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**NAPRAPATHIC MANUAL
THERAPY AND OTHER
FACTORS OF IMPORTANCE
FOR THE PROGNOSIS OF
NECK AND BACK PAIN**

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To my family

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ABSTRACT

Introduction: Neck and back pain common health problems causing economic burden and individual suffering worldwide.

Aim: The overall aim of this thesis was to increase understanding of naprapathic manual therapy and other factors of potential importance for the prognosis of back and neck pain. **Specific aims:** *Study I:* 1) to assess and compare the sex-specific recovery from spinal pain and psychological distress as single and comorbid conditions, 2) to describe the interrelationships between these conditions at baseline and at follow-up and 3) to explore whether spinal pain is a risk factor for onset of psychological distress and vice versa. *Study II:* to explore the role of the role of good sleep on the prognosis of non-specific neck and/or low back pain. *Studies III and IV:* to compare the occurrence and severity of adverse events (study III) and the treatment effect (study IV) of naprapathic manual therapy between different treatment technique combinations as part of naprapathic manual therapy.

Methods: *Study I:* a cohort study based on The Stockholm Public Health Cohort including 23,794 participants. A random sample of the population in Stockholm was approached with postal questionnaires at baseline and at follow-up five years later. *Study II:* a cohort study that was a secondary analysis of data from a randomized controlled trial. Information was used from baseline and follow-up questionnaires at 12 and 52 weeks. *Studies III and IV:* a randomized controlled trial. Participants were recruited among patients, ages 18–65 years, seeking care for neck and/or back pain. Participants were randomly assigned to one of three treatment arms: 1) naprapathic manual therapy (i.e. spinal manipulation, spinal mobilization, stretching and massage), 2) naprapathic manual therapy excluding spinal manipulation or 3) naprapathic manual therapy excluding stretching. Treatments were provided by students in the seventh semester of a total of eight.

Results: *Study I:* comorbidity of spinal pain and psychological distress was twice as common among women as among men. Recovery was less likely with comorbidity than with single conditions of spinal pain or psychological distress. Overall, 24% of women and 17% of men with spinal pain without psychological distress at baseline had psychological distress at follow-up. The corresponding figures for spinal pain among participants with psychological distress without spinal pain at baseline were 24% and 20%. Spinal pain was a determinant of psychological distress and vice versa. *Study II:* patients with good sleep at baseline were more likely to experience a clinically important improvement in pain and pain-related disability compared to patients with impaired sleep at the 1-year follow-up. *Study III:* adverse events after combined manual therapy were common and mostly mild and transient. The most common adverse events were muscle soreness, increased pain and stiffness. No differences were found between the treatment arms. Women more often had short and long moderate adverse events compared to men. *Study IV:* There were no disparities between the treatment arms in clinically important improvement in pain or pain-related disability after 1 year of follow-up, in men or in women.

Conclusion: Spinal pain with psychological distress is common, especially among women. Comorbidity of neck and/or back pain and psychological distress had a negative effect on the prognosis of these conditions. Good sleep had a positive effect on the prognosis of non-specific neck and/or back pain. Adverse events after manual therapy were common and transient. There were no differences in the occurrence of adverse events or in treatment effects when either spinal manipulation or stretching was excluded from the treatment arsenal of combined manual therapy for non-specific neck and/or back pain.

List of Publications

- I. **Paanalahti K**, Holm LW, Magnusson C, Carroll L, Nordin M, Skillgate E.
The sex specific interrelationship between spinal pain and psychological distress across time in the general population. Results from the Stockholm Public Health Study.
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- II. **Paanalahti K**, Wertli MM, Held U, Åkerstedt T, Holm LW, Nordin M, Skillgate E.
Spinal pain – good sleep matters: a secondary analysis of a randomized controlled trial.
Submitted

- III. **Paanalahti K**, Holm LW, Nordin M, Asker M, Lyander J, Skillgate E.
Adverse events after manual therapy among patients seeking care for neck and/or back pain. A randomized controlled trial.
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- IV. **Paanalahti K**, Holm LW, Nordin M, Höijer J, Lyander J, Asker M, Skillgate E.
The effect of different treatment technique combinations within naprapathic manual therapy for neck and/or back pain: A randomized controlled trial.
Manuscript

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LIST OF ABBREVIATIONS

BCE	Before the Common Era
BP	Back Pain
CI	Confidence Interval
CPQ	Chronic Pain Questionnaire
GEE	Generalized Estimating Equation
GHQ-12	General Health Questionnaire-12
MCID	Minimal Clinically Important Difference
NMT	Naprapathic Manual Therapy
NP	Neck Pain
NRS	Numerical Rating Scale
OR	Odds Ratio
PD	Psychological Distress
RCT	Randomized Controlled Trial
RR	Relative Risk
SD	Standard Deviation
SP	Spinal Pain

1 INTRODUCTION

The aim of this thesis, in the field of epidemiology, is to broaden knowledge of the prognosis of neck and back pain. "Prognosis is a description of the probable course or prediction of the outcome of a health condition over time" [1]. To investigate prognosis, study participants have a disease or complaint at the start of the study, in contrast to studies of risk factors for a disease in which participants are initially disease free.

Neck and back pain are among the most common disorders worldwide, causing huge economic burden for countries and suffering for individuals [2-5]. Nevertheless, it is interesting that only marginal attention has been focused on neck and back pain. According to the 2004 report of the Global Burden of Disease (GBD) study, back pain was not even among the top 100 diseases of greatest global burden. However, the most recent update of the GBD study showed that low back pain was the leading cause of years lived with disability (YLD) worldwide [4].

In this thesis, factors of interest for the prognosis of neck and back pain were psychological distress, sleep and naprapathic manual therapy. Further, the issue of adverse events after manual therapy was explored. The data used were based on already collected material (studies I and II) and on data collected for the purposes of this thesis (studies III and IV). The study designs included cohort studies (studies I and II) and randomized controlled trial (RCT; studies III and IV).

Psychological conditions often accompany neck and/or back pain. It has been shown that mental disorders are more common among individuals with neck and/or back pain, with no clear disparities between developed and developing countries [6, 7].

Concerning differences between sexes, women seem to have more neck and back pain complaints than men, and similarly mental disorders and impaired sleep are more common in women [6, 8, 9]. Impaired sleep is common among individuals suffering from neck and back pain [10, 11].

Manual therapy is a common treatment for neck and back pain [12-18]. Naprapathy is commonly practiced in Finland, Norway, Sweden and the USA, and has many similarities with chiropractic, osteopathy and physiotherapy. In Finland and Sweden, naprapathy has been a registered profession since 1994 and controlled by governmental institutions. In this thesis, the effect of different combinations of treatment techniques within naprapathic manual therapy, as well as the risk of adverse events, was explored.

2 BACKGROUND

2.1 EPIDEMIOLOGY

‘Epidemiology is the study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health-related problems. Various methods can be used to carry out epidemiological investigations: surveillance and descriptive studies can be used to study distribution, and analytical studies are used to study determinants’ [19].

The focus of this thesis is clinical epidemiology. This area of epidemiology involves the study of the natural course of a disease in the population and prognostic factors, and assesses the effects of diagnostic procedures and treatments [20].

2.2 THE BIOPSYCHOSOCIAL MODEL

In 1977, the psychiatrist George Engel stated: ‘Medicine’s crises stems from the logical inference that since “disease” is defined in terms of somatic parameters, physicians need not to be concerned with psychosocial issues which lie outside medicine’s responsibility and authority’ [21]. Engel proposed this model as a new approach to understanding the complexity of disease and suffering. The model has been widely used to examine pain experience and for educational purposes in various institutions [22-25].

The biopsychosocial model is a product of understanding that body and mind are dimensions that act together. Figure 1, describes theoretically the response to acute and chronic low back pain according to this model. Tissue damage activates pain perception (nociceptive mechanism; biological component) which in turn activates the affective and cognitive mechanisms (psychological and social components) which lead to different reactions and behaviour caused by pain which may include increased pain perception, pain-related disability, psychological distress and/or impaired sleep.

Pain experience includes biological, psychological and social dimensions. The biological component is the activation of nociceptors, the psychological component is the interpretation of these signals and the social component includes factors such as the individual’s surroundings, family, workplace, socioeconomic position and culture. The biological and psychological dimensions of pain have been studied in this thesis.

The biopsychosocial model is an important theoretical framework for studying pain. Different characteristics of the individual such as grade of pain and disability, general health, physical activity, gender, age, psychological distress, manual therapy and impaired sleep have been explored within the biopsychosocial framework of this thesis to investigate how they affect the prognosis for neck and/or back pain.

ACUTE PAIN



CHRONIC PAIN

(? tissue damage)

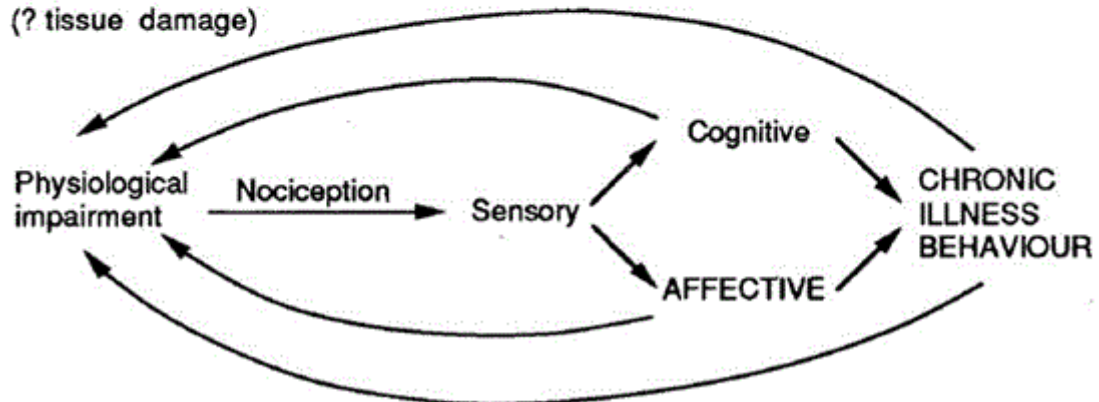


Figure 1. A Comparison of the biopsychosocial elements of acute and chronic low back pain and illness behaviour[26].

2.3 PAIN

The purpose of pain is to warn the individual of something that is potentially going to cause harm. This is crucial in terms of survival. A classic example is the reaction to touching a hot plate; removing the hand rapidly after the sensation of the stimulus that may harm the individual is important. If this warning system is not properly functional, a potential burn injury could lead to tissue damage which in turn leads to pain sensation.

Various factors affect the perception of pain such as emotional status, control over the situation, cultural differences, attitudes, personality and gender. This indicates the complexity of pain. The International Association for the Study of Pain (IASP) has defined pain as: 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' [27].

Pain perception includes different components that may increase or decrease the experience of pain:

- 1) Discriminative: the subjective evaluation of pain intensity, location and duration.
- 2) Affective: the degree of unpleasantness of pain and urge to escape.

3) Cognitive: thoughts about pain, expectations, cultural values, distraction and quality [28].

Pain can be classified into:

1) Nociceptive pain: receptors that react to harmful or potentially harmful stimuli are termed nociceptors. These receptors (mechanoreceptors, chemoreceptors and thermal and polymodal receptors) are free nerve endings that react to painful (noxious) stimuli such as pressure, chemicals and temperature. The nervous system is intact, undamaged [27].

2) Neuropathic pain: due to injury to the nervous system, i.e. a lesion in a peripheral nerve or in the central nervous system (brain and spinal cord) [27].

3) Complex regional pain syndrome (CRPS): a syndrome characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of pain after trauma or other type of lesion [29]. The aetiology of CRPS is poorly understood [30].

4) Psychogenic pain: no nociceptive or neuropathic origin. Pain often precedes a psychiatric condition such as depression or anxiety [28].

In this thesis the duration of pain has been classified as: acute (from hours to several weeks), subacute (less than 3 months and more than several weeks) and chronic (more than 3 months). Acute, subacute and chronic pain conditions were considered in the analyses in all studies in this thesis (studies I–IV).

2.3.1 Measuring pain, pain-related disability and recovery

The measurement of pain is of primary importance in musculoskeletal disorders. Pain is the main predictor of disability caused by low back pain [31]. The measurement of pain, due to its multifactorial nature, may be problematic and therefore great attention should be directed towards the use of reliable measuring instruments. The concept of recovery may be another important issue. It has been suggested that the meaning of recovery may vary between individuals even when estimated pain levels are the same. Thus individuals may define themselves as ‘recovered’ even when the pain is still present but when 1) they experience less pain, 2) the pain becomes tolerable, 3) they are adjusting to the level of everyday living to be able to avoid the pain or 4) the pain is accepted as part of life [32].

Pain and disability can be measured using different self-administered tools: pain can be measured using the Visual Analogue Scale (VAS) [33], Numerical Rating Scale (NRS)[33] and Verbal Rating Scale (VRS) [33, 34], Chronic Pain Questionnaire (CPQ) [35, 36] and the Nordic Pain Questionnaire [37, 38]; disability can be measured using, for example, the Roland-Morris Disability Questionnaire (RDQ) [39, 40], Neck Pain Disability Questionnaire (NDI) [41, 42], Oswestry Disability Index (ODI) [35, 40, 43].

CPQ , which measures both pain and pain-related disability was used to assess these conditions at baseline and follow-up in studies II and IV.

2.4 NECK AND BACK PAIN

The first documented back problems in humans date back to 1500 BCE [23]. Since the Second World War, back problems have escalated substantially and this effect seems likely to continue in the coming decades [23, 44]. Today, both neck and back pain are ranked among the four most disabling conditions worldwide (low back pain in first place and neck pain fourth) [45].

The prevalence of neck and back pain can be measured using different prevalence periods such as lifetime, annual, monthly or point prevalence; the figures are high regardless of the prevalence period, varying from about 10% (point prevalence) to 80% (lifetime prevalence) in the adult general population worldwide [6, 46]. The prevalence of back pain is increasing among children and adolescents, and is at about the same level as in adults [47, 48]. Back pain is a recurrent condition and may continue through life for one-third of individuals among the populations studied [49]. The proportion of individuals without back pain is reported to vary from 23% to 35% in the general adult population [50-52].

Neck and/or back pain can stem from different structures and causes including muscles, ligaments, vertebrae, annulus fibrosis, facet joints, sacroiliac joints, nerves, fractures, tumours, inflammation and infections. The development of these pain conditions may depend on psychological and social factors, especially with regard to chronicity of symptoms. Therefore careful anamnesis and examination of patients is important to determine the origin of pain and how it affects patients and even their social environment.

Regarding low back pain, in about 85% of cases the cause of such pain is unknown [53]. Non-specific neck and/or back pain has been examined in three of the four studies in this thesis (studies II–IV). In study I, neck and/or back pain was studied in the general population which includes persons with specific as well as non-specific pain.

There is no clear consensus regarding the definition of neck and back pain. This makes assessment of the effect of different interventions as well as classification of such pain challenging. Global comparisons are also difficult because of the use of different prevalence periods.

Three distinct populations have been studied in this thesis: the general population, the working population and the care-seeking population.

2.4.1 General population

The lifetime prevalence of neck and back pain in the general population is up to 80% [45, 49, 54, 55]. The 12-month prevalence of neck pain is estimated to be between 30% and 50%. Of those individuals with neck or back pain, 2% to 24% experienced limitations in their everyday life due to the pain [56-58]. It has been suggested that musculoskeletal pain is more common today than it was 40 years ago [59].

The general population was investigated in study I.

2.4.2 Working population

It is estimated that approximately between 10-45% of workers suffer from back pain in Europe [60]. The 1-year prevalence of neck pain among workers is estimated to be between 27% and 48%. Of those individuals with neck or back pain, 11–20% experienced pain-related disability that affected their everyday life [61, 62].

The working population was investigated in study II.

2.4.3 Care-seeking population

Pain is the most common reason for visiting a general practitioner (GP) in Sweden, with approximately 20–40% of visits because of pain complaints [63]. In the USA, back pain is the second most common reason for seeking care in the primary care setting, and healthcare utilization as a result of this condition appears to be increasing [64, 65].

In studies III and IV, the care-seeking population was investigated.

2.5 FACTORS OF IMPORTANCE FOR PROGNOSIS

A wide variety of factors and their effects on the prognosis for neck and back pain have been studied. These include factors such as pain intensity at baseline, fear avoidance, psychological and social factors, age, gender, physical activity, work demands, smoking, duration of pain, comorbidity, education, sleep, social support and general health [66-68].

In this thesis, the prognostic effect of psychological distress, good sleep and manual therapy on non-specific neck and/or back pain has been evaluated. The prognostic impact of these factors is important for patients, healthcare providers and decision makers to be able to predict the future needs of and costs for society of a certain disease. Neck and back pain cause a heavy burden for healthcare in many countries [69]. Therefore it is necessary to explore the effect of different factors that may modify the course of neck and back pain. This is also important for clinicians when planning the care for the individual patient [66].

2.5.1 Psychological distress

Psychological distress is a marker for mental health. It is often used in population surveys and epidemiological studies to determine the degree of general mental non-well-being in the population. The term psychological distress includes symptoms of depression such as: hopelessness, anxiety, lack of ability to concentrate, loss of sleep due to worry, playing a useful part in society, capable of making decisions, constantly under strain couldn't overcome difficulties, enjoy normal activities, face up to problems, feeling unhappy, losing confidence in yourself, thinking of yourself as worthless, feeling reasonably happy and/or catastrophizing [70].

2.5.2 Comorbidity

Pain and psychiatric conditions are both common disorders among individuals in primary care [71]. It has been shown that pain may cause psychiatric illness such as depression and anxiety, and vice versa [72, 73]. Therefore it is important to identify these conditions and understand how they affect the prognosis of neck and back pain.

In this thesis, comorbidity is defined as the co-existence of spinal (neck and/or back) pain and psychological distress. A single disorder refers to spinal pain without psychological distress or psychological distress without spinal pain.

The effect of spinal pain and/or psychological distress on recovery from these conditions in the general population has been studied in this thesis.

2.5.3 Impaired sleep

The prevalence of impaired sleep is approximately 30% in the general population, and insomnia symptoms are associated with daytime consequences in 10–20% of individuals [74, 75]. The prevalence of impaired sleep among individuals suffering from neck and back pain may be as high as 64% [10, 11, 76].

The definition of insomnia encompasses difficulties in falling asleep and waking up at night with difficulty in returning to sleep. A diagnosis of insomnia also depends on the individual having a daytime consequence such as feeling tired during the working day. Insomnia is a common disease that affects individuals and society on different levels. Insomnia often co-exists with other diseases including anxiety, depression and neck and back pain [77-81].

2.5.4 Manual therapy

Spinal manipulative therapy is a widely used treatment modality for neck and back pain. The first evidence of the use of spinal manipulation comes from around 400 BCE,

with manipulative therapy described by Hippocrates in 460–385 BCE [82]. The main indication for spinal manipulation is neck and back pain [17]. Treatments are given by chiropractors, naprapaths, osteopaths, physicians and physiotherapists. Manual therapy has been suggested to be a cost-effective treatment alternative for neck and back pain in comparison with conservative care such as GP care, physiotherapy or exercise [15]. The positive effect of manual therapy including spinal manipulation has been shown in comparison with other treatment modalities [83-86].

In this thesis the effects of combinations of manual therapy techniques provided by naprapaths are compared. These techniques include massage, stretching, spinal manipulation and spinal mobilization, and the main purpose of their use is to treat musculoskeletal pain and disability.

2.5.4.1 Naprapathy

In this thesis we have explored the effect of different combinations of treatment techniques used as part of naprapathic manual therapy. In Scandinavia, naprapathy is defined as a system for specific examination, diagnosis, manual treatment and rehabilitation of shortened or pathological soft and connective tissue resulting in pain and dysfunction in the musculoskeletal system. Naprapathic manual therapy is also known as soft and connective tissue manipulation (SCTM), and is a combination of techniques [87].

The profession of naprapathy was introduced in 1907 in the USA by Oakley Smith, and in Sweden in 1970 by Björn J:son Berg. Naprapathy has many similarities with chiropractic, osteopathy, and physiotherapy and is today practised mainly in Sweden, Finland and Norway as well as in the USA. There are education centers in Sweden, in Finland and in the USA. In Finland and Sweden, naprapathy has been a registered profession since 1994, part of the health care system and controlled by governmental institutions.

In previous studies naprapathy has been suggested to be an effective treatment for non-specific back and neck pain [85, 86]. It has also been implied to be a cost effective treatment to consider for orthopedic outpatients with disorders unlikely to benefit from surgery [88, 89].

2.5.4.2 Adverse events

Adverse events are defined as any unfavourable and unintended (medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical examination or laboratory finding), symptom or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research [90].

Adverse events after manual therapy have been shown to be mostly mild or moderate in intensity with a short duration [91-93].

In study III, the occurrence of adverse events shortly after naprapathic manual therapy has been investigated. The effect of different naprapathic treatment technique combinations has been compared in study IV.

3 AIMS

The overall aim of this thesis was to increase understanding of naprapathic manual therapy and other factors of potential importance for the prognosis of patients with neck and back pain.

3.1 STUDY I

The aims were 1) to assess and compare the sex-specific recovery rate of spinal pain and psychological distress as single and comorbid conditions, and 2) to describe the interrelationships between these conditions at baseline and at follow-up 5 years later. In addition, we explored whether spinal pain is a risk factor for the onset of psychological distress, and vice versa.

3.2 STUDY II

The aim was to explore the role of good sleep on prognosis for patients with non-specific neck and/or low back pain.

3.3 STUDY III

The main aim was to investigate differences in the occurrence of adverse events of varying severity and duration among patients receiving 1) manual therapy (a combination of spinal manipulation, spinal mobilization, muscle stretching and/or massage), 2) manual therapy without spinal manipulation or 3) manual therapy without muscle stretching. An additional aim was to compare the occurrence of adverse events in men and women.

3.4 STUDY IV

The main aim was to compare the treatment effect of naprapathic manual therapy (including spinal manipulation, spinal mobilization, stretching and massage) and naprapathic manual therapy without either spinal manipulation or stretching in patients with non-specific neck and/or back pain. An additional aim was to investigate whether treatment effects varied in men and women patients.

4 MATERIALS AND METHODS

4.1 STUDY I

Study 1 is based on data from The Stockholm Public Health Cohort, a prospective cohort study set within the framework of the Stockholm County Council Public Health Surveys. These extensive surveys, with the aim of collecting data for regional public and occupational health reports, included questions about spinal pain, psychological distress and other health-related parameters such as lifestyle, labour market status, physical and psychosocial work environment [94]. Data were collected initially in 2002 and at follow-up in 2007 (Figure 2).

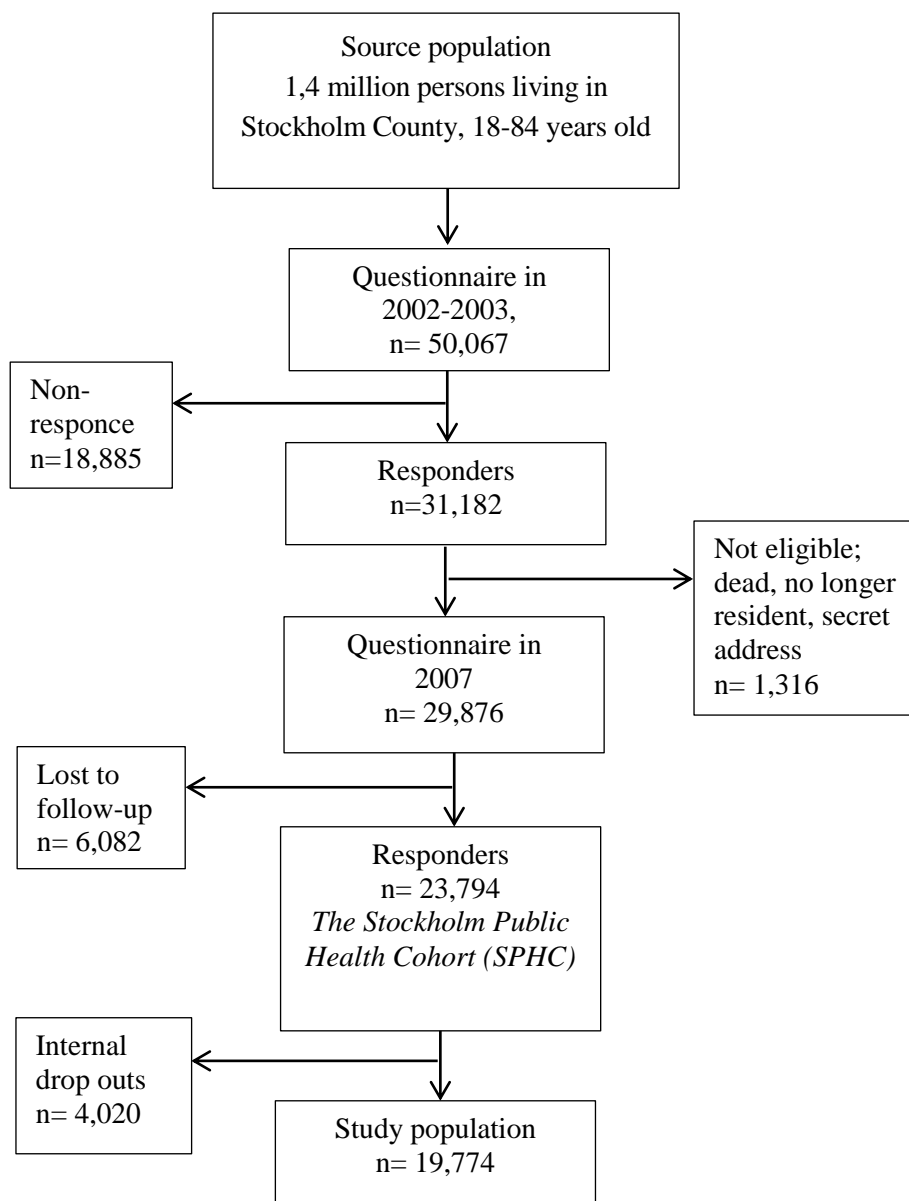


Figure 2. Flow chart showing the selection of study participants in The Stockholm Public Health Cohort.

To be able to describe the interrelationships among different combinations of neck pain, back pain and psychological distress in a valid way, participants with missing values for any of the questions measuring neck pain, back pain or psychological distress at either baseline or follow-up were excluded from the analyses (n=4,020). Accordingly, the study population comprised 19,774 participants divided into four subcohorts according to the presence of spinal pain and psychological distress at baseline. These subcohorts were used to assess and compare recovery from spinal pain and psychological distress as single and comorbid conditions, and to describe the interrelationships between these conditions at baseline and at follow-up 5 years later. As shown in Figure 3, analyses were conducted in two subcohorts to investigate whether spinal pain was a risk factor for the onset of psychological distress, and vice versa.

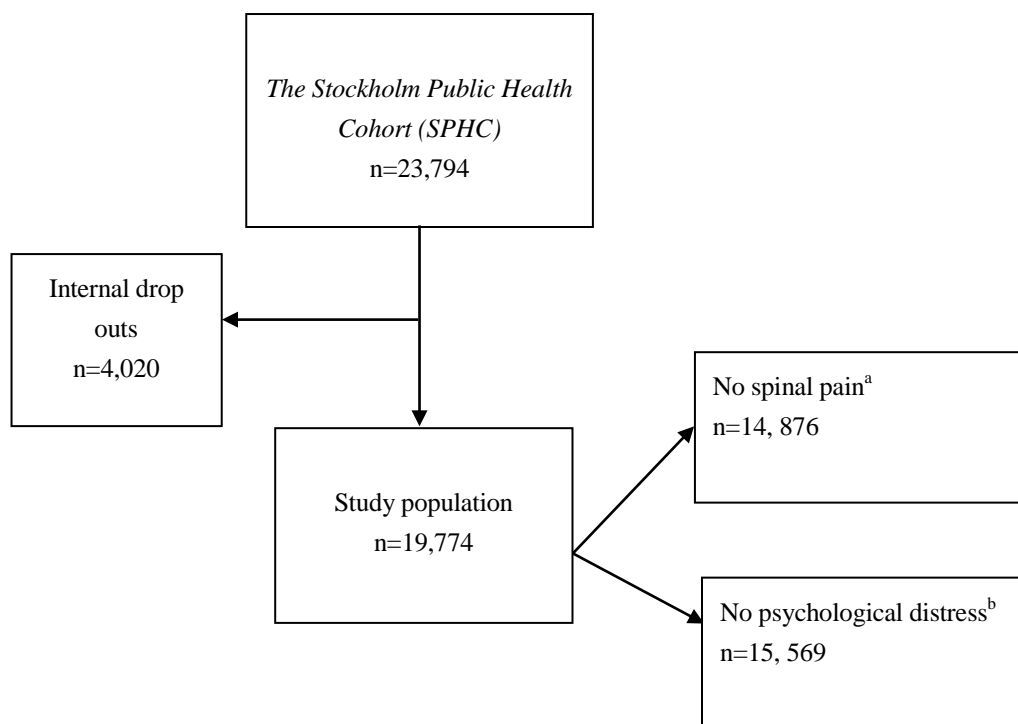


Figure 3. Flow chart showing the selection of study participants in The Stockholm Public Health Cohort.

^aAt risk of developing spinal pain at follow-up; i.e. participants with psychological distress at baseline (n=2,650) and those with neither spinal pain nor psychological distress (n=12,226).

^bAt risk of developing psychological distress at follow-up; i.e. participants with spinal pain at baseline (n=3,343) and those with neither psychological distress nor spinal pain (n=12,226).

The study was approved by the ethical review board in Stockholm (approval number 2009/5:4).

4.1.1 Measures

In this study, spinal pain was measured using a slightly modified form of the Standardized Nordic Questionnaire [37] and the General Health Questionnaire-12 (GHQ-12) was used to measure psychological distress [95, 96].

4.1.2 Definitions

At baseline

Neck pain at baseline was measured with the following question: ‘During the previous 6 months, have you experienced pain in your upper back or neck?’. The possible answers were: 1) No, never; 2) Yes, 2 days in the last 6 months; 3) Yes, on average 2 days a month; 4) Yes, on average 2 days a week; or 5) Yes, every day. Participants who gave answers 4 or 5 were considered to have neck pain.

Back pain at baseline was measured with the same question, but substituting ‘lower back’ for ‘upper back or neck’.

Spinal pain at baseline was defined as the presence of neck pain and/or back pain at baseline.

At follow-up

Neck pain at follow-up in 2007 was assessed with the following question: ‘During the last 5-year period have you had neck pain for at least 3 consecutive months that has bothered you considerably?’ and ‘During the last 5-year period have you had neck pain, on at least 7 consecutive days but for less than 3 consecutive months, that has bothered you considerably?’. If the answer was ‘yes’, to either or both of these questions, a second question was asked to assess in which year(s) such episodes of neck pain occurred. Participants who answered ‘yes’ and specified that this occurred in the year 2007 were defined as having neck pain at follow-up.

Back pain at follow-up was assessed in the same way as neck pain, but substituting ‘back’ for ‘neck’ in the questions.

Spinal pain at follow-up was defined as having at least one episode of neck and/or back pain at follow-up.

The questions to assess spinal pain at baseline and follow-up were different with regard to prevalence period. At baseline the questions about spinal pain were related to the pain experienced during the previous 6 months. At follow-up, the questions about spinal pain were limited to the pain experienced in the year 2007. The follow-up questionnaires were sent out from 14 March to 15 August 2007. This covers a 3- to 8-month period in that year, which is similar to the prevalence period regarding spinal pain at baseline of 6 months.

4.1.3 Psychological distress

The GHQ-12 was used [96] to determine the presence of psychological distress. The original version of this questionnaire has 60 questions and the shorter versions have 30, 28 and 20 items. It has been shown that the questionnaire with 12 items is comparable to and as reliable as the 30-item version. In this thesis, we used the 12-item GHQ-12, which covers areas such as anxiety and depressed mood, social function and loss of confidence during the preceding weeks.

As recommended, a sum score of ≥ 3 out of a maximum of 12 (using the standard 0-0-1-1 scoring for the four possible answers: 1) Better than usual, 2) As usual, 3) Worse than usual and 4) Much worse than usual) was used to denote significant psychological distress [97]. This instrument has been found to be valid and reliable for male and female subjects, in young and adult populations in different countries [98-101]. This instrument identifies psychological distress during the previous weeks. GHQ-12 is not designed to detect severe psychiatric conditions but only transient and common mental disorders [102].

4.1.4 Comorbidity at baseline and follow-up

Comorbidity was defined as the presence of spinal pain (neck and/or back) with concurrent psychological distress at baseline or at follow-up.

4.1.5 Statistical analysis

The sample of the population used in this study from the Stockholm County was treated as a complete random sample because weighted preliminary analyses according to the stratified sampling scheme showed only negligible differences in the prevalence of spinal pain and psychological distress.

To compare data between women to men, we calculated the relative risk (RR), with corresponding 95% confidence interval (95% CI). The chi-squared test was used to calculate the one-tailed p-value for differences between women and men, with one degree of freedom. Mantel-Haenszel analyses were used to test whether the age differences confounded the comparisons of occurrences between men and women. Logistic regression was used to analyse the odds for onset of spinal pain for a given baseline level of psychological distress and the odds for onset of psychological distress for a given baseline level of spinal pain. Factors tested for potential confounding in these analyses were age at baseline (continuous variable), sex, home and household work ≥ 3 hours/day (yes/no), Sweden born (yes/no), socioeconomic status (blue collar workers/white collar workers/self-employed), daily smoking (yes/no), alcohol consumption (yes/no), body mass index (continuous variable) and sedentary leisure time (yes/no).

All calculations were carried out using Stata SE version 12.0 [103].

4.2 STUDY II

This cohort study is a secondary analysis of data from the Björn-trial, an RCT with the aim of comparing naprapathic manual therapy and evidence-based physician care for patients with non-specific neck and/or back pain [85]. The two interventions that were compared were naprapathic manual therapy such as spinal manipulation/mobilization, massage and stretching (index group) and evidence-based care provided by a physician (control group). In the index group patients received a maximum of six treatments by a licensed and experienced naprapath.

The patients participating in this study were recruited from public companies in Stockholm, Sweden (n=409). All participants had non-specific neck and/or back pain lasting at least 2 weeks which had bothered them considerably.

The trial was approved by the ethical review board in Stockholm (approval numbers 03-657 and 2014/190-32), and was registered in a public registry (Current Controlled Trials ISRCTN56954776).

4.2.1 Measures

Sleep at baseline was measured using the Karolinska Sleep Questionnaire [104] and the ‘unwinding and recovery’ questions of Aronsson et al [105]. The CPQ [35] was used at baseline and follow-up (7, 12, 26 and 52 weeks) to measure pain and pain-related disability.

4.2.2 Good sleep

The definition of impaired sleep in the present study was based on international diagnostic criteria and the available literature: difficulty initiating and/or maintaining sleep accompanied by daytime consequences [75].

Three groups were compared with regard to their sleep status and the minimal clinically important difference (MCID) in pain and pain related disability.

4.2.3 Exposure

1) ‘Impaired sleep’ (reference group): patients who reported difficulty falling asleep (‘Do you have trouble falling asleep?’) or maintaining sleep (‘Do you wake up several times at night and sometimes have difficulty going back to sleep?’), and reported daytime consequences (‘Do you feel very tired during your work day (shift)?’) several times per week or every day. The first two questions were derived from the reliable Karolinska Sleep Questionnaire [106] and the last question was taken from the ‘unwinding and recovery’ questions by Aronsson et al [105].

2) ‘Good sleep’: patients who had no problems initiating and maintaining sleep, or problems less than several times per week.

3) ‘Impaired sleep without daytime consequences’: patients who reported having problems several times per week or every day in initiating and maintaining sleep but had no daytime consequences.

4.2.4 Outcome

The study outcome was MCID in pain and pain related disability from baseline to follow-up at 3 and 12 months. Pain and pain related disability were measured with a slightly modified CPQ (the original scale based on recall of the previous 6 months was changed to the previous 4 weeks) [35].

Patients rated their pain according to three pain items (current pain, worst pain, average pain) and measured how the pain affected their daily activities, using three disability items (interference with activities related to daily living, recreation and social life or work). Items were rated on an NRS of 0–10 (0=no pain/no interference, 10=worst pain/unable to continue with these activities). The NRS has been shown to be a reliable instrument when measuring pain intensity [36, 107-109].

The outcome, MCID on the pain score, was defined as a decrease of at least two points compared to the baseline value. An MCID in the disability score was defined as a decrease of at least one point compared to the baseline value [110, 111]. Pain and disability scores were calculated as the mean of the three pain and three disability items, respectively. If only two pain or disability questions were answered, the calculation was based on those questions (n=3). Patients for whom the pain or disability score at baseline was too low (i.e. cannot have a MCID at follow-up according to our definition), were not included in the analysis (pain: n=4, disability: n=94).

4.2.5 Confounding

Potential confounding factors for the analyses of the association between neck and/or back pain and good sleep were identified a priori by members of our research group based on the currently available literature [112, 113]. The following potential confounding factors were identified: treatment modality (design variable), age (continuous), gender, education, pain duration, pain intensity at baseline, pain-related disability at baseline, pain site, smoking, physical activity, obesity (≥ 30 kg/m²), marital status, one or more major life event during the previous year (e.g. serious conflict with spouse or partner, or serious illness of a close person), work stress, job satisfaction, bullying, depression, anxiety.

4.2.6 Statistical analysis

Logistic regression was used to analyse the association between good sleep and MCID in pain and disability at 3 and 12 months. Each potential confounding factor was tested separately by building a series of multiple regression models with the main exposure (impaired sleep) and the potential confounding factor. If the inclusion of a factor resulted in $\geq 10\%$ change in the effect estimate of the determinant of outcome (i.e. MCID in pain or disability), the factor was considered a confounding factor and included in the final model [114].

The statistics program Stata version 12.0 was used for the analysis [103].

4.3 STUDIES III AND IV

This RCT, the Stockholm Manual Intervention Trial (MINT), studies III and IV are based on, was carried out at the educational clinic of the Scandinavian College of Naprapathic Manual Medicine, Stockholm. The patients participating in these studies were seeking care for neck and/or back pain at this clinic during the period 1 January 2010 to 30 June 2012 (study III) or 1 January 2010 to 31 December 2012 (study IV).

4.3.1 Design

The three-arm RCT was approved by the ethical review board in Stockholm (approval number 2009/1848-31/2), and was registered in a public registry (Current Controlled Trials ISRCTN92249294).

4.3.2 Setting

The treatments were given at the educational clinic of the Scandinavian College of Naprapathic Manual Medicine, Stockholm. The students, who provided the treatments were in their seventh semester of a total of eight, and they had regularly (2 days a week) treated patients during the previous five semesters. These treatments included spinal mobilization techniques during the previous three semesters and spinal manipulation techniques during the previous two semesters under the supervision of experienced registered naprapaths. Therapists participating in the current study had passed all practical clinical examinations at this level of the education. The therapists as well as the supervising experienced registered naprapaths were thoroughly trained in different aspects of the study protocol during a number of meetings before the start of the study. Uncertainties and questions were discussed in regular weekly meetings during the inclusion period.

4.3.3 Participants

Patients (18–65 years of age) seeking care for neck and/or back pain who had not visited the educational clinic during the previous month were eligible for inclusion in the trial.

Figures 4 (study III) and 5 (study IV) show the progress of participants through the two studies based on the trial.

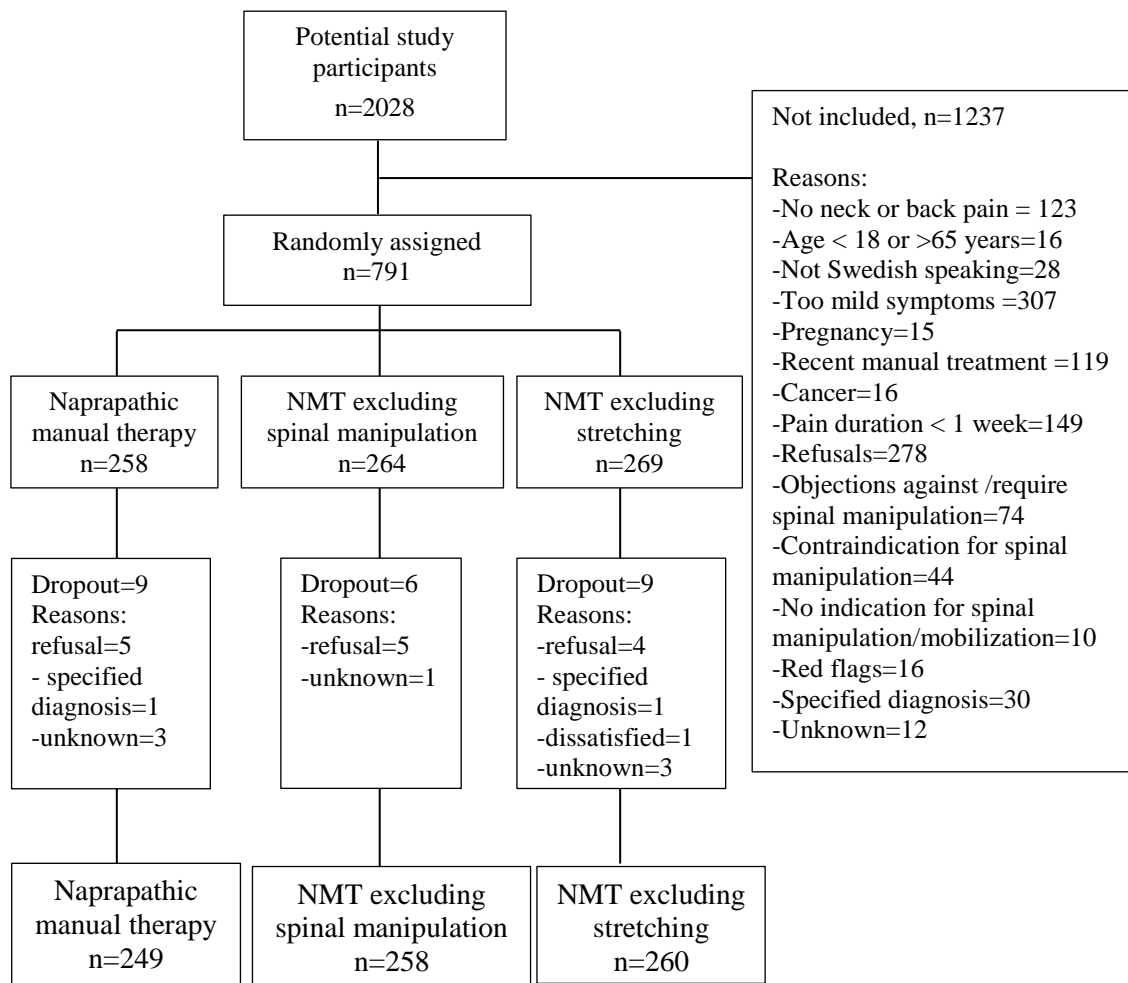


Figure 4. Flowchart of recruitment, randomization and follow-up in study III.

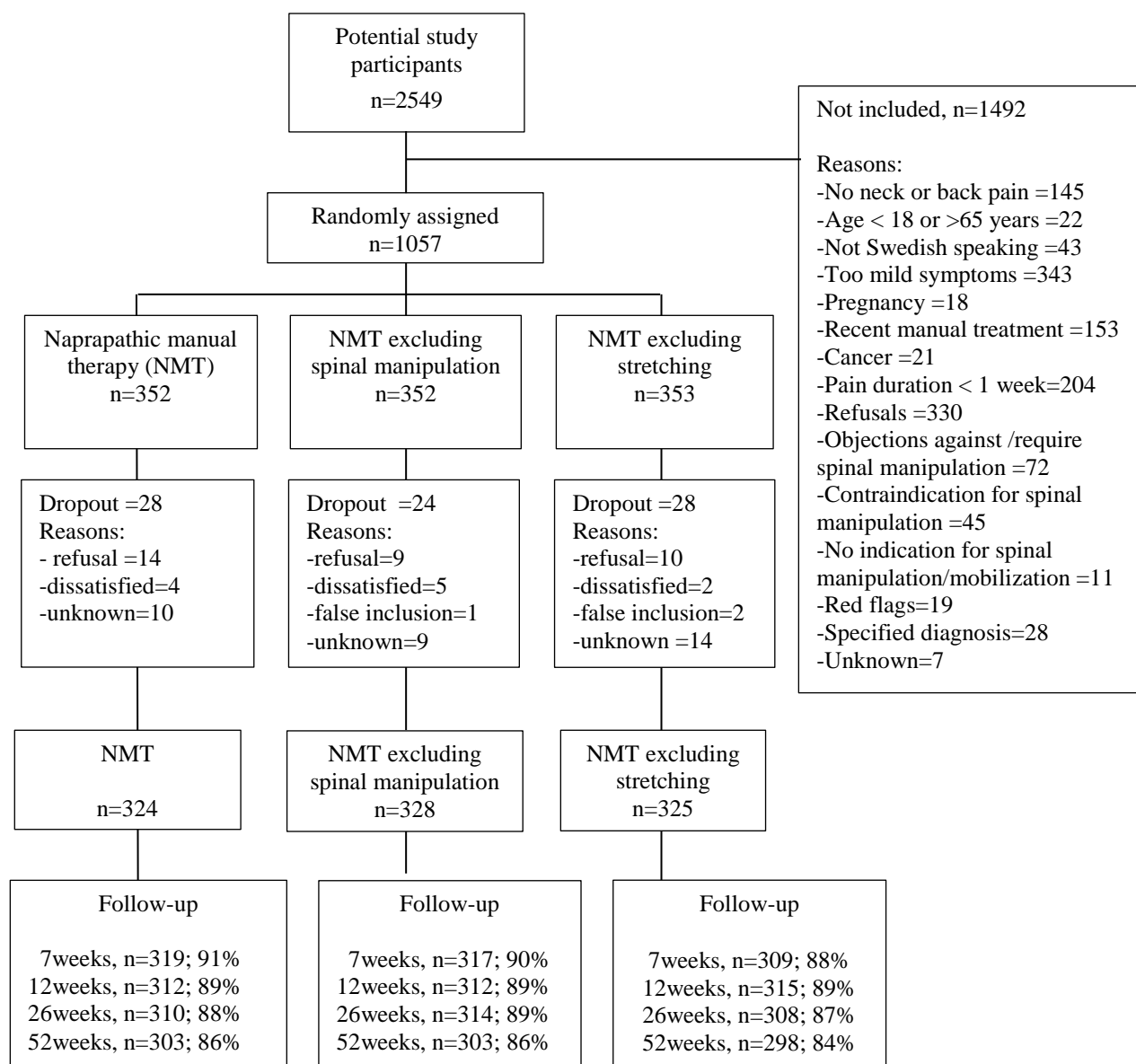


Figure 5. Flowchart of recruitment, randomization and follow-up in study IV.

4.3.4 Exclusion criteria

The exclusion criteria for these studies were 1) lack of proficiency in the Swedish language, 2) score of <2 on an NRS (0–10) in two questions regarding pain intensity (pain at the present time and the worst pain during the past 4 weeks) in the neck and/or back, 3) pregnancy, 4) current or previous cancer diagnosis, 5) having previously received treatments for the current complaint by a chiropractor, naprapath, osteopath or physiotherapist during the past month, 6) duration of the current complaint less than 1 week, 7) demanding/refusing spinal manipulation/stretching, 8) contraindication for spinal manipulation according to the Swedish Board of Social Welfare [115], 9) no indication for spinal manipulation in the area of complaint, 10) ‘red flags’ (e.g. previous trauma, inflammatory or rheumatic diseases, drug addiction or large rapid weight loss), 11) specific diagnoses (e.g. ankylosing spondylitis, spinal stenosis and rheumatoid arthritis) and 12) on sick leave due to planned/completed surgery for neck and/or back pain.

4.3.5 Randomization

A trained research assistant carried out the randomization in advance and prepared sequentially numbered opaque and sealed envelopes with folded cards numbered 1, 2 or 3, by drawing these cards from a box. Stratified randomization was used, based on the location of pain: 1) neck and upper back (including neck/shoulders and upper back, above the 11th thoracic vertebra, upper extremities and chest), 2) lower back (including the area below the 10th thoracic vertebra, gluteal area and lower extremities) and 3) neck and back (pain equally bad in the neck and upper back and lower back). For each stratum, block randomization was used so that there were equal allocations to the three treatment arms in each block of 99 patients.

At the first visit, potential participants were informed about the study. Informed consent was obtained and the patient completed the baseline questionnaire appropriate for the area of pain before physical examination and diagnostic assessment were carried out by the therapist. Both patient and therapist were unaware of the group assignment until after all baseline data were collected. Treatment allocation was accomplished by the therapist after the physical examination and completion of the baseline questionnaire. Therapists were told not to reveal the result of the randomization to patients if possible, but this cannot be considered as patient blinding to the treatment.

4.3.6 Baseline questionnaire

The baseline questionnaire was based on questionnaires used in our previous studies [85, 116] and included questions about socio-demographic factors, physical activity, smoking habits, previous similar pain conditions and how the current complaint began, expectations of recovery related to treatment and general health [117]. A modified CPQ was used to assess pain intensity and pain-related disability at baseline and at follow-up [35]. The original scale that was based on recall of the past 6 months was modified to recall of the past 4 weeks [35, 36].

4.3.7 Interventions

Three interventions were compared:

- 1) Naprapathic manual therapy (NMT): i.e. spinal manipulation, spinal mobilization, muscle stretching and massage could be used by the therapist.
- 2) NMT excluding spinal manipulation: all available NMT techniques, excluding spinal manipulation, were allowed.
- 3) NMT excluding muscle stretching: all NMT techniques, excluding muscle stretching, were allowed.

Each treatment session was scheduled for 45 minutes, maximum six visits.

4.3.8 Follow-up: study III

In study III the follow-up was completed at each return visit. The patient filled in an adverse event questionnaire in the waiting room before undergoing treatment.

If the patient did not show up for a scheduled visit, the therapist contacted the patient and made a new appointment. If the therapist could not, for any reason, contact the patient or if the previous visit was the last visit in the treatment series, the research assistant contacted the patient and completed the questionnaire.

4.3.8.1 Outcomes

In study III the adverse events of concern were events that had occurred within 24 hours following the treatment [118-120]. The adverse event questionnaire contained questions to determine: 1) whether the patient had experienced an event as an effect of the treatment given at the latest visit (yes/no), 2) the duration of the event (how many hours the event lasted) and 3) to what extent the event had bothered the patient, measured by an 11-point NRS (0=not bothered at all, 10=had bothered them in the worst possible way).

The choice of eight adverse events to include in the questionnaire was based on the results from previous studies [85, 93, 121, 122]: tiredness, soreness in muscles, stiffness, increased pain, nausea, headache, dizziness or 'other'.

4.3.8.2 Categorized outcomes

For the data presentation and analyses, adverse events were divided into five categories with definitions based on duration and/or severity of the reaction: 1) short minor (duration <24 hours; NRS ≤3), 2) long minor (duration ≥24 hours; NRS ≤3), 3) short moderate (duration <24 hours; NRS >3), 4) long moderate (duration ≥24 hours; NRS >3) and 5) serious adverse events (e.g. loss of bowel/bladder function, stroke, fracture or hospitalization).

4.3.9 Follow-up: study IV

In study IV the follow-up regarding the outcomes was carried out by self-administered postal or web-based questionnaires after 7, 12, 26 and 52 weeks. If a patient did not answer or if the questionnaire was not completely filled in, a trained research assistant contacted the patient by phone, mail or letter as a reminder, a maximum of three times.

4.3.9.1 Outcomes

In study IV patients graded their pain according to three pain items (current pain, worst pain, average pain) each measured with an NRS of 0–10 (0=no pain, 10=pain as bad as possible) using a slightly modified CPQ [35]. Three questions assessed disability and concerned to what degree pain 'interfered with your daily activities', 'changed your ability to take part in recreational, social and family activities' and 'changed your ability to work (including housework)' in the past 4 weeks. These items were rated using an NRS of 0–10 (0=no interference, 10=unable to continue with these activities).

Mean pain and mean disability scores were calculated based on the answers to these questions.

4.3.9.2 *Dichotomized primary outcomes*

An MCID in pain was defined as a decrease of at least two points in the mean pain score at follow-up compared to the baseline value and an MCID in disability was defined as a decrease of at least one point in the mean disability score at follow-up compared to the baseline value [110, 111].

4.3.9.3 *Secondary outcome*

Perceived recovery was measured by the question ‘Which of the following statements is most consistent with how you feel your problem in the neck/back has changed since you joined this study?’. The possible answers were 1) ‘Is completely free from pain and have no other complaints originating from neck/back’, 2) ‘Is considerably improved’, 3) ‘Is slightly improved’, 4) ‘No change’, 5) ‘Is slightly worse’ and 6) ‘Is much worse’. For the comparison between groups the answers were dichotomized: recovered (answers 1 and 2)/not recovered (answers 3–6).

4.3.10 **Statistical methods**

In study III, descriptive statistics were used to summarize baseline characteristics and describe the frequency and proportion of different types of adverse events after each visit. Odds ratios (ORs) and 95% CIs were calculated with Generalized Estimating Equations (GEEs) to examine the association between adverse events (four levels) and treatment (three arms) and sex respectively in the longitudinal data [123, 124]. The baseline characteristic factors listed in Table 5 were considered as potential confounding factors. No confounding was identified. Additional analyses were performed to determine the number and proportion of patients who had experienced any kind of adverse events, regardless of duration and severity, after every visit or any visit, or who had no adverse events after any of at least three treatments

In study IV, an intention to treat approach was used for analyses. Logistic regressions using GEEs were conducted to determine whether there were any differences between the treatment arms in MCID in pain and pain related disability and to test for confounding. Further, linear regressions with GEEs were used to test whether there were any differences in mean pain/disability score [123, 124]. The analysis of perceived recovery was performed using ordinal logistic regression with cluster-robust standard errors. The analyses in study IV were made by a biostatistician who was not involved in the randomization process or data collection.

All analyses were conducted using Stata version 13.0 [125].

5 RESULTS

5.1 STUDY I

The mean age of the study population was 47.6 years, and 55% were women. Twenty-seven percent were blue collar workers and 3% were unemployed.

Spinal (neck and/or back) pain with concurrent psychological distress (comorbidity) was significantly more common among women than men (women 11%, men 4%; RR=2.4, 95% CI: 2.1–2.7). The risk of neck pain (but not back pain) with concurrent psychological distress was more than three-fold higher for women than men (RR=3.2, 95% CI: 2.7–3.9). Spinal pain without psychological distress (women 20%, men 14%; RR=1.4, 95% CI: 1.3–1.5) and psychological distress without spinal pain (women 15%, men 12%; RR=1.2, 95% CI: 1.2–1.3) were also more common in women. Age adjustment did not significantly change the results of the comparisons between men and women.

Among participants with spinal pain as a single condition, 41% of women and 44% of men had recovered at follow-up; among those with psychological distress as a single condition, 49% of women and 52% of men had recovered at follow-up. Fewer women and men with both spinal pain and concurrent psychological distress at baseline (comorbidity) recovered (26% and 27%, respectively), and those with all three conditions (neck pain, back pain and psychological distress) had the poorest prognosis for recovery (18% for both sexes). Recovery from spinal pain and/or psychological distress was similar among men and women. The effect of comorbidity of spinal pain and psychological distress on the likelihood of recovery is shown in Figure 6.

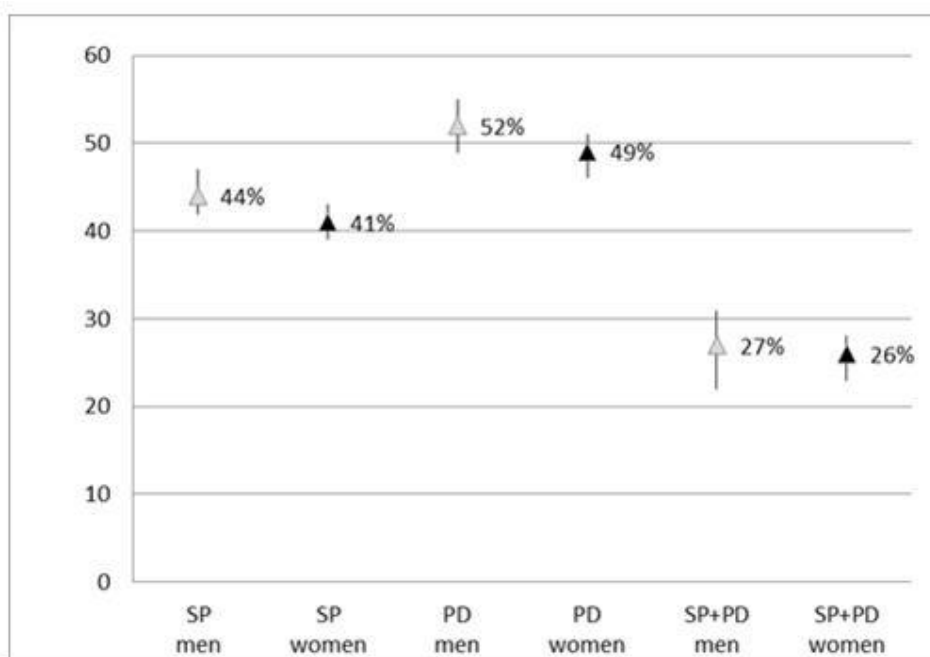


Figure 6. The proportion of study participants (men, grey; women, black) with spinal pain (SP), psychological distress (PD) or SP with concurrent PD who recovered (neither spinal pain nor psychological distress) from baseline to follow-up. The corresponding 95% confidence intervals are shown.

The risk of developing psychological distress at follow-up in participants with spinal pain as a single condition at baseline was slightly higher (adjusted OR=2.6, 95% CI: 2.3–2.9) than that of developing spinal pain at follow-up in participants with psychological distress as a single condition at baseline (adjusted OR=2.0, 95% CI: 1.8–2.2). Only sex and age were found to confound these associations.

5.2 STUDY II

Of the patients included in the original trial (n=409), 105 reported sleep problems consistent with the definition of impaired sleep. Of the remaining patients, 238 reported no sleep problems (good sleep) and 66 reported some sleep problems without daytime consequences. The mean age of the study population was 46.86 (SD 10.60) years, and 71% were women. Patients with impaired sleep had a lower level of education, were more likely to be single and smokers, and had depression and anxiety more often than those with good sleep or impaired sleep without daytime consequences.

Table 1 shows the OR values for MCID in pain and disability from baseline to follow-up for patients with good sleep and impaired sleep without daytime consequences, compared to patients with impaired sleep. Patients with good sleep were more likely to experience an MCID in pain (OR=2.03, 95% CI: 1.22–3.38) and pain related disability (OR=1.85, 95% CI: 1.04–3.30) at the 12-month follow-up compared to patients with

impaired sleep. The OR for MCID in pain in the fully adjusted model was 2.51 (95% CI: 1.45–4.38) at the 12-month follow-up and the corresponding figure for pain related disability was 1.88 (95% CI: 1.05–3.35). The adjusted OR values for MCID in pain and pain related disability for patients with impaired sleep without daytime consequences in comparison to patients with impaired sleep at 12 months were 2.15 (95% CI: 1.05–4.46) and 1.36 (95% CI: 0.62–2.17), respectively.

Table 1. The odds ratio for minimal clinically important difference in pain and disability from baseline to follow-up for patients with good and impaired sleep without daytime consequences compared to patients with impaired sleep.

Follow-up	3 months		12 months	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Minimal clinically important difference in pain ^a				
Impaired sleep ^b	Ref.	Ref.	Ref.	Ref.
1. Good sleep ^c	1.14 (0.71-1.86)	1.61 (0.94-2.75)	2.03 (1.22–3.38)	2.51 (1.45–4.38)
2. Impaired sleep without daytime consequence ^d	1.20 (0.63-2.29)	1.80 (0.90-3.64)	1.65 (0.84-3.24)	2.15 (1.05–4.46)
Minimal clinically important difference in disability ^e				
Impaired sleep	Ref.	Ref.	Ref.	Ref.
1. Good sleep	1.21 (0.69-2.12)	1.21 (0.69-2.13)	1.85 (1.04–3.30)	1.88 (1.05–3.35)
2. Impaired sleep without daytime consequence	1.35 (0.62-2.94)	1.35 (0.62-2.95)	1.31 (0.60-2.83)	1.36 (0.62-2.17)

^a Minimal clinically important difference in pain: defined as at least a two-point decrease from baseline to follow-up, measured with a numerical rating scale of 0–10 (0=no pain, 10=pain as bad as possible).

^b Impaired sleep: defined as difficulty initiating and/or maintaining sleep, for several nights per week or every day, and accompanied by a daytime consequence (feeling tired during work).

^c Good sleep: defined as having no problems or having problems less than several times per week in initiating and maintaining sleep.

^d Impaired sleep without daytime consequences: defined as having problems in initiating or maintaining sleep several times per week or every day but having no daytime consequence.

^eMinimal clinically important difference in disability: defined as at least a one-step decrease from baseline to follow-up, measured with a numerical rating scale of 0–10 (0=no interference, 10=unable to continue with these activities).

^fMinimal clinically important difference in pain was adjusted for pain intensity at baseline (>5 vs ≤5) and anxiety (yes vs no). Minimal clinically important difference in disability was adjusted for pain intensity at baseline.

5.3 STUDY III

Of the 2027 eligible study patients, 1236 did not fulfill the inclusions criteria, and accordingly 791 study participants were randomly assigned to one of the three treatment arms. A total of 24 patients dropped out after randomization (14 wanted to leave the study, two had specific diagnoses and one was dissatisfied; the reasons were unknown for the remaining seven). Therefore the study population consisted of 767 patients. The participation rate was 97%, and an additional 6% of patients were lost to follow-up (of these 6% of patients, data were not available for the first, last or any treatment for 29%, 51% and 20%, respectively). This missing data were equally distributed between the three treatment arms.

Baseline characteristics of the patients in the trial are presented in Table 2.

Table 2. Baseline characteristics of patients stratified by treatment arm (n=767).

	MT ^a	MT excluding spinal manipulation	MT excluding stretching
	n = 249	n = 258	n = 260
Mean age (SD)	35.0 (12.4)	35.3 (12.3)	35.7 (11.3)
Women, %	67	74	75
Painful area, %			
Back	35	33	33
Neck	54	54	54
Back/Neck	11	13	13
Duration of the pain, %			
1 week	17	17	18
2-4 weeks	28	23	25
1-3 months	17	21	20
3-6 months	9	10	6
>6 months	29	29	31
^b Pain at baseline (SD)	5.5 (1.7)	5.3 (1.7)	5.5 (1.8)
^c Disability at baseline (SD)	2.5 (2.2)	2.5 (2.3)	2.6 (2.2)
Education, %			
1-9 years	3	5	3
10-12	40	37	36
13-15	46	46	47
>16	11	12	14
General health, %			
Excellent	16	15	18
Very Good	46	48	43
Good	31	30	35
Somewhat	6	7	3
Bad	1	0	1
Daily smoking, %	18	14	17

^aManual therapy (spinal manipulation/mobilization, stretching and massage).

^bPain at baseline was based on three pain items: current pain, worst pain and average pain during the past 4 weeks, measured with a numerical rating scale of 0–10 (0=no pain, 10=pain as bad as possible) and calculated as an average pain score for these items.

^cDisability at baseline was based on three disability items: interference with 1) daily activities, 2) recreational and social activities and 3) work activities, measured with a numerical rating scale of 0–10 (0=no interference, 10=unable to continue with these activities) and calculated as an average disability score for these items.

The most common adverse event was soreness in the muscles followed by increased pain, stiffness and tiredness. There were no clear differences between the treatment groups regarding the occurrence of adverse events (Table 3).

Table 3. Comparison of different levels of adverse events between treatment arms.

Treatment arms	Adverse events			
	Short minor ^a OR (95% CI)	Long minor ^b OR (95% CI)	Short moderate ^c OR (95% CI)	Long moderate ^d OR (95% CI)
1. MT ^e	Ref.	Ref.	Ref.	Ref.
2. MT excluding spinal manipulation	1.09 (0.83-1.43)	1.37 (0.91- 2.08)	0.82 (0.58- 1.16)	1.09 (0.79-1.52)
3. MT excluding stretching	1.09 (0.84- 1.43)	1.24 (0.82-1.89)	0.97 (0.70-1.37)	1.11 (0.81-1.53)

^aDuration <24 hours, numerical rating scale (NRS) ≤3; ^bduration ≥24 hours, NRS ≤3;

^cduration <24 hours, NRS >3; ^dduration ≥24 hours, NRS >3.

NRS of 0–10: 0=not bothered at all and 10= had bothered them in the worst possible way.

^eManual therapy (MT; spinal manipulation/mobilization, stretching and massage).

Comparison between women and men showed that women more often experienced both short moderate (OR=2.19, 95% CI: 1.52–3.15) and long moderate adverse events (OR=2.49, 95% CI: 1.77–3.52). Adverse events, regardless of severity or duration, were investigated in a sub-cohort of 556 patients who had received at least three treatment sessions. The results showed that approximately half (51%) of patients experienced at least one event after some of the treatments, 37% did so after every visit, and 13% reported no events. The overall comparison showed that most of the adverse events lasted less than 24 hours and were graded less than or equal to three on the NRS of severity of the event.

Table 4 shows the number and proportion of patients who experienced at least one adverse event after each visit.

Table 4. Proportion of patients who experienced at least one adverse event after each visit.

Visit number	1. n=767 (%)	2. n=685 (%)	3. n=556 (%)	4. n=389 (%)	5. n=211 (%)	6. n=84 (%)
Adverse event						
Short minor ^a	270 (35)	218 (32)	147 (26)	89 (23)	55 (26)	32 (38)
Long minor ^b	34 (4)	110 (16)	64 (12)	37 (10)	27 (13)	12 (14)
Short moderate ^c	135 (18)	147 (21)	87 (17)	57 (15)	24 (11)	10 (12)
Long moderate ^d	121 (16)	117 (17)	80 (14)	44 (11)	18 (9)	7 (8)

^aDuration <24 hours, numerical rating scale (NRS) ≤ 3 ; ^bduration ≥ 24 hours, NRS ≤ 3 ; ^cduration <24 hours, NRS >3; ^dduration ≥ 24 hours, NRS >3. NRS of 0–10: 0=not bothered at all and 10= had bothered them in the worst possible way.

5.4 STUDY IV

Of the 2549 eligible study patients, 1492 did not fulfill the inclusions criteria, and accordingly 1057 study participants were randomly assigned to one of the three treatment arms. After randomization, 80 patients dropped out: 33 wanted to leave the study, three were false inclusions, 11 were dissatisfied and 33 dropped out due to unknown reasons. The dropouts were equally distributed between the treatment arms.

Baseline characteristics of the study participants are shown in Table 5.

Table 5. Baseline characteristics of the patients (n=1057).

	NMT ^a	NMT excluding spinal manipulation	NMT excluding stretching
	n = 352	n = 352	n = 353
Mean age (SD)	35 (12.2)	36 (11.9)	36 (11.4)
Sex, %			
Women	68	72	71
Painful area, %			
Back	35	33	33
Neck	54	54	54
Back/Neck	11	13	12
Duration of the pain, %			
1 week	17	16	18
2-4 weeks	29	23	26
1-3 months	18	22	21
3-6 months	9	19	7
>6 months	28	28	27
Similar previous complaints, %			
Yes	73	79	80
Mean pain at baseline ^b (SD)	5.5 (1.6)	5.4 (1.7)	5.5 (1.7)
Mean disability at baseline ^c (SD)	2.6 (2.2)	2.6 (2.2)	2.6 (2.2)
Education, %			
1-9 years	3	4	3
10-12	37	39	37
13-15	50	46	46
>16	11	11	14
General Health, %			
Excellent	14	17	19
Very Good	46	45	42
Good	34	30	34
Somewhat	6	7	4
Bad	1	-	1
Smoking, %			
Daily	18	14	17
Physical activity, % on medium or high level ^e	33	33	43
Mean expectations of recovery ^d (SD)	6.1 (3.0)	5.9 (2.9)	5.9 (2.9)
Obesity, %	7	8	7

^aNaprapathic manual therapy (NMT; spinal manipulation/mobilization, stretching and massage).

^bPain intensity at baseline was based on three pain items: current pain, worst pain and average pain during the past 4 weeks, measured with a numerical rating scale of 0–10 (0=no pain, 10=pain as bad as possible) and calculated as an average pain score for these items.

^cDisability at baseline was based on three disability items: interference with 1) daily activities, 2) recreational and social activities and 3) work activities, measured with a numerical rating scale (NRS) of 0–10 (0=no interference, 10=unable to continue with these activities) and calculated as an average disability score for these items.

^dExpectations of recovery were measured with an NRS of 0–10 (0=recovery not at all likely and 10=recovery very likely).

^ePhysical activity: medium (effort that would make it difficult to hold a conversation) or high (you have a high pulse, you feel strained and become sweaty) level at least twice/week.

The total number of treatments in this study was 4627, mean 3,6 per patient (SD 1.46). For the analysis regarding MCID in pain, it was required that, at baseline, the patient should have a pain score of at least 2/10. Therefore, another six patients were excluded from these analyses. For the analysis regarding MCID in disability, it was required that the patients should have a disability score at baseline of at least 1/10. Consequently, 286 patients were excluded from these analyses. The analyses of the associations between the treatment alternatives and the primary outcomes were not confounded by any of the characteristics presented in Table 5.

There were no significant differences in MCID in pain and pain related disability or perceived recovery for patients seeking care for non-specific neck and/or back pain between those who received NMT (spinal manipulation, spinal mobilization, stretching and massage) and those who received NMT excluding either spinal manipulation or stretching over 1 year (Table 6). Further, we found no significant differences in any of these effects in sex-specific analyses.

Table 6. The odds of a minimal clinically important difference (MCID) in pain intensity, disability and perceived recovery following naprapathic manual therapy (NMT) excluding either manipulation or stretching compared to complete NMT, at follow-up after 7, 12, 26 and 52 weeks.

Treatment arms	NMT ^d Ref.	NMT excluding manipulation OR (95% CI)	NMT excluding stretching OR (95% CI)
Follow-up in weeks			
MCID in pain ^a (n=971)			
7	1.0	0.93 (0.68-1.27)	1.00 (0.73-1.37)
12	1.0	0.74 (0.54-1.03)	0.96 (0.70-1.33)
26	1.0	0.83 (0.60-1.15)	0.85 (0.62-1.17)
52	1.0	0.84 (0.61-1.17)	0.83 (0.60-1.15)
MCID in disability ^b (n=691)			
7	1.0	1.08 (0.72-1.64)	1.44 (0.93-2.21)
12	1.0	1.01 (0.65-1.59)	1.38 (0.86-2.20)
26	1.0	1.21 (0.77-1.91)	1.05 (0.67-1.64)
52	1.0	0.99 (0.61-1.61)	0.73 (0.46-1.17)
Perceived recovery ^c (n=977)			
7	1.0	1.21 (0.88-1.65)	1.12 (0.82-1.53)
12	1.0	0.90 (0.66-1.23)	0.98 (0.72-1.34)
26	1.0	0.90 (0.66-1.24)	1.04 (0.76-1.43)
52	1.0	1.00 (0.73-1.38)	0.89 (0.65-1.22)

^aMCID in pain intensity was defined as at least a two-point decrease from baseline to follow-up, measured with a numerical rating scale of 0–10 (0=no pain, 10=pain as bad as possible).

^bMCID in disability was defined as at least a one-point decrease from baseline to follow-up, measured with a numerical rating scale of 0–10 (0=no interference, 10=unable to continue with these activities).

^cPerceived recovery dichotomized into recovered ('Is completely free from pain and have no other complaints originating from neck/back' or 'Is considerably improved')/not recovered ('Is slightly improved', 'No change', 'Is slightly worse' or 'Is much worse').

^dNaprapathic manual therapy (spinal manipulation, mobilization, stretching and massage).

Table 7 shows perceived recovery at follow-up.

Table 7 Perceived recovery at follow-up.

Follow-up in weeks (n)	7 (n=945)	12 (n=939)	24 (n=932)	52 (n=904)
Perceived recovery	n (%)	n (%)	n (%)	n (%)
Is completely free from pain and have no other complaints originating from neck/back	64 (7)	104 (11)	130 (14)	134 (15)
Is considerably improved	413 (44)	365 (39)	334 (36)	289 (32)
Is slightly improved	333 (35)	311 (33)	266 (29)	238 (26)
No change	114 (12)	131 (33)	166 (29)	190 (21)
Is slightly worse	18 (2)	22 (2)	24 (3)	39 (4)
Is much worse	3 (0.3)	6 (0.6)	3 (0.3)	14 (2)

6 DISCUSSION

6.1 MAIN FINDINGS AND RELATION TO OTHER STUDIES

6.1.1 Study I

The main finding of this study was the negative effect of comorbidity (neck and/or back pain with psychological distress) on recovery (not having any of these conditions). If only one of these conditions was present at baseline, the proportion of patients who recovered was twice as high compared to those with comorbidity. To our knowledge, this is the first longitudinal study showing the effect of comorbidity on recovery from spinal pain with psychological distress in the general population. The findings were equivalent for men and women.

The risk of developing either spinal pain or psychological distress at follow-up using one of the conditions as a determinant of the other was compared. It was found that spinal pain was a slightly stronger determinant of developing psychological distress than vice versa (over a 5-year period).

We found sex-specific differences in the prevalence of neck and/or back pain and psychological distress. All conditions, neck pain, back pain, neck/back pain and psychological distress, were more common in women than in men. The prevalence estimate for comorbidity was nearly two and a half times higher for women. The greatest sex difference was in the prevalence of neck pain (but not back pain) with comorbid psychological distress. The risk of this comorbid condition was more than three times higher for women than men. Our findings are similar to those of other studies [73, 126-131]. Fillingim et al extensively reviewed current research regarding the reasons for gender differences in the prevalence and experience of pain [132]. They noted that the prevalence of common pain is higher among women. The reasons for this are not clear, although various factors such as hormones, the endogenous pain control system (diffuse noxious inhibitory control), differences in treatments, gender roles and coping strategies may be important. The authors also showed that there were clear gender differences when algescic substances were used for stimulation of muscular pain, indicating that women may be more sensitive to this type of pain. This may be part of the explanation for the higher prevalence of neck and/or back pain among women in this thesis. The reason for the sex differences in pain perception is not clear, and according to Fillingim et al the disparity may depend on biopsychosocial factors [132].

6.1.2 Study II

The main finding of this study was that good sleep was an independent and important prognostic factor for improvement in neck and/or back pain and pain-related disability. The results indicate approximately a two-fold increase in clinically important improvement in pain and pain-related disability after 1 year in patients who reported good sleep at baseline compared to those with impaired sleep with daytime consequences. After adjustment in the model for pain intensity at baseline and anxiety, the effect of good sleep on MCID in pain and pain-related disability was enhanced.

These findings are in line with and complement those of previous studies [133-135] showing the negative effect of impaired sleep on pain and pain-related disability.

6.1.3 Study III

The main finding of this study was that most of the adverse events after combined manual therapy were of short duration (lasted less than 24 hours) and mild (≤ 3 on the NRS). The most common adverse event was muscle soreness, followed by increased pain and stiffness. No serious adverse event was reported.

The sex-specific comparison showed that women experienced more than twice as many short- and long-term moderate adverse events than men. No sex differences in short- and long-term minor events were found.

In a subcohort of 556 patients who had undergone at least three treatment sessions, half of the patients experienced at least one adverse event after some of the treatments; 13% reported no events.

The results show that adverse events after manual therapy are common and transient. Similar findings have been reported by others [12, 93, 120, 136-138].

We found no evidence that the use of spinal manipulation in combined manual therapy was associated with more adverse events than treatment without spinal manipulation. Our results are similar to those of previous studies [139, 140]. Others have found disparities in the use of spinal manipulation and mobilization with regard to the occurrence of adverse events. Hurwitz et al reported more adverse events among patients treated with spinal manipulation compared to those treated with spinal mobilization [141]. This disparity in the results may have depended on the pain location. Hurwitz et al studied adverse events in a population with neck pain [141]. Cagnie et al found that patients with neck pain experienced more adverse events compared to individuals with low back pain after treatment with spinal manipulation [120]. In this thesis, the study population consisted of patients with neck (54%), back (34%) and neck and back (12%) pain; this may have affected the occurrence of adverse events.

Further, no differences in occurrence of adverse events were found in study III when stretching was excluded from the manual treatment arsenal. No previous published studies were found to support or contradict these findings.

6.1.4 Study IV

In this study we compared the effect of different treatment technique combinations within naprapathic manual therapy for non-specific neck and/or back pain. Perceived recovery and MCID in pain and pain-related disability were measured at follow-up to assess the effect of the treatment.

There were no differences between the treatment arms in recovery or clinically important improvement in pain or disability. Similar results have been reported previously [12, 142, 143]. No differences in the results were seen in comparisons between men and women in the stratified analysis.

6.2 METHODOLOGICAL CONSIDERATIONS

6.2.1 Internal validity

Selection bias

Selection bias can be present when the association between the exposure and the outcome differs for study participants and non-participants [144].

In study I, most of the responders were women with higher income and educational level, whereas non-responders (38%) were mostly men, foreign-born, younger individuals with lower income and educational level. This produces a potential selection bias when interpreting the sex-specific prevalence of the studied outcomes.

The rate of loss to follow-up (24%) and the proportion of internal dropouts (17%) in this study were high. This problem may reduce the external validity. However, the main focus in this study was on gender differences and thus stratified analyses were performed between men and women; therefore this potential selection bias on sex is unlikely to affect the external validity of the results.

With regard to the explanatory analyses of the dependence of the risk of onset of spinal pain on baseline psychological distress and vice versa, there is a potential risk of selection bias, even though the prospective design makes it unlikely that attrition is related to the outcome.

Selection bias is unlikely to be a problem in studies II–IV, due to the low attrition rate in all these studies. High participation and low attrition rates increase the internal validity by lowering the possibility of selection bias among participants.

Misclassification of exposure and disease

Misclassification occurs when individuals are categorized incorrectly by their exposure or disease status. This happens if the exposed individuals are categorized as unexposed or vice versa, and individuals with disease categorized as non-diseased or vice versa [145].

In study 1 there may have been a potential misclassification of pain status due to different wording of the questions at baseline and at follow-up, and regarding different prevalence periods. This is probably, if at all, a non-differential misclassification with a dilutive effect on the results.

In addition, due to the social non-acceptability of mental illness, it is possible that individuals might report pain instead of psychological distress. However, it is not likely that this will have introduced a major source of bias. Also, there is a possibility that the questionnaire used in this study (GHQ-12) did not capture all individuals with psychological distress. This questionnaire is designed to detect transitory psychological distress during the past weeks. A potential misclassification may have occurred if individuals with a chronic psychological condition were classified as non-diseased, resulting in a lower specificity of psychological distress. However, the proportion of individuals with severe psychiatric conditions such as major depression is low (5.2%) in the general population [146]. Furthermore, it is possible that those with severe psychiatric conditions may not even participate in large surveys.

In study II, self-reported sleep problems may be a source of misclassification of exposure. It has been suggested that self-reported sleep problems may be imprecise [134, 147]. However, this is likely to be a non-differential misclassification which may have a dilutive effect on the results.

In study III, a potential misclassification of disease may have occurred in the reporting of adverse events. Most of the adverse events (65%) were reported by patients within 2 weeks. It is debatable whether or not this time interval was too long in order to be able to report the events accurately. It is possible that patients were not able to remember correctly the duration or the severity of the event. However, there is no reason to believe that this potential misclassification of disease differs between treatment groups and therefore it is probably non-differential and has a dilutive effect on the results. Nevertheless, it is possible that this potential bias may have contributed to the negative results in this study, in terms of lack of difference between the treatment arms.

In study III, a potential source of misclassification is the origin of the adverse event. It is possible that the event could be caused by something other than the treatment itself. However, this potential misclassification of disease should be non-differential because it is independent of the exposure. If this was the case, there would be a potential overestimation of the occurrence of adverse events.

In study III, the questionnaire measuring adverse events was not validated. The adverse events included in the questionnaire were based on events measured in previous studies [85, 93, 121, 122] and the clinical experience of the research team. The questions explored whether or not the patient had experienced an event (within 24 hours after the treatment), as well as the duration (hours) and severity of the event (NRS 0–10). However, if the questionnaire is not valid, this may lead to a potential non-differential misclassification of the disease and may have a dilutive effect on the results. Nevertheless, the questionnaire used to measure adverse events in this study showed many similarities with a recently published expert group statement regarding how these events after manipulation therapy should be measured [148].

In study IV, perceived recovery represented the change in patients' complaints compared to baseline. It may be difficult to recall a change in condition after 1 year but there is no reason to believe that there would be differences in recall between the treatment groups. Therefore, this potential misclassification of disease-based measurement error should be non-differential, with a dilutive effect on the results. This may have contributed to the negative findings in terms of lack of difference between the treatment arms.

In studies III and IV there may have been a potential misclassification of exposure if the treatment was not carried out according to the protocol. However, we examined a random sample of the patients' records (6%), and it was found that the treatments were carried out according to the randomization.

Therapists in studies III and IV were students in the seventh semester of a total of eight. It is possible that their experience and skills were different from those of experienced registered naprapaths. This may have introduced a potential non-differential misclassification of exposure, and may have had a dilutive effect on the results.

Confounding

Confounding is defined as confusion, or mixing, of effects. 'The effect of the exposure is mixed together with the effect of another variable, leading to bias' [114]. If not controlled for in the analysis, the effect of confounding can lead to over- or under-estimation of the results.

The risk of confounding is more problematic in observational studies where the distribution of different potential confounding factors is not random between exposed and unexposed individuals.

RCTs are considered to be the gold standard in intervention studies. The aim of the randomization process is to achieve similar treatment groups; the patients within each group should be as similar as possible with regard to different characteristics, such as demographic variables, that might affect the comparisons. If randomization is successful and the study population is sufficiently large, both known and unknown confounding factors are equally distributed in comparison groups thus lowering the risk of confounded results.

We have controlled for confounding factors in all studies in this thesis. The selection of factors was based on the current literature and on discussions within the research group.

In study I, out of nine tested factors only age and gender were found to be confounders. However, there may still be residual and unmeasured confounding that could affect the results.

In study II, we controlled for a large number of potential confounders. It was found that only anxiety and pain intensity at baseline confounded the results for MCID in pain. Despite extensive control, residual and unmeasured confounding may still affect the results.

In studies III and IV, which are based on a large RCT, confounding is less likely to be a problem compared with observational studies. Nevertheless, we controlled for confounding in these studies and as a consequence none of the potential factors tested confounded the results.

Strengths

The strengths of study I were the large study population (n=19,744) and the prospective cohort design.

A high participation rate (85%), access to comprehensive information about potential confounders and the prospective cohort design were the major strengths of study II.

The main strengths of studies III and IV were the design (RCT), the large study populations, high participation rate, low attrition rate and the large number of therapists who performed the treatments. In these two studies the data collection, data input and randomization were performed by a trained research assistant.

The analyses in study IV were performed by a biostatistician who was not involved in data collection or the randomization process.

Detailed information about adverse events and the use of MCID in pain and pain related disability measures at follow-up increase the usefulness of the results.

6.2.2 External validity

In study I, the external validity of the results when measuring spinal pain and psychological distress may be reduced by the large number of non-responses at baseline in 2002 and losses to follow-up and internal dropouts at follow-up 5 years later. Furthermore, men were more likely to be non-responders, which could have an impact on the results; however, the comparisons of the prevalence of spinal pain and psychological distress in 2002 and 2007 were stratified by gender and therefore the effect of this should not be significant.

Our results from study II can be compared with those of several studies investigating the association between pain and sleep. Further, the large study population and high participation rate in study II increase the external validity.

In study III, there were differences in the study population in comparison with patients treated at other naprapathy clinics in Stockholm (Joakim Ahlgren, unpublished observation); our patients were younger and had less experience of naprapathic treatments. This may limit the external validity of the results in comparison to the general population.

In studies III and IV, a large number of therapist provided treatment. Thus the results of these studies are more likely to be dependent on the treatment itself rather than the individual therapists. On the other hand, the fact that the therapists in these studies were inexperienced compared to qualified manual therapists may limit the external validity of the results.

6.3 CLINICAL IMPORTANCE

The results of this thesis are clinically important. The findings highlight the poor prognosis when spinal pain coexists with psychological distress, and indicate that the proportion of individuals who recovered was significantly lower for those with both conditions compared to those with a single condition. This finding of the prognostic effect of comorbidity is valuable for clinicians when planning patient care.

Good sleep was an important prognostic factor for improvement in pain and pain related disability. The use of MCID in outcome measures increases the usefulness of the results in clinical practice. This emphasizes the need to consider sleep status when planning patient care. The results are also relevant for the patient to understand the effect of sleep and how important it is in the recovery process.

Further, the findings show that the occurrence of adverse events is common and transient after manual therapy. Most of the events were mild (≤ 3 on an NRS of 0–10) and lasted less than 24 hours. There were no differences in the occurrence of adverse events or the effects of treatment between treatment arms.

From a women's health perspective, the results suggested that neck and back pain with psychological distress is more common in women than in men. Also, women experienced more adverse events after manual therapy. Thus it is important to take these findings into consideration when planning care for women.

6.4 RESEARCH IMPLICATIONS

In future studies of the treatment effect of manual therapy, it may be interesting to conduct different subgroup analyses based on factors such as pain duration, location and onset, as these variables may be important when choosing treatment methods.

Gender differences in the occurrence of adverse events after manual therapy should be explored, to determine an appropriate gender-specific treatment approach.

The biopsychosocial model was proposed in the 1970s and is included in the educational programme for students in healthcare professions. Is it possible that this model is not used in the real-life situation? If this is the case, the reasons should be explored.

7 CONCLUSIONS

Comorbidity of neck and/or back pain and psychological distress had a negative effect on the prognosis of these conditions. Good sleep had a positive effect on the prognosis of non-specific neck and/or back pain. Adverse events after manual therapy were transient and the severity of such events was mild. There were no differences in the occurrence of adverse events or the treatment effect of combined manual therapy when either spinal manipulation or stretching was excluded from the treatment arsenal for non-specific neck and/or back pain.

8 SVENSK SAMMANFATTNING

Inledning: Nack- och ryggsmärta är vanliga hälsoproblem som förekommer över hela världen och som orsakar ekonomisk belastning för samhället och lidande för individen.

Syfte: Det övergripande syftet med avhandlingen var att öka kunskapen om naprapati och om andra faktorer som eventuellt kan vara viktiga för prognosen vid nack- och ryggsmärta. **Specifika syften:** *Studie I:* 1) att jämföra tillfrisknande från nack-/ryggsmärta och psykisk ohälsa var för sig och som samsjuklighet, mellan män och kvinnor, 2) att beskriva inbördes relationer mellan dessa tillstånd vid baslinjen och uppföljningen, 3) att studera om nack-/ryggsmärta är en riskfaktor för psykisk ohälsa och vice versa. *Studie II:* att studera vilken betydelse god sömn har för prognosen vid ospecifik nack-/ryggsmärta. *Studie III och IV:* att jämföra förekomst och svårighetsgrad av oönskade behandlingsreaktioner (studie III), och behandlingseffekter (studie IV) vid behandling av ospecifika nack-/ryggbesvär, mellan olika kombinationer av behandlingstekniker som används inom naprapati.

Metod: *Studie I:* en kohort-studie baserad på Stockholms folkhälsokohort. Ett frågeformulär skickades till slumpvis utvalda stockholmare vid baslinjen och fem år senare. *Studie II:* en kohort-studie som var en sekundär analys av data från en randomiserad kontrollerad studie. Information från baslinjen samt från uppföljningen 12 och 52 veckor senare användes. *Studie III och IV:* en randomiserad kontrollerad studie. Deltagarna var patienter i åldrarna 18-65 år som sökte vård för nack- och/eller ryggsmärta. De lottades till en av tre behandlingsgrupper: 1) naprapatisk manuell terapi (i.e. spinal manipulation, spinal mobilisering, stretching och massage), 2) naprapatisk manuell terapi utan spinal manipulation och 3) naprapatisk manuell terapi utan stretching. Behandlingarna utfördes av naprapatstudenter som studerade på sjunde terminen av totalt åtta. Uppföljning av resultat skedde efter varje behandlingstillfälle (studie III) samt efter 7, 12, 26 och 52 veckor (studie IV).

Resultat: *Studie I:* samsjuklighet av nack-/ryggsmärta och psykisk ohälsa var dubbelt så vanligt hos kvinnor som hos män. Nack-/ryggsmärta med eller utan psykisk ohälsa var också vanligare hos kvinnor än hos män. Samsjuklighet gjorde tillfrisknandet betydligt mindre sannolikt jämfört med om enbart ett av tillstånden var närvarande. Tjugofyra procent av kvinnorna och 17 % av männen som hade nack-/ryggsmärta utan psykisk ohälsa vid baslinjen hade utvecklat psykisk ohälsa vid uppföljningen fem år senare. Motsvarande andel som utvecklat nack-/ryggsmärta hos de med psykisk ohälsa utan nack-/ryggsmärta vid baslinje var 24 % och 20 %. Nack-/ryggsmärta kan orsaka psykisk ohälsa och vice versa. *Studie II:* patienter med god sömn hade bättre chans att tillfriskna ett år senare jämfört med de som uppgav att de hade dålig sömn. *Studie III:* oönskade behandlingsreaktioner efter kombinerad manuell terapi var vanligt men oftast milda i karaktären och övergående. De vanligaste behandlingsreaktionerna var ömhet i muskulaturen, ökat smärta och stelhet. Inga skillnader hittades mellan behandlingsgrupperna. Kvinnor löpte större risk att utveckla oönskade behandlingsreaktioner än män. *Studie IV:* inga skillnader hittades mellan behandlingsgrupperna angående kliniskt relevant förbättring av smärta och

smärtrelaterad funktionsnedsättning under ett års uppföljning. Resultatet var lika för män och kvinnor.

Slutsats: Samsjuklighet av nack- och/eller ryggsmärta och psykisk ohälsa har en negativ effekt på prognosen. God sömn har en positiv effekt på prognosen för icke-specifik nack-/ryggsmärta. Oönskade behandlingsreaktioner efter manuell terapi är vanligt, relativt milda och övergående. Det finns inga skillnader i förekomsten av oönskade behandlingsreaktioner eller i behandlingseffekter när spinal manipulation eller stretching tas bort som en del av behandlingen för patienter med ospecifik nack-/ryggsmärta som behandlas med olika kombinationer av manuella tekniker.

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