. 2017. The risk associated with spinal manipulation: an overview of reviews. *Systematic reviews, BioMed Central* 6, 1–19.

Oppenheim, J.S., Spitzer, D.E. & Segal, D.H. 2005. Nonvascular complications following spinal manipulation. *The Spine Journal* 5, 660–667.

Paanalahti, K., Holm, L.W., Nordin, M., Asker, M., Lyander, J. & Skillgate, E. 2014. Adverse events after manual therapy among patients seeking care for neck and/or back pain: a randomized controlled trial. *BMC Musculoskeletal Disorders*, 15, 1–10.

Paanalahti, K., Holm, L.W., Nordin, M., Höijer, J., Lyander, J., Asker, M. & Skillgate, E. 2016. Three combinations of manual therapy techniques within naprapathy in the treatment of neck and/or back pain: a randomized controlled trial. *BMC Musculoskeletal Disorders* 17, 1–10.

Page, P. 2012. Current concepts in muscle stretching for exercise and rehabilitation. *The International Journal of Sports Physical Therapy* 7, 109–119.

Park, K.-N., Kwon, O.-Y., Yi, C.-H., Cynn, H.-S., Weon, J.-H., Kim, T.-H. & Choi, H.-S. 2016. Effects of motor control exercise vs muscle stretching exercise on reducing compensatory lumbopelvic motions and low back pain: a randomized trial. *Journal of Manipulative and Physiological Therapeutics* 39, 576–585.

Pohjolainen, T. 2009a. Niskakivut. In Kalso, E., Haanpää, M. & Vainio, A. (eds.). Kipu. 3rd edition. Helsinki: Kustannus Oy Duodecim, 340–347.

Pohjolainen, T. 2009b. Selkäkivut. In Kalso, E., Haanpää, M. & Vainio, A. (eds.). Kipu. 3rd edition. Helsinki: Kustannus Oy Duodecim, 348–349.

Pohlman, K. A., O'Beirne, M., Thiel, H., Cassidy, J. D., Mior, S., Hurwitz, E. L., Westaway, M., Ishaque, S., Yager, J. & Vohra, S. 2014. Development and validation of providers' and patients' measurement instruments to evaluate adverse events after spinal manipulation therapy. *European Journal of Integrative Medicine* 6, 451–466.

Rajendran, D., Bright, P., Bettles, S., Carnes, D. & Mullinger, B. 2012. What puts the adverse in "adverse events"? Patients' perceptions of post-treatment experiences in osteopathy – A qualitative study using focus groups. *Manual Therapy* 17, 305–311.

Rajendran, D., Bright, P., Mullinger, B. & Froud, R. 2015. Reporting patterns and predictors of common minor adverse events following osteopathic treatment: Lessons learned from a prospective, patient-administred questionnaire feasibility study in a UK teaching clinic. *European Journal of Integrative Medicine* 7, 634–644.

Rothman, K. 2012. Epidemiology: An Introduction. 2nd edition. New York: Oxford University Press, Inc., 85–86, 126–128, 133–136.

Rothwell, D.M., Bondy, S.J. & Williams, J.I. 2001. Chiropractic Manipulation and Stroke: A Population-Based Case-Control Study. *Stroke* 32, 1054–1060.

Rubinstein, S.M., Leboeuf-Yde, C., Knol, D.L., de Koekkoek, T.E., Pfeifle, C.E. & van Tulder, M.W. 2007a. The benefits outweight the risks for patients undergoing chiropractic care for neck pain: A prospective, multicenter, cohort study. *Journal of Manipulative and Physiological Therapeutics* 30, 408–418.

Rubinstein, S.M., Leboeuf-Yde, C., Knol, D.L., de Koekkoek, T.E., Pfeifle, C.E. & van Tulder, M.W. 2007b. Predictors of Adverse Events Following Chiropractic Care for Patients with Neck Pain. *Journal of Manipulative and Physiological Therapeutics* 2, 94–103.

Rubinstein, S.M. 2008. Adverse Events Following Chiropractic Care for Subjects With Neck or Low-Back Pain: Do the Benefits Outweigh the Risks? *Journal of Manipulative and Physiological Therapeutics* 6, 461–464.

Rubinstein, S., van Middelkoop, M., Assendelft, W., de Boer, M. & van Tulder, M. 2011. Spinal manipulative therapy for chronic low-back pain. *Cochrane Database of Systematic Reviews* 16.

Rubinstein, S., Terwee, C., Assendelft, W., de Boer, M. & van Tulder, M. 2012. Spinal manipulative therapy for acute low-back pain. *Cochrane Database Systematic Review* 9.

Sarna, S. 2012. Kliinisen biostatistiikan kurssi, sanasto.

Schuller, W., Ostelo, R., Rohrich, D., Apeldoorn, A. & de Vet, H. 2017. Physicians using spinal manipulative treatment in The Netherlands: a description of their characteristics and their patients. *BMC Musculoskeletal Disorders* 18, 1–8.

Senstad, O., Leboeuf-Yde, C. & Borchgrevink, C. 1996. Predictors of side effects to spinal manipulative therapy. *Journal of Manipulative and Physiological Therapeutics* 7, 441–445.

Senstad, O., Leboeuf-Yde, C. & Borchgrevink, C. 1997. Frequency and characteristics of side effects of spinal manipulative therapy. *Spine* 22, 435–440.

Skillgate, E., Vingård, E., Josephson, M., Holm, L. & Alfredsson, L. 2009. Is smoking and alcohol consumption associated with long-term sick leave due to unspecific back or neck pain among employees in the public sector? Results of a three-year follow-up cohort study. *Journal of rehabilitation medicine* 41, 550–556.

Smith, W.S., Johnston, S.C., Skalabrin, E.J., Weaver, M., Azari, P., Albers, G.W. & Gress, D.R. 2003. Spinal manipulative therapy is an independent risk factor for vertebral artery dissection. *Neurology* 60, 1424–1428.

Stevinson, C., Honan, W., Cooke, B. & Ernst, E. 2001. Neurological complications of cervical spine manipulation. *Journal of the Royal Society of Medicine* 94, 107–110.

Suomen Naprapaattiyhdistys. 2018. WWW document. Available at: http://www.naprapaattiyhdistys.fi/naprapatia/mita-on-naprapatia/ [accessed 11.4.2018].

Svenska Naprapatförbundet. 2017. The history of naprapathy. WWWdocument. Available at: http://naprapater.se/en/naprapathy/historical-review [accessed 11.4.2018].

Tabell, V. 2015. The role of adverse events after naprapathic manual therapy as a prognostic factor. University of Jyväskylä. Sports and Exercise Medicine. Master's thesis.

Tsertsvadze, A., Clar, C., Court, R., Clarke, A., Mistry, H. & Sutcliffe, P. 2014. Cost-effectiveness of manual therapy for the management of musculoskeletal conditions: a systematic review and narrative synthesis of evidence from randomized controlled trials. *Journal of Manipulative and Physiological Therapeutics* 37, 343–362.

Tunwattanapong, P., Kongkasuwan, R. & Kuptniratsaikul, V. 2016. The effectiveness of a neck and shoulder stretching exercise program among office workers with neck pain: a randomized controlled trial. *Clinical Rehabilitation* 30, 64–72.

US Burden of Disease Collaborators. 2013. The state of US health, 1990-2010: Burden of diseases, injuries, and risk factors. *JAMA* 310, 591–608.

Viikari-Juntura, E., Heliövaara, M., Solovieva, S. & Shiri, R. 2012. Tuki- ja liikuntaelinsairaudet. In Koskinen,S., Lundqvist, A. & Ristiluoma, N. Terveys 2011 – tutkimuksen perustulosraportti Terveys, toimintakyky ja hyvinvointi Suomessa 2011. Helsinki: Terveyden ja hyvinvoinnin laitos. Available at: http://www.julkari.fi/handle/10024/90832 [accessed: 1.3.2018], 92–95.

Walker, B.F., Hebert, J.J., Stomski, N.J., Clarke, B.R., Bowden, R.S., Losco, B. & French, S.D. 2013. Outcomes of usual chiropractic. The OUCH randomized controlled trial of adverse events. *Spine* 38, 1723–1729.

A. DATUM

B. LÖPNUMMER

C. SMÄRTOMRÅDE

☐ *NACKE/SKULDRA/ÖVRE DEL AV RYGG*

☐ *NEDRE DELEN AV RYGG*

☒ *NACKE/RYGG*

.....

NEDANSTÅENDE UPPGIFTER FYLLS I AV TERAPEUTEN

D. ☐ EXKLUDERAD PÅ GRUND AV (KRITERIENUMMER)_____

E. ☐ 1. INKLUDERAD **ALLT** ☐ 2. INKLUDERAD **EJ MAN**

☐ 3. INKLUDERAD **EJ STR**

Mint | Manual Intervention Trial

Karolinska Institutet

1. Namn_____

2. Gatuadress_____

Postnummer_____ Postort_____

3. Telefonnummer (dagtid och kvällstid) _____

4. Personnummer: _____

5. ☐ Jag har fått muntlig och skriftlig information om studien och accepterar att delta i denna

6. På vilket sätt önskar du att få uppföljningsenkäter?

☐ e-post ☐ postutskick

E-postadress: _____

Upprepa e-postadress: _____

---

7. Vilken är din högsta skolutbildning?

☐ Grundskola (1-9 år)
☐ Gymnasieskola/yrkesskola (10-12 år)
☐ Universitet/högskoleutbildning (13 -15 år)
☐ Högre akademisk utbildning (16 år eller mer)

---

8. Röker du dagligen?

☐ Nej ☐ Ja

9. Hur mycket väger du? _____kg

10. Hur lång är du? _____cm

11. Följande frågor handlar om i vilken utsträckning du ägnar dig avsiktligt åt motions-, idrotts- eller friluftsverksamhet. OBS! Gäller fritiden och du får endast räkna med det som överstiger 20 minuters aktivitet per gång. Hur ofta motionerar du vanligtvis på nedanstående aktivitetsnivåer? *(Markera ett alternativ för varje aktivitetsnivå)*

a) Hård ansträngningsnivå *(du har hög puls och blir ansträngd och svettig)*

☐ Aldrig
☐ Oregelbundet
☐ En gång per vecka
☐ Två gånger per vecka
☐ Tre gånger per vecka eller oftare

b) Medelhög ansträngningsnivå *(ansträngningsnivån ska vara sådan att det hjälpligt skulle gå att föra ett samtal med någon)*

- ☐ Aldrig
- ☐ Oregelbundet
- ☐ En gång per vecka
- ☐ Två gånger per vecka
- ☐ Tre gånger per vecka eller oftare

c) Låg ansträngningsnivå *(t.ex. lugna promenader och cykelturer)*

- ☐ Aldrig
- ☐ Oregelbundet
- ☐ En gång per vecka
- ☐ Två gånger per vecka
- ☐ Tre gånger per vecka eller oftare

Frågor om smärta i nacke och rygg.

12. Har du haft perioder av liknande besvär förut?

☐ Nej ☐ Ja, vid _____tillfällen

13. Hur länge har besvären pågått denna gång?

☐ 1 vecka ☐ 2-4 veckor ☐ 1-3 månader

☐ 4-6 månader ☐ mer än 6 månader

14. Hur började besvären denna gång?

- ☐ Plötsligt påkommande efter lättare belastning/våld (t.ex. hastig rörelse)
- ☐ Plötsligt påkommande efter tyngre belastning/våld (t.ex. fallolycka eller tungt lyft)
- ☐ Smygande debut under flera dagar
- ☐ Smygande debut under flera veckor
- ☐ Vet ej

---

15. Har du tidigare fått behandling av naprapat av någon anledning?

☐ Nej ☐ Ja, vid enstaka tillfällen ☐ Ja, vid flertal tillfällen

---

16. Enligt din bedömning hur sannolikt är det att du är **helt besvärsfri i nacke och rygg om sju veckor**? *(Markera den siffra du tycker stämmer bäst)*

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls sannolikt att jag är helt besvärsfri

Mycket sannolikt att jag är helt besvärsfri

17. Vilken betydelse tror du att den behandling du kommer att få har för tillfrisknandet? *(Markera den siffra du tycker stämmer bäst)*

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen betydelse — Helt avgörande

18. På frågorna nedan ska du svara på hur stark/intensiv din smärta eller värk i **nacke och rygg** är, genom att ange en siffra på en skala mellan 0 – 10, där 0 = ingen smärta/värk alls och 10 = värsta tänkbara smärta/värk.*(Markera den siffra du tycker stämmer bäst)*

a) Hur stark bedömer du att din smärta eller värk i nacken/ryggen är **för tillfället**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen smärta — Värsta tänkbara smärta

b) Hur intensiv har din **värsta** smärta/värk i nacke och rygg varit **de senaste fyra veckorna**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen smärta — Värsta tänkbara smärta

c) Hur intensiv har din smärta/värk varit i nacke och rygg i **genomsnitt de senaste fyra veckorna**? *(Med det menas hur smärtan/värken vanligtvis varit när du haft smärta)*

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Ingen smärta — Värsta tänkbara smärta

Frågor om funktion

19. Under hur många dagar **de senaste fyra veckorna** har du inte kunnat utföra dina normala aktiviteter (arbete, studier och/eller hushållsarbete) på grund av smärta eller värk i nacke och rygg?

a) Antal dagar:.....

Besvara frågorna nedan genom att ange den siffra du tycker stämmer bäst.

b) Hur mycket har smärta eller värk i nacke och rygg hindrat dig i dina dagliga aktiviteter **de senaste fyra veckorna?**

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls — Omöjligt att utföra dessa aktiviteter

c) Hur mycket har smärta eller värk i nacke och rygg hindrat dig att ta del i fritidsaktiviteter, sociala aktiviteter och familjeaktiviteter **de senaste fyra veckorna?**

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls — Omöjligt att utföra dessa aktiviteter

d) Hur mycket har smärtan/besvären i nacke och rygg hindrat dig att arbeta (inkluderat studier/hemarbete) **de senaste fyra veckorna**?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10

Inte alls — Omöjligt att utföra dessa aktiviteter

SF-12

	Utmärkt	Mycket god	God	Någorlunda	Dålig
20. I allmänhet, skulle du vilja säga att din hälsa är:	☐	☐	☐	☐	☐

De följande två frågorna handlar om aktiviteter som du kan tänkas utföra under en vanlig dag.

***Är du på grund av ditt hälsotillstånd** begränsad i dessa aktiviteter **nu**? Om så är fallet, hur mycket?*

	Ja, mycket begränsad	Ja, lite begränsad	Nej, inte alls begränsad
21. **Måttligt ansträngande aktiviteter**, som att flytta ett bord, dammsuga, skogspromenader eller trädgårdsarbete?	☐	☐	☐
22. Gå uppför **flera** trappor?	☐	☐	☐

Under **de senaste fyra veckorna**, har du haft något av följande problem i ditt arbete eller med andra regelbundna dagliga aktiviteter **som en följd av ditt kroppsliga hälsotillstånd**?

	Ja	Nej
23. **Uträttat mindre** än du skulle önskat?	☐	☐
24. Varit hindrad att utföra **vissa** arbetsuppgifter eller andra aktiviteter?	☐	☐

Under **de senaste fyra veckorna,** har du haft något av följande problem i ditt arbete eller med andra regelbundna dagliga aktiviteter **som en följd av känslomässiga problem** (som t.ex. nedstämdhet eller ängslan)?

	Ja	Nej
25. **Uträttat mindre** än du skulle önskat?	☐	☐
26. Inte utfört arbete eller andra aktiviteter så **noggrant** som vanligt?	☐	☐

27. Under **de senaste fyra veckorna,** hur mycket har **värken eller smärtan** stört ditt normala arbete (innefattar både arbete utanför hemmet och hushållssysslor)?	Inte alls	Lite	Måttligt	Mycket	Väldigt mycket
	☐	☐	☐	☐	☐

*Frågorna här handlar om hur du känner dig och hur du haft det **under de senaste fyra veckorna.** Ange för varje fråga det svarsalternativ som bäst beskriver hur du känt dig.*

Hur stor del av tiden under **de senaste fyra veckorna**…

	Hela tiden	Största delen av tiden	En hel del av tiden	En del av tiden	Lite av tiden	Inget av tiden
28…har du känt dig lugn och harmonisk?	☐	☐	☐	☐	☐	☐
29…har du varit full av energi?	☐	☐	☐	☐	☐	☐
30. ..har du känt dig dyster och ledsen?	☐	☐	☐	☐	☐	☐
31. Under **de senaste fyra veckorna**, hur stor del av tiden har **ditt kroppsliga hälsotillstånd eller dina känslomässiga problem** stört dina möjligheter att umgås (t ex hälsa på släkt, vänner, etc)?	☐	☐	☐	☐	☐	☐

FRÅGOR OM BEHANDLINGSREAKTIONER

A. DATUM_____

B. NAMN_____

C. PERSONNUMMER_____

D. ÅTERBESÖKSTILLFÄLLE NUMMER _____

Mint | Manual Intervention Trial

Karolinska Institutet

Det händer att patienter upplever oönskade behandlingsreaktioner i samband med manuell behandling. Därför undrar vi om du som en direkt effekt av behandlingen upplevt något av följande? **OBS! Ange endast symtom som har debuterat inom 24 timmar efter behandlingen**.

1. Trötthet?

☐ Nej - Gå till fråga 2

☐ Ja - Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt

2. Ömhet i muskler?

☐ Nej - Gå till fråga 3

☐ Ja - Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt

3. Ökad stelhet?

☐ Nej - Gå till fråga 4

☐ Ja - Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt

4. Ökad smärta?

☐ Nej - Gå till fråga 5

☐ Ja - Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt

5. Ostadighet/yrsel?

☐ Nej - Gå till fråga 6

☐ Ja - Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt

6. Huvudvärk?

☐ Nej - Gå till fråga 7

☐ Ja - Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt

7. Illamående?

☐ Nej – Gå till fråga 8

☐ Ja - Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt

8. Annat?

☐ Nej

☐ Ja - Vad? _____

Reaktionen pågick i _____ timmar

Hur mycket besvärade det dig?

0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Inte alls — På värsta tänkbara sätt