Neck pain

– clinical course and pain trajectories

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“I do not know what I appear to the world; but to myself I seem to have been only like a boy playing on a seashore, and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me.”

-Sir Isaac Newton

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Husk at leve, mens du gør det

(Live while you’ve got life to live)
Piet Hein

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Summary in English

Background: Studies on the clinical course of pain challenge the common classification of pain as either acute or chronic. Instead, spinal pain appears to be a dynamic condition that is characterized by episodes and fluctuations. An overview on low back pain trajectory studies identified similar trajectory patterns across studies. The authors recommended that future studies on the course of pain should include a combination of three constructs: pain variation patterns, pain intensity, and speed of improvement. A Danish research group operationalized the recommendations into definitions of trajectory patterns and subgroups from weekly SMS measures on low back pain patients. There are few trajectory studies on neck pain patients, but it has been hypothesized that low back pain trajectories could also fit neck pain patients. Moreover, little is known about the stability of pain trajectories over time, or if patients can accurately identify or recall their own pain trajectory through illustrations of common trajectories (visual trajectories).

Hence, the main aims of this thesis were first to investigate if previously identified SMS-based definitions of patterns and subgroups for low back pain were applicable to neck pain patients. Second, to explore to what extend the patients shifted from one SMS-based pattern to another in periods of four quarters in the 1-year follow-up. Last, to explore visual trajectories in neck pain in terms of the patients prospectively reported clinical course and SMS-based pattern classification.

Methods: We conducted a prospective cohort study including 1476 patients with neck pain consulting chiropractors in Norway. Patients were followed for 1 year with weekly SMS' that included questions on number of days with pain during the past week (0-7) and their typical pain intensity the past week on a Numeric Rating Scale (NRS, 0-10). In addition, they answered self-reported questionnaires at baseline and 1-year follow-up.

We classified patients into four patterns from weekly days with pain (ongoing, persistent fluctuating, episodic, single episode) and subsequently subdivided each pattern into four subgroups based on weekly pain intensity (severe, moderate, mild, minor) for the last 43 weeks of follow-up, in accordance with the Danish low back pain study. Based on findings from Paper I, the SMS-based patterns and subgroups were modified for analyses for Paper II into 11 subgroups in each quarter of the 1-year follow-up. To assess the stability of the patterns, we defined patients classified with the same pattern in the first and fourth quarter as having a stable trajectory pattern. We used Sankey diagrams to explore the flow of patients between patterns. For Paper III, data from the Visual Trajectory Pattern Questionnaire at 1-year follow-up was used. The patients had selected one of the five drawings and descriptions of neck pain trajectories that best represented their experienced clinical course the past year: Single episode, Episodic, Mild ongoing, Fluctuating, and Severe ongoing. For each of the five visual trajectories, we described the patients' clinical course by details of the weekly SMS'. This data included

the duration and frequency of pain-free and painful weeks, and the proportion of weeks in the pain intensity categories. We described patient characteristics and their SMS-based classification for both the 1-year and last quarter follow-ups for each visual trajectory.

Results: We found that the trajectories developed for low back pain fit well for the neck pain patients in our cohort. Most patients were classified as either persistent fluctuating (48%) or episodic (45%). A pain episode could last longer than three months, and complete recovery was rare. Patients classified as persistent fluctuating scored significantly higher on all clinical factors than all other patterns ($p \leq 0.006$). A total of 785 (70%) patients were in a stable trajectory (same trajectory in first and fourth quarter). Of these, 82% (648/785) were in a stable persistent fluctuating pattern and scored significantly higher on psychosocial factors and reported more reduced function than patients in any other stable or shifting pattern. The majority of patients were classified as episodic (49%) or persistent fluctuating (48%) when examining data for the whole year. The most commonly selected self-reported visual trajectories at 1-year were Episodic (37%), Fluctuating (36%), and Single episode (14%). We found large variations of individual pain trajectories (from SMS) among patients selecting each of the five visual trajectories. However, there was a general resemblance between the selected visual trajectory and the 1-year clinical characteristics and SMS-based classification on a group level. This resemblance improved when using data from the last quarter only. There was an increase in severity of symptoms, functional disability, psychosocial and psychological distress from patients selecting Single episode through to those selecting Severe ongoing visual trajectory. Only negligible differences were found between patients selecting the Mild ongoing and Episodic visual trajectories.

Conclusion: Most neck pain patients in chiropractic care report pain that is either persistent fluctuating or episodic. Low back pain trajectory definitions appear to fit well to neck pain patients. Persistent fluctuating pain is more stable over time, but these patients also have pain with a higher negative impact on functional disability and psychosocial distress. Our findings are similar to the Danish low back pain study, as well as studies on other spinal and musculoskeletal regions. The visual trajectories reflected the clinical course of pain on a group level, where patients differed on symptoms and characteristics. However, only negligible differences were found between patients selecting Episodic and Mild Ongoing visual trajectory. Patients with mild pain seem to struggle the most to identify a visual trajectory that most reflect their reported 1-year clinical course and appear predisposed to recall bias. Our results suggest that the visual trajectories embrace more aspects of the pain experience than just pain intensity and the course of pain. Based on our results and results from previous studies, the visual trajectories seem to have potential for use in clinic and research. In addition, our study lends support to the ongoing debate on treating musculoskeletal pain as one entity in research and clinical work, rather than separate regions.

Norsk sammendrag

Bakgrunn: Studier på kliniske smerteforløp utfordrer den vanlige klassifiseringen av smerte som enten akutt eller kronisk. I stedet virker spinale smerter å være en dynamisk tilstand som er preget av episoder og fluktueringer. En oversikt over studier på smerte-trajektorier på korsryggs-pasienter identifiserte lignende trajektorier på tvers av studier. Forfatterne anbefalte at fremtidige smerteforløp studier bør inkludere en kombinasjon av tre konstruksjoner: smertevariasjonsmønstre, smerteintensitet, og forbedringshastighet. Fra disse anbefalingene, lagde en dansk forskergruppe på korsryggs pasienter definisjoner for smerte-mønstre og undergrupper basert på ukentlige SMS. Få trajektorie-studier er gjort på nakkesmertepasienter, men det er antatt at trajektorier for korsryggs pasienter også kan passe pasienter med nakkesmerter. Dessuten er lite kjent om trajektorienes stabilitet over tid, eller om pasienter nøyaktig kan identifisere eller huske sin egen smerte-trajektorie gjennom illustrasjoner av vanlige trajektorier (visuelle trajektorier).

Hovedmålene med denne oppgaven var derfor først å undersøke om tidligere identifiserte SMS-baserte definisjoner av mønstre og undergrupper for korsryggsmerter var anvendelige for nakkepasienter. Deretter å utforske i hvilken grad pasientene skiftet fra ett SMS-basert mønster til et annet i fire kvartaler på 1 år. Sist, å utforske visuelle trajektorier for pasienter med nakkesmerte basert på prospektivt rapportert klinisk forløp og SMS-basert mønsterklassifisering.

Metode: Vi gjennomførte en prospektiv kohortstudie med 1476 nakkesmerte pasienter hos norske kiropraktorklinikker. Pasientene ble fulgt i 1 år med ukentlig SMS som inkluderte spørsmål om siste ukes antall dager med smerte (0-7) og typisk smerteintensitet på en nummerskala (NRS, 0-10). I tillegg leverte de selvrapporterte spørreskjemaer ved baseline og 1-års oppfølging.

Vi klassifiserte pasienter i fire mønstre fra ukentlige dager med smerte (pågående, vedvarende fluktuerende, episodisk, enkelt episode) og delte deretter hvert mønster inn i fire undergrupper basert på ukentlig smerteintensitet (alvorlig, moderat, mild, minimal) for de siste 43 ukene av oppfølgingen, i henhold til den danske studien på korsryggsmerter. Basert på funn fra Artikkel I, ble mønstrene og undergruppene modifisert til 11 undergrupper i hvert kvartal av 1-års oppfølgingen for analyser for Artikkel II. For å vurdere mønstrenes stabilitet, definerte vi pasienter klassifisert med samme mønster i første og fjerde kvartal til å ha en stabil trajektorie. Vi brukte Sankey-diagrammer til å utforske flyten av pasienter mellom mønstre over tid. For Artikkel III brukte vi data fra Visual Trajectory Pattern Questionnaire' ved 1-års oppfølging. Pasientene valgte en av fem tegninger og beskrivelser av smerte-trajektorier som best representerte deres siste års kliniske forløp: Enkelt episode, Episodisk, Mildt vedvarende, Fluktuerende og Alvorlig vedvarende. Vi beskrev pasientenes kliniske forløp med detaljer fra de ukentlige SMS for hver av de fem visuelle trajektoriene, inkludert varigheten og hyppigheten av smertefrie og smertefulle uker, og andelen uker i smerteintensitetskategoriene. Vi beskrev

pasientkarakteristikker og deres SMS-baserte klassifisering for både 1-års og siste kvartals oppfølginger for hver visuell trajektorie.

Resultater: Vi fant at trajektoriene utviklet for korsryggs pasienter passet godt til nakkesmertepasientene i vår kohort. De fleste pasientene ble klassifisert som enten vedvarende fluktuerende (48 %) eller episodiske (45 %). En smerteepisode kunne vare lenger enn tre måneder, og fullstendig bedring var sjelden. Pasienter klassifisert som vedvarende fluktuerende rapporterte signifikant høyere på alle kliniske faktorer enn de andre mønstrene ($p \leq 0{,}006$). Totalt 785 (70 %) pasienter var i en stabil trajektorie (samme trajektorie i første og fjerde kvartal). Av disse var 82 % (648/785) i et stabilt vedvarende fluktuerende mønster og rapporterte signifikant høyere på psykososiale faktorer og mer redusert funksjon enn pasienter i noe annet stabilt eller skiftende mønster. Flertallet av pasientene ble klassifisert som episodisk (49 %) eller vedvarende fluktuerende (48 %) ved undersøkelse av data for hele året. De vanligste selvrapporterte visuelle trajektoriene ved 1 års oppfølging var Episodisk (37 %), Fluktuerende (36 %), og Enkeltepisode (14 %). Det var store variasjoner i individuelle smerte-trajektorier (fra SMS) blant pasienter som valgte hver av de fem visuelle banene. Det var imidlertid en generell likhet på gruppenivå mellom valgte visuelle trajektorien og 1-års kliniske karakteristika og SMS-basert klassifisering. Denne likheten var bedret ved bruk av data kun fra siste kvartal. Det var en økning i alvorlighetsgrad på symptomer, funksjonshemming og psykososiale plager for pasienter som valgte Enkeltepisode til de som valgte Alvorlig vedvarende synsbane. Bare ubetydelige forskjeller ble funnet mellom pasienter som valgte Mildt vedvarende og Episodiske visuelle trajektorie.

Konklusjon: De fleste nakkesmertepasienter i kiropraktisk praksis rapporterer smerte som enten er vedvarende fluktuerende eller episodisk. Definisjoner for korsryggs pasienter ser ut til å passe godt til nakkepasienter. Vedvarende fluktuerende smerte er mer stabil over tid, men disse pasientene har også smerter med høyere negativ innvirkning på funksjon og psykososiale plager. Funnene våre ligner den danske studien på korsryggsmerter, og også studier på andre rygg- og muskelskjelettregioner. De visuelle trajektoriene reflekterte det kliniske smerteforløpet på gruppenivå, der pasientene var forskjellige på symptomer og karakteristika. Vi fant kun ubetydelige forskjeller mellom pasienter som valgte Episodisk og Mildt vedvarende visuell trajektorie. Pasienter med mild smerte ser ut til å slite mest med å identifisere en visuell trajektorie som best reflekterer deres rapporterte 1-årige kliniske forløp og ser ut til å være påvirket av hukommelses bias. Resultatene våre tyder på at de visuelle trajektoriene omfatter flere aspekter av smerteopplevelsen enn bare smerteintensitet og smerteforløp. Basert på våre resultater, og resultater fra tidligere studier, virker de visuelle trajektoriene å ha potensiale for bruk i klinikk og forskning. I tillegg gir våre funn støtte til den pågående debatten om behandling av muskel- og skjelettsmerter som én enhet i forskning og klinisk arbeid, snarere enn separate regioner.

List of papers

Paper I

Irgens P, Kongsted A, Myhrvold K, Waagan K, Engebretsen KB, Natvig B, Vøllestad NK & Robinson HS **Neck pain patterns and subgrouping based on weekly SMS-derived trajectories -**BMC Musculoskeletal Disorders 2020 Vol. 21 Issue 1. doi: 10.1186/s12891-020-03660-0

Paper II

Irgens P, Myhrvold K, Kongsted A, Waagan K, Engebretsen KB, Vøllestad NK & Robinson HS **The clinical course of neck pain: Are trajectory patterns stable over a 1-year period? -** European Journal of Pain 2022 Feb;26(2):531-542. doi: 10.1002/ejp.1879.

Paper III

Irgens P, Myhrvold K, Kongsted A, Natvig B, Vøllestad NK & Robinson HS **Exploring visual pain trajectories in neck pain patients, using clinical course, SMS-based patterns and patient characteristics** - Submitted to BMC Chiropractic and Manual Therapies May 2022

List of Figures and Tables

Abbreviations

ANOVA	Analysis of variance
CRP	Chronic Regional Pain
CWP	Chronic Widespread Pain
DALYs	Disability-Adjusted Life Years
EQ-5D	EuroQol-5 dimensions questionnaire, (a generic instrument measuring Health Related Quality of Life)
EMA	Ecological Momentary Assessment
GP	General Practitioner
HRQoL	Health-Related Quality of life
HSCL	The ten-item Hopkins Symptom Check List
HUNT	The Trøndelag Health Study
IASP	International Association for the Study of Pain
ICD-11	International Classification of Diseases, the Eleventh revision
ICF	International Classification of Functioning, Disability and Health
IQR	Inter-Quartile Range
LCA	Latent Class Analysis
LCGA	Latent Class Growth Analysis
LCMM	Latent Class Mixed Model
LBP	Low Back Pain
MIC	Minimal Important Change
MRI	Magnetic Resonance Imaging
MSK	Musculoskeletal
NDI	Neck Disability Index
NICE	National Institute for Health and Care Excellence
NP	Neck Pain
NPQ	Nordic Pain Questionnaire
NRS	Numeric Rating Scale
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
NSP	Neck-Shoulder Pain
RCT	Randomized Controlled Trial
SD	Standard Deviation
SMS	Short Messaging Services
TSD	Tjenester for Sensitive Data/Services for sensitive data
UK	United Kingdom
VAS	Visual Analogue Scale
VTQ-P	Visual Trajectory Questionnaire - Pain

Background

I have worked in primary care as chiropractor for more than 20 years and met patients seeking treatment for a variety of musculoskeletal pain problems. I very early experienced how difficult it was to prioritize between patients presenting with different needs and complexities for what appeared to be the same condition. It was a feeling I realized many of my colleagues also experienced on a regular basis; the firm belief that chiropractic treatment "worked", yet a group of patients had little to no improvement. Why was that? Attempting to find answers, I tried my own empirical investigations. For each treatment I noted in the patients' journal four grades of outcome (from complete recovery to specialist referral) for four consecutive weeks. I found that the individual patients appeared to have varied response to treatment in those four weeks irrespective of treatment type or frequency. What surprised me was that I found very little indication that the majority of patients improved or recovered on the days I felt like a queen of chiropractic, or the opposite outcome when I felt like a failure. In fact, my success or failure had very little connection to patients' outcome other than my distinct memory of it being so.

About the same time, in 2013, I was approached by the Norwegian Chiropractic Association regarding the possibility of doing research on the course and prognosis of neck pain. Finally, in 2015, I was given the chance to become a PhD student with a group of supervisors with backgrounds from manual therapy, physiology, chiropractic, physiotherapy, and medicine. Combined with part-time clinical work as a chiropractor, this gave me the opportunity to gain deeper knowledge on the subgroups of neck pain patients' clinical course, and after a while, how our findings may be a part of the cogwheel to improve the methods of identifying them.

1 Introduction

This thesis is one part of a larger project studying the clinical course and prognostic factors of neck pain patients in a chiropractic cohort. This introductory chapter gives an overview of the prevalence, risks, and prognosis of neck pain in primary care. It then goes on to provide a summary of how neck pain is usually measured and classified. It subsequently provides an overview on the course of pain that includes the historical background, methodology, and terminology for descriptors of the clinical course of neck pain. Finally, it summarizes trajectory research for the last decade, with an in-depth look at different methodologies used.

1.1 Neck pain

1.1.1 Prevalence, health care utilization, and costs

Neck pain is one of the most common musculoskeletal disorders worldwide (1, 2). The most recent Global Burden of Disease Study (1990-2017) revealed neck pain as number four in terms of years lived with disability globally, and the second most common musculoskeletal condition after low back pain (3). The age adjusted point prevalence is estimated to be between 5%-8% and 1-months prevalence close to 23%, with 50% to 90% of adults likely to experience an episode of neck pain at least once in their lifetime (2, 4).

The mean annual prevalence of neck pain in the general population ranges from 30% to 80% (5-7), and is estimated to be 48% in Norway (8-10). The large ranges are likely due to differences in methodology making figures difficult to compare (11, 12). There was a small, but significant decrease in global point prevalence of neck pain from 4.9% in 2010 to 3.5% in 2017 (4). Still, neck pain is listed as number twenty-five in leading causes of global Disability-Adjusted Life Years (DALYs), with a 116% increase since 1990 (2). More females are likely to have neck pain than males across all age groups, and the peak prevalence occurs between 45-49 years for men, and 45-54 years for women (2). A higher prevalence for neck pain is found in urban areas compared to rural areas, as well as in the working compared to non-working population (13). People with sedentary, office-based jobs have a higher risk of developing neck pain than the rest of the population (2). Neck pain is associated with reduced quality of life, sleep disturbance, and work absenteeism, and as a result has a large economic impact from healthcare costs (both public and private) and work absence (1, 7, 14, 15). Norway has the highest point prevalence and annual incidence of neck pain globally (2), where neck pain accounts for close to 3% of disability benefits and 4% of sick leave (16) .

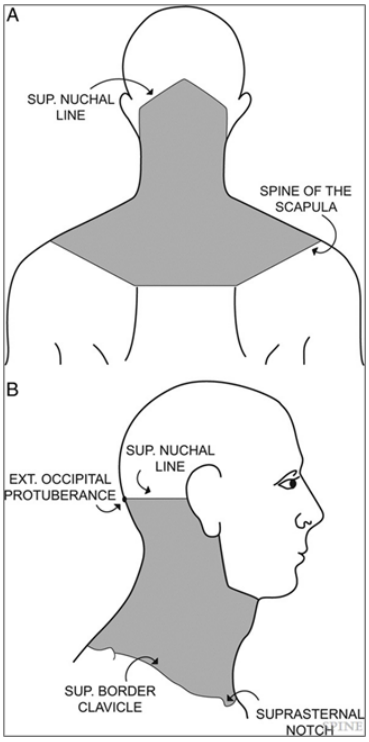
Despite extensive research to improve the understanding of neck pain and develop evidence-based treatments, the burden has not changed in the period 1990-2017 (4).

1.1.2 What is non-specific neck pain?

Neck pain is a heterogeneous symptom and not a disease. It varies greatly in individual presentations, descriptions, and causes (1, 17). It can be caused by specific diseases such as inflammatory joint disease, cervical disc herniation, dislocations, or fractures, which are easily diagnosed by imaging (18-23). In the large majority of patients, however, no identifiable disease, abnormal anatomic structure, or specific cause can be identified (24, 25). This pain condition is therefore typically diagnosed only on clinical grounds and is referred to as non-specific neck pain. A conceptual model for neck pain was introduced by the Bone and Joint Decade Task Force on neck pain in 2008 (17). They defined neck pain as “an unpleasant sensory and emotional experience”, ranging between the superior nuchal line to the

upper thoracic region, across the spine of the scapula and the superior border of the clavicle, to the suprasternal notch (Figure 1) (17).

Figure 1 The anatomic region of the neck from the back (A) and the side (B) as defined by The Bone and Joint Decade 2000–2010 Task Force on Neck Pain and its Associated Disorders (17). Reproduced with permission from Spine.



Bogduk indicates that this is an area that is sensed by the patient, and not necessarily means that the underlying cause originates in the described anatomical neck area (26). In this thesis, the focus is on non-specific neck pain, and will be referred to as neck pain throughout, unless otherwise specified.

Neck pain is commonly associated with a multifactorial etiology (27, 28). Patients with neck pain frequently experience other symptoms like headache, shoulder pain, low back pain, and radiating pain to the upper limb (29), but also stiffness of neck and shoulder muscles, limited cervical range of motion, weakness, sensitivity, fatigue, and dizziness (30, 31). The focus of the pain history is usually on the area of pain, mode of onset, duration and frequency of the neck pain episode, the history of previous musculoskeletal pain, and type and intensity of the neck pain. The clinical examination aims to identify probable contributing factors and, if possible, exclude significant pathology through area-standardized musculoskeletal and neurological tests (29, 32, 33). The main aim of the pain history and clinical tests is to exclude red flags that indicate serious pathology. However, few diagnostic tests for neck pain have demonstrated good diagnostic validity and specificity (34). In addition, present evidence does not support a relationship between imaging findings and neck pain symptoms beyond age-related changes (21, 35).

1.1.3 Brief overview of chiropractic care

Chiropractors are specialized in the diagnosis and management of musculoskeletal conditions. Most patients with low back or neck pain in Norway seek primary care practitioners. Of these, 16% consult a chiropractor (24). At present, approximately 700 (75%) of the chiropractors are members of The Norwegian Chiropractic Association, and most hold a 4-or 5-year master's degree. Close to 50% work in a multidisciplinary clinic (36).

Chiropractic is a protected professional title in Norway, and chiropractors have full state authorization as primary care health providers, a right given in 1998 (by the Norwegian Directorate of Health (Helsedirektoratet)). In 2006, chiropractors received extended rights to provide sick leave for patients up to 12 weeks, and permission to refer patients directly to physical therapy, medical specialists and radiology related to the musculoskeletal system. The Norwegian health care system is patient and tax-funded (both national and municipal). Chiropractors are a first contact in primary care, yet only approximately 10-15% of the treatment fee is reimbursed by the Norwegian Health Economics Administration (HELFO). Most chiropractors are private practitioners and have no legal financial agreement with the municipality. There is no established chiropractic education in Norway.

Patients in this thesis were recruited from chiropractic clinics. The most common clinical interventions of chiropractic care are spinal manipulation and mobilization (manual therapy) (37), which is recommended as a component of multimodal care in clinical practice guidelines (38, 39). Still, other modalities such as soft tissue work and exercise therapy, as well as patient education and lifestyle advice, are frequently used (36, 40). Chiropractors treat all joints in the body; however, the most common area is the spine. Although there is evidence of some treatment effect of manual therapy, it is mostly mild to moderate, and the mechanisms behind the treatment are uncertain (41, 42) Suggested explanatory models include biomechanical and neuromuscular/neurophysiological mechanisms such as muscle tension, motor control and sensorimotor integration (43-45).

A traditional approach to musculoskeletal care that is distinctive to chiropractic is maintenance care. This includes continued care at regular intervals that goes beyond the reduction or elimination of symptoms (46-48). The purpose of maintenance care is to prevent future pain, i.e., to help keep the patient healthy and free from pain, and to keep status quo or prevent flare-ups in patients with persistent, long-term pain and/or dysfunction (49). Howe common this treatment approach is in chiropractic care varies, but the proportion of patients on a maintenance treatment plan in Scandinavia ranges from 22-41% (40, 50). Some studies support the effectiveness of maintenance care (51, 52), but not of cost-effectiveness (49).

1.1.4 The clinical course of neck pain

The clinical course of pain is defined as the course subsequent to diagnosis and treatment initiation (53).

The purpose of the first ever systematic review on the course of neck pain was to improve the estimation of prognosis (31). Due to the lack of studies for the review, both randomized controlled trials (RCTs) and observational studies were included. The studies had short follow-up times and were too few for the authors to conclude on the clinical course. However, close to half of the patients did report a general improvement. The authors recommended future studies to focus patients having their first time with neck complaints (inception cohort (54)) and follow-up periods of at least one year. Another review on course and prognostic factors of neck pain in the general population came ten years later with results from the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders (27). Only six studies qualified for inclusion, and two were from the same cohort of schoolchildren (55, 56). Between 22-37% of patients reported resolution of pain at the end of a follow-up period ranging from 6 months to five years (57-59), however most patients reported pain one to five years after inclusion (57, 60). The studies varied on population, methodology, and definitions of neck pain, making comparisons difficult. In conclusion, neck pain was described as episodic or persistent in nature, with multifactorial causes and risk factors (17, 27).

Very few studies focused purely on identifying the course of neck pain. Common to most studies on the course of neck pain is irregular measurements over shorter periods (27, 31). In addition, conclusions are based on cohort, rather than individual, means, which hamper the identification of the natural fluctuations of neck pain (61). Pain fluctuates, and measuring outcome based on a single point in time provides only a "snapshot" of the actual course of pain, and rarely captures the real change in pain over time as found in individual pain trajectories.

A pain trajectory (the pattern of pain over time) describes an individual's or a group of individuals' course of pain symptoms measured repeatedly for a specified time-period (62).

For instance, a study based on data from the Norwegian HUNT studies (the Trøndelag Health Study) found that the natural course of neck pain was a decrease in average pain intensity during the first three months of follow-up in patients reporting some neck/shoulder pain at recruitment (63). Nevertheless, a large majority of the patients did not recover. A study by Ailliet et al found that 75% of patients with neck pain reported to be much improved or completely recovered at three months, yet only 50% were recovered at 1-year follow-up (64). However, most studies on the course of musculoskeletal pain are low back pain patients. In this thesis, low back is defined as "pain and discomfort located below the costal margin and above the gluteal folds, with or without leg pain" (65), and thoracic pain is defined as "as pain experienced in the region of the thoracic spine, between the boundaries of T1–T12 and across

the posterior aspect of the trunk" (66). Many studies indicate that there are similarities between low back and neck pain in characteristics, risks and prognostic factors, and clinical course (63, 64, 67, 68), and some postulate that neck, low back, and thoracic pain are one condition; i.e., spinal pain (69-74). Given this, parts in this thesis that lack information on the course of neck pain will be described and explained by studies on low back pain.

1.1.5 Neck pain; Risk, prognosis, and care

Risk

Neck pain is multifactorial (28). Numerous modifiable (that can be changed, such as obesity) and non-modifiable (that cannot be changed, for example age) risk factors related to the development of neck pain or transition from occasional to persistent pain are known (11, 15, 75).

Gordon Waddell introduced the biopsychosocial model of low back already in 1987 (76). This resulted in a shift of focus of seeing back pain as purely biologically related pain that has a clear pathological cause and functional disability, to also address the psychological and social aspect of the condition. Hence, risk factors can be separated into three categories: psychosocial, individual (demographic), and physical factors (75). Psychosocial risk factors for neck pain include workplace related factors (77, 78), health perceptions (79, 80), perceived muscle tension, history of neck and low back pain (81), and depressed mood (82). Individual risk factors are high body mass index (79), marital status and family size of three or more (80), as well as being male with low income and high perceived economic stress with low income (83). Lastly, physical factors like having the possibility of adjusting sitting position, and working in sustained or awkward positions are also factors that increase the risk of neck pain (81). Factors found to be protective against developing persistent neck pain include working in a good social climate with empowering leadership (84), good cervical extensor endurance (82), and sufficient levels of leisure physical activity (85).

Prognosis

Prognostic research aims to predict future outcomes in patients with a specific condition (86). The underlying mechanisms for the progression of neck pain, being short term, recurrent, or persistent pain, are not clear (28). However, knowledge about factors influencing the clinical course of pain is important in clinical practice. Known prognostic factors include previous neck pain, concomitant low back pain and headache, presence of kinesiophobia, older age, and being male (58, 87, 88). However, most studies on prognosis of neck pain are of low to very low quality (88), and are also difficult to compare. The most common causes for this are inadequate methodology and the use of different definitions (88). A review of systematic reviews and meta-analyses (umbrella review) of self-reported prognostic factors for neck and low back pain identified seven factors with a moderate confidence for robust findings:

disability/activity limitation, mental health, pain intensity and severity, coping, expectation of outcome/recovery, and fear-avoidance (89). A recently published Delphi study on pain after first episode of neck pain by Verwoerd et al, concluded on potentially modifiable factors and categories that mostly involved psychosocial factors, emphasizing the importance of addressing such factors early in the treatment plan (90). Prognostic factors can be combined into prognostic and prediction models (91). An increasing number of prognostic models for neck pain have been published (92-94). Prognostic models aim to distinguish patients with a favorable outcome from those with an unfavorable outcome (91). They are particularly useful decision-making tools to select appropriate treatment strategies in clinical practice (91). A recent systematic review on prognostic models for neck pain concluded that none of the models had sufficient clinical utility, and the methodology used was often of poor quality (92). Most prognostic studies on neck pain have been exploratory (27, 87, 92), and only two prognostic models have been externally validated but not found to be effective (93, 95).

Neck pain management approaches

Traditional neck pain treatments include treating movement restriction with mobilization or manipulations (96), or more specific exercise therapy to restore or improve motor control (97, 98). However, no single treatment modality has to date been found to be superior to others (41, 99). The evidence of the effectiveness of different interventions for musculoskeletal pain is often summarized in clinical guidelines with the aim to improve efficiency and effectiveness in the treatment of pain. There are numerous of guidelines available for the assessment and treatment of neck pain (100-103). Two systematic reviews of guidelines have concluded that most of the guidelines recommend manual therapy (manipulation and mobilization), and the combination of manual therapy with exercises, as well as education on prognosis and advice to stay active (38, 104). Inconsistent evidence for interventions like laser therapy, acupuncture, yoga, massage, psychosocial interventions, and pharmacological treatments were found. However, the evidence for treatment effect is mostly mild to moderate at best, and often not assessed in different populations (38). However, the vast number of treatment options, combined with frequently questionable methodological quality, validity, and reliability concerning many of the studies and instruments used, make it challenging to evaluate guidelines (38, 104). Most recommendations target biopsychosocial factors (29, 101, 105), yet there are no clinical tests to guide the selection of specific treatment for intervention strategies (106-109). This thesis included patients who received treatment at the chiropractor's discretion, but treatment modality and effect are not studied in this thesis.

Musculoskeletal pain is costly for both the individual and society. This, combined with the lack of treatment with good effect, have given the study of progression from occasional to persistent pain a high research priority (38, 110). In particular, two care approaches show promise. With the stepped-care approach patients are given the same core treatment or advice. It involves variations of the "wait-

and-see"-approach (111), where follow-up is only given if the patient does not improve (112). However, the stepped-care approach does not consider the recurrent aspect of pain and psychosocial distress (113, 114). In addition, patients with different pain presentations, causes of pain, or personal characteristics are likely to respond differently to the same treatment (115). Lastly, clinical evaluations are likely done by a combination of theoretical knowledge, experience, and what clinicians themselves often put down to intuition (116). Early research suggested that matching diagnostic subgroups to classification-based management strategies could lead to improvement in clinical, individual, and cost-related outcomes (117-119). Commonly used risk-prediction tools to subgroup patients based on risk for poor clinical outcome are the STarT Back Tool (115), the ÖMPQ-10 (120), and the PICKUP (121) used in the NICE guidelines in the UK (122). Identifying patients' risk profile, and subsequently how to match the patient with a certain type of treatment or treatment plan, is called stratified or matched care (111, 123-129). With this treatment approach, comprehensive care is given to patients with high risk of a poor outcome, while patients with low risk of poor outcome might only require advice and education. However, these subgrouping and management approaches are still in an early stage, and reviews conclude that these systems to date are of poor to moderate quality and are not more effective than standardized care alternatives (104, 130-135). Furthermore, primary care physicians rarely integrate stratified care in their treatment strategy (136). The overall conclusion is that both subgrouping and stratification are potentially important, but they demand a lot of knowledge and understanding from the health care provider to have any effect (137). In addition, improved methodology, reporting of results, external validation, as well as strategies for implementation in practice are needed (111, 123, 138, 139).

Many musculoskeletal guidelines and stratification studies recommend similar approaches for assessment and management of neck and low back pain, as well as other musculoskeletal pain (38, 39, 140, 141). An important common finding is that musculoskeletal conditions are frequently comorbid (142-145). Prognostic and risk factors (146-152), as well as clinical course (63, 69, 73, 148, 153) , are also found to be similar across conditions. Additionally, recent studies have identified phenotypes across different conditions (154, 155). There is a call to shift the management of musculoskeletal pain from condition-specific care to a patient-specific management (70, 156). The evidence is strongly suggestive towards knowledge being transferrable between spinal regions, and perhaps also several other musculoskeletal conditions. Localized pain at a single site only is rare (157), and 40% to 75% of patients report pain at multiple sites (8, 73, 74, 144), and may form part of the explanations for the similarities between musculoskeletal pain disorders. Thus, prognosis rather than diagnosis may be a more appropriate framework for treatment selections and planning (113).

1.2 The classification of pain

Pain is an individual and subjective experience and has a connection to both pathophysiology and biopsychosocial factors (76, 158-162). It is defined by the International Association for the Study of Pain (IASP) as (163) :

> "an unpleasant sensory and emotional experience associated with, or resembling that *associated* with, actual or potential tissue damage"

Furthermore, IASP goes on to specify that pain is a personal experience influenced by biopsychosocial factors. It is not only a result of present pathology, but also learnt. In addition, patients' experiences should be respected, and that pain may have psychosocial and functional adverse effects. Consequently, this complexity makes pain difficult to measure as well as compare between individuals (163, 164).

How to measure pain

No single, objectively measured characteristic has been identified for pain (160, 165, 166), nor is there a consensus on a single standardized tool for pain assessment. Pain assessment tools can be unidimensional or multidimensional (167). A common multidimensional pain assessment tool is the McGill Pain Questionnaire that assesses three components of the pain experience (sensory intensity, emotional impact, and cognitive evaluation of pain) (168). Unidimensional tools measure pain intensity, defined as "how much a patient hurts, reflecting the overall magnitude of the pain experience" (169). The IASP recently released a new Classification of Chronic Pain for the International Classification of Diseases (ICD-11) with extension codes that for the first time contained a more detailed description for the pain intensity measure of chronic pain (163). They state that pain should be assessed either verbally or on a numerical or visual rating scale. The Visual Analogue Scale (VAS) is a self-reported scale that consists of a 100 mm long vertical or horizontal line. The scale has anchors at the extreme ends with verbal descriptors that describes the corresponding pain status at that anchor (170). Similarly, the Numeric Rating Scale (NRS) is a numbered version of the VAS, where the patient selects the number that best represents their pain intensity (171). The most common number scale is 0-10, with descriptive anchors at each extreme. The anchor descriptors, recall period, and introductory text vary between studies for both VAS and NRS (172). The benefit of these scales is that they can be used across languages (173, 174). Pain intensity measured by VAS and NRS can be used as a continuous scale, but also categorized as mild, moderate, and severe pain, or resolved and non-resolved (175, 176). However, no standard cutoff points exist across pain studies (177). Both VAS and NRS have shown varying degrees of measurement properties (174, 178-180). The weakness of the unidimensional pain assessment tools is that the single measure relies purely on the patient's interpretation of the number describing their pain intensity. This may vary due to different tolerance for pain, previous experiences,

and a range of psychosocial factors in patients with the same pain scores (181-185). Studies have found that individuals express difficulties with quantifying their pain intensity with numbers, and particularly the middle parts of the scale seem to require degrees of abstract thinking regarding what their pain should be compared with (186, 187). A recent study found that participants expressed doubt that pain could, in fact, be measured (188, 189). Furthermore, pain measure is vulnerable to recall bias when measured retrospectively (190-193), and as a single measure it is not able to represent the variability of pain over time (68, 194, 195). Nevertheless, pain intensity is essential to patients and clinicians, as well as being an important outcome measure (196-203).

1.2.1 Common pain classifications

Pain has many domains (162). Pain classifications are used to systematically identify subgroups within one or more domains in order to guide specific interventions and treatment plans (204, 205), and aim to improve treatment effect (206-209).

Neck pain is commonly classified based on symptom duration, pain location, underlying pain mechanisms (for instance, nociceptive, idiopathic, or specific/nonspecific), pain intensity, and the pain pattern (burning, aching, stabbing) (17, 29, 32). Classifying pain based on pain intensity is considered a core outcome domain in research (210), and is a simple method used to order the reported intensity into categories that corresponds to differences in severity (211). Due to this, pain intensity is often used to guide treatment selection, define successful outcome in trials, and as inclusion criteria for research studies (212). The most common categories are mild, moderate, and severe (211, 213-215). The cutoff values for intensity depend on the pain scale used, of which the 0-10 NRS is the most common (175). The challenge with cutoff scores is that while they can be defined for a whole cohort, it is uncertain whether they fit the individual patient (215). Hirschfeld et al identified a range of optimal cutoff points of NRS within one sample (216). They concluded that using cutoffs can be misleading, as larger variability is found even in homogenous groups of patients (216-219). Therefore, using cutoffs as standardized criteria in research studies or for pain management is questionable.

Many classification systems combine pain domains (17, 29, 117, 220, 221). Childs et al proposed a classification system based on the overall goal of treatment that included dysfunction, centralization of symptoms, exercise tolerance, pain control, and headache (117). The commonly used Quebec Task Force grading system is based on four categories ranging from neck pain without physical signs, to neck pain with fracture or dislocation (220). A study assessing the difference in baseline characteristics and outcome in neck pain patients using the Quebec system found only small differences between the four groups (222). Classifications based on clinical manifestations were presented by the 2000-2010 Bone and Joint Decade Task Force on Neck Pain and its Associated Disorders in 2008 (17). This model included a four-degree system based on signs and symptoms of major structural pathologies (yes or no) and

interference on daily activities (minor to major). The World Health Organization's International Statistical Classification of Diseases and Related Health Problems (ICD-11) and the associated International Classification of Functioning, Disability and Health (ICF) are commonly used across health care professions (221, 223). Based on the ICF, a classification system for clinical practice guidelines in physical therapy suggested yet another four categories for neck pain based on concomitant presentations of mobility deficit, movement coordination deficit, headache, and neurological signs (29).

Classification by pain duration

Pain duration is considered one of the strongest predictors for treatment outcome in neck pain (32, 224). Patients have traditionally been classified as suffering from acute, subacute, or chronic pain (53, 195, 225). The IASP has defined chronic pain as pain that persists past the usual time of healing, and more specifically, as ongoing or recurring pain for three or more months (163). However, there is no consistent definition in the literature relating to the time frames used to categorize duration (226), and the cutoff at three months is arbitrary (227). In addition, the definition of 'subacute' appears to be a mixture of 'acute' and 'chronic' (228), and therefore dependent upon the definitions used for 'acute' and 'chronic'. Dunn et al (229) found no obvious dichotomy of pain duration, nor other patient characteristics, at baseline for low back pain patients' when comparing their 12-month clinical course. This supports the previous criticism of the traditional division (230). In fact, they concluded that pain duration of a pain episode of three years appeared to be a better cutoff point than 3 months concerning patients' clinical course (229). A limitation using the term 'chronic' is that it is based on symptoms that last for over three months and does not distinguish between different pain intensities. This, in theory, can include patients with persistent severe pain, persistent mild pain, and those reporting fluctuations of pain for longer than three months. In other words, several definitions of chronic would be necessary, depending on the aims of the study. Nonetheless, while most clinical studies agree on the cutoff points for 'chronic' patients as >3 or >6 months for most chronic conditions (227), categorization of 'acute' pain ranges from <1 week (107), <3 weeks (231), <4 weeks (232), or <6 weeks or longer (25, 233). A study assessing various categories of pain duration regarding treatment outcome found that a duration of pain from zero to four weeks was the best definition for 'acute' pain (233). A limitation of the term 'acute' is that it does not differentiate between a first-time episode of pain, a recent onset of an episode of recurrent pain, nor a recent flare-up of a persistent pain problem. Consequently, describing the course of pain based simply on three time-based categories: 'acute', 'subacute', and 'chronic', does not adequately match the experience of most individuals living with the condition. Studies have shown that pain can vary greatly within one day and from one day to another (234). This variability is largely explained by psychosocial factors and how pain is modulated on an individual level (235-238). This experience is better described by a classification that includes patients' course of pain over time (225, 239, 240).

1.2.2 Defining the clinical course of pain

It is almost 30 years since the first indications of a paradigm shift emerged regarding the course of pain (53, 241-243). In order to clarify the classification terminology concerning the course of pain, Von Korff defined six types of clinical course of low back pain: transient, recurrent, chronic, acute, first onset, and flare-up (53). At the same time, Waddell commented that predictive models for pain needed to include the progress over time, rather than at a single time-point (241). Croft et al (242) suggested that low back pain, instead, should be viewed as "a problem with untidy patterns of grumbling symptoms and periods of relative freedom from pain and disability interspersed with acute episodes, exacerbations and recurrences". In addition, Cedraschi et al (243) found discrepancy between researchers, clinicians, and patient population in the definition of chronic low back pain, labeling the term chronic unclear.

To characterize the course of pain as described by Von Korff (53), this requires studies with frequent measurements and follow-up that goes beyond the duration of an initial episode of pain. Individual variations concerning the course of pain should also be considered (244). The knowledge on clinical course at the time was mostly based on studies with few follow-ups (ranging from two to six) and a varied study duration (ranging from three to twelve months) (245-248). In comparison, the number of comparable neck pain studies were vastly inferior to low back pain studies, with even less frequent follow-ups over and shorter time (31). Until 2010, only one study on low back pain had collected data at monthly intervals for six months with the aim to identify the clinical course (240). There was no consensus for the definitions of clinical course nor on the prevalence of the suggested course patterns (249). However, there was an overall agreement between the studies that, for a large group of patients, low back pain was a recurrent condition with either repeated episodes or persistent pain (229, 240, 242, 244).

Dionne et al (225) conducted a modified Delphi study to provide a framework to interpret and compare studies on low back pain. The consensus rounds resulted in seven elements considered important for defining the prevalence of low back pain: timeframe of measure (set to four weeks), site, symptoms observed (like pain radiating into limb), duration and frequency of symptoms, the severity of pain (cutoff set as ≥7 for severe pain, <7 was termed mild pain on a 0-10 NRS), and exclusions (225). The conclusion was that uniform definitions to describe, study, and report the course of pain in studies on prevalence, intervention, and predictions for future outcome were needed (225). Up until 2011, the discussion centered around how to define the different terminology suggested by Von Korff (53) and Croft (242), terminology that is still used today when describing pain duration and frequency. Below is a summary of the most common terminology used in clinical course studies. This is followed by a summary of results and methodology for the studies on pain trajectories the last decade.

Clinical course terminology

Episode

The term 'episodic', and 'episode', has been frequently used in clinical practice and research settings. However, the first proposed definition of the term did not come until 2002. A group of researchers performed a literature review on the studies mentioning episodes of low back pain and found that the definitions were largely heterogenous in the few studies that actually provided a definition (250). The definitions ranged from "visits or series of visits" (251) to specific duration and intensity within a six-month period (252). The group of researchers therefore settled on definitions for pain episodes that were, for the most part, based on discussion sessions (250). These discussions centered on the applicability of the definition in research and clinical practice, as well as the justifications for the suggested pain-free period connected to the episode. In addition, the discussion was restricted to pain or disability, and had to be anchored, where possible, in previous literature. This resulted in definitions of episodes for low back pain, care for low back pain, and work absence due to low back pain. An episode of low back pain was defined as (250):

> *"A period of pain in the lower back lasting for more than 24 hours, preceded and followed by a period of at least one month without back pain".*

The researchers' argument behind the choice of one-month remission period preceding and succeeding the episode was two-fold. First, pain recall could constitute a significant bias if the pain-free duration prior to the onset of an episode was too long, and one month was considered realistic. Second, the pain intensity was not included in this definition, as very few studies specified the intensity of episodes. Third, disability was left out of the definition to decrease the possibility for misunderstanding by the patient and make the measure more precise. Lastly, the authors state that the definitions are most applicable to patients with a clear episode of back pain. For individuals with persistent pain with periods of exacerbations, the term "flare-up" proposed by Von Korff should be applied (53). The prevalence of the four consecutive pain-free weeks has since been studied in several populations and has been found to represent a good marker for non-episodes in three studies (253-255).

Recurrence

The term 'recurrence' of pain has also been part of clinicians' vocabulary for decades. Earlier studies have shown that low back pain recurred rather than remained steady (230). The earliest reports showed that recurrence of low back pain ranged from 37% to 68% of cases(256-258). Recurrence was first defined as "pain recurring after a pain-free interval" (259) The first suggestions of a definition to separate 'recurrence' from an episode was published by Von Korff, defining it as back pain that was present less than half the days during 1 year, and occurring in multiple episodes over that year (53). In a study on neck and shoulder pain using this definition, they found that the recurrence of neck pain in a 3-year period was 65% (260). Croft et al, however, argued that the definitions of recurrence and episode

were arbitrary, and more research was needed to categorize the course of pain (80). The only review on neck pain that mentions 'recurrence' is from the Task force on neck pain and its associated disorders (Results of the Bone and Joint Decade 2000-2010), who defined a recurrent course as "recovery to no neck pain, followed by aggravation" (27). However, the definitions still lacked specification on both intensity, duration, and frequency of the pain episodes in a recurring condition. Only two studies have since reviewed the use and definitions of the term 'recurrence' (261, 262). They found that definitions varied greatly between studies (262) and only eight percent of the studies had used the definitions proposed by Von Korff 16 years earlier (53). They suggested the use of the definition of recovery in relation to an episode by de Vet et al (250) to separate recurrent episodes, and that recurrence of pain should be defined as "pain that returns and persists for more than 24 hours" (261, 262). Based on these reviews, Stanton et al conducted a modified Delphi approach to standardize low back pain recurrence terminology that included factors such as the minimum duration of pain, and definitions of recovery, minimum intensity of pain, maximum duration between current and previous episode, and minimum functional impact (263). Stanton et al subsequently defined recurrence of an episode of low back pain as (263):

> *"A return of low back pain lasting at least 24 hours with a pain intensity of >2 on an 11-point NRS (>20mm on a 100mm VAS) following a period of at least 30 days pain-free"*

In addition, for a condition to be described as recurrent, at least two recurrences had to occur over the past year. They also recommended that function be assessed when applying the consensus definition to patients.

We have not been able to find recent studies with an updated definition of recurrence. A systematic review found a risk of recurrence of low back pain of 40% to 69% (264), and studies on neck pain indicate a recurrence rate of 22% (265, 266).

Recovery

Defining and identifying an episodic or recurrent pattern depends largely on the definition of recovery. Recovery is also a large part of patients' expectation of treatment outcome (267, 268). Patients' views on recovery embrace a range of factors that not only include absence of pain itself (268, 269). de Vet et al suggested recovery to be a period of at least four weeks without pain (250), however, the Delphi study from Stanton et al on the definition of "recurrent pain", expressed concern that this number was arbitrarily selected (263). Only two studies have used the exact same criterion for recovery of neck pain, and as a result, recovery rates ranged from 16% to 98.9% (270).

Myburgh et al found that, although pain was central in the recovery of recurrent low back pain, patients included more qualitative features like "redefinition" and "readjustment" when defining recovery (271). In other words, patients' definition of recovery could change over time with more knowledge and

experience of pain. A low back pain study assessed recurrences, or relapses, after a defined period of recovery (272), using the definitions by de Vet et al (250). They found that as many as 43% of patients classified as recovered at three months would experience at least one new pain episode during the 1-year follow-up (272). They challenged whether these patients then could, or should, be defined as recovered. There are increasing debates as to whether recovery necessitates complete freedom of pain (95, 273-276), and if the continued use of recovery as a completely pain-free state results in unrealistic expectations of treatment outcome (277). As the definitions of the clinical course of pain involves the requirement of a completely pain-free state for episodic and recurrent pain, these discussions highlight the complexity of such definitions.

Pain fluctuations

Steady, ongoing pain is rare (278, 279). Pain variations also occur in an already ongoing pain state and is usually described as 'fluctuating pain' (53, 240, 280, 281). In contrast to episodic and recurrent pain, fluctuating pain does not have a specific definition nor strict descriptors. However, studies have shown that the fluctuations that occur in a persistent complaint influence patient in different ways. For instance, persistent pain with only mild variations is predictable, and thus easier for patients to live with (279, 282-284). However, a constant variation in pain intensity that rarely, if ever, reaches a mild state is often unpredictable and a higher burden on patients (282, 285, 286). Frequently, the word 'flare' is used to describe such pain variations (287), which is defined as "…a worsening of your condition that lasts from hours to weeks that is difficult to tolerate and generally impacts your usual activities and/or emotions" (288-290). This definition builds on the proposal by Von Korff (53), and flares are considered meaningful events by patients even though they occur in a persistent pain state (285, 289, 291, 292). However, the definitions of episodes, recurrence, recovery, and fluctuations are proposed and defined by clinicians and researchers. Evidence suggest that these definitions do not always match patients' perspectives (269, 273).

In summary, there is consensus on the definitions of episodic and recurrent pain, and for flares that represent pain variation in a persistent pain complaint (250, 263, 288). In contrast, the term recovery has no commonly accepted definition, reflected in reviews and more recent findings on the complexity of pain (270, 273, 274). A particular challenge when investigating the terms episodes, recovery, and recurrence of pain within a clinical course is that, while one definition might suit the cohort and condition in one study, it can be unsuitable for another study. For instance, individuals with a long pain-free period, or several very short episodes of pain with long pain-free periods in between, are likely to have a different prognosis than individuals with two long episodes of pain during the last year (240, 279). This introduces the possibility of incorrect inclusion and/or exclusion into observational studies, with a subsequent possible bias in estimates of outcome in intervention studies (12, 293, 294). In

addition, uniform terminology will ease comparability between studies and allow for better study of causative factors and develop appropriate treatment options for neck pain (295).

1.3 Pain trajectory research

To be able to compare results between studies, it is important that uniform terminology is used in research (195, 225, 250, 263). The paradigm shift from acute-chronic pain to temporal variations like episodic, recurrent, and recovery, aids in establishing that pain is a recurrent or fluctuating condition regardless of the spinal origin (296). However, measuring outcome at arbitrarily selected time points, like three, six, and 12 months after inclusion, is likely to miss the temporal variations known to characterize pain (297). The selected time points then only represent a snapshot of the course of events. Pain varies extensively between and within individuals between hours (284, 298-303), weeks (192, 279, 284, 304), months (240), and years (305, 306). Consequently, presenting a clinical course based on mean pain in the cohort for each follow-up point is likely to show only one, smooth clinical course, as the individual variations are superimposed on to each other. Advances in data collection and statistical methodology at the turn of the century opened up the possibilities to assess the models proposed by Van Korff et al (244), Croft et al (242), and Dionne et al (225). The first study to use such methodology was done by Dunn et al in 2006, where data were collected monthly and analyzed with latent class analysis (LCA) (240). Four trajectory patterns were identified, providing the first basis for classification of clinical course.

Frequent collection of data with long follow-up periods increases the possibility to identify real turning points for pain exacerbation or improvement. This, in turn, enables differentiation of a diverse array of trajectories. The data collection method is also ideal to quantify the duration and number of pain-free weeks between episodes (240, 278, 297). Equally important is the minimizing of potential recall bias, as the time between follow-up points is short (307). Conditions like neck pain that often span over a lifetime, require close monitoring of the progression to be able to adjust care in relation to the expected course. Such information lets the clinician predict the expected progression and thus aid with decisions regarding in the planning of individualized treatments (113). It also allows for the identification of those at greatest risk for adverse trajectories and events (195). The information on ‘how it is likely to go’ may help to improve the communication between the health care provider and the patient on what to expect and enable patients to adapt their lives and expectations accordingly.

1.3.1 Studies on pain trajectories

As discussed above, most of the research on trajectories and development of terminology is performed on low back pain. To be able to understand the development of neck pain trajectories and the basis for this thesis, we present below a summary of important studies and reviews on low back pain followed by the research on neck and general musculoskeletal trajectories.

Low back pain trajectories

In 2016, a group of researchers summed up the research on low back pain trajectories (195) (hereafter called the 'Trajectory Overview Group'), and identified ten studies that collected data weekly or monthly for 6-12 months (177, 240, 279, 305, 308-313). Although the studies differed in type, numbers, and proportions of patients within the trajectory patterns, there was a clear trend across settings and countries. In general, five common trajectory patterns were identified: persistent, recovery, improvement, fluctuating, and episodic, with the persistent pattern being the most common. Table 1 gives an overview of trajectory studies.

Table 1 Overview of trajectory studies on musculoskeletal pain

Author Setting Design Measurement tool	Year	Pain region	Sample size (N)	Timeline Duration	Outcome measure	Analytical method	Trajectories identified
Our cohort **Primary care** **Observational** **SMS**	**2022**	**NP**	**1213**	**Weekly** **1 year**	**Neck bothersome**	**SMS-based defined subgroups**	**48% Persistent fluctuating** **48% Episodic** **2% Recovery** **1% Single episode**
Neck pain							
Pico-Espinosa (194) General population RCT SMS	2021	NP	617	Weekly 1 year	NP intensity	LCMM	42% Small improvement 24% Moderate improvement 22% Persistent 7% Large improvement 3% Slightly fluctuating 2% Largely fluctuating
Ailliet (68) Primary care RCT SMS	2018	NP LBP	NP: 153 LBP: 259	Weekly 6 months	NP intensity	LCGA NP: LBP:	76% Recovering from mild 16% Recovering from severe 7% Severe chronic 3% Recovering from mild, with flare-up 58% Recovering from mild pain 30% Recovering from severe pain 6% Moderate-chronic 5% Slowly recovering from severe pain
Walton (314) Primary care Observational Questionnaire	2014	NP	50	Weekly 1 month	NP intensity	LGCA	52% Improvement 48% General stability
Hallman (315) Workers Observational SMS	2018	Neck shoulders	748	Monthly 1 year	NP intensity	LCGA	28% Moderate recovering 24% Strong fluctuating 18% Low recovering 11% Asymptomatic 10% Very low pain 9% Severe persistent

Low back pain									
Tamcan (309) General population Observational Diary	2010	LBP	305	Weekly 1 year	LBP intensity	LCA		35% 34% 20% 10%	Moderate Fluctuating Mild Severe
Kongsted (279) Primary care Observational SMS	2015	LBP	1082	Weekly 1 year	LBP intensity	LCA LCGA	5 cluster:	29% 26% 20% 13% 12%	Mild episodic Recovery Moderate/Severe Improvement w/relapse Slow improvement
							8 cluster:	22% 21% 14% 12% 11% 10% 6% 5%	Recovery Mild episodic Moderate ongoing non-daily Late recovery Improvement w/relapse Slow improvement Severe ongoing Moderate ongoing daily
Hestbaek (316) Primary care Observational SMS	2019	LBP	30	Weekly 1 year	LBP intensity	Visual inspection, categorized by authors		40% 30% 20% 10%	Episodic Single episode Fluctuating Ongoing
Axen (310) Primary care Observational SMS	2011	LBP	176	Weekly 6 months	Days with bothersome low back	Hierarchial cluster		41% 24% 15% 13% 6%	Rapid improvement Stable mild Slow improvement Fast improvement Not classified
Kent (311) Secondary care RCT SMS	2012	LBP	322	Monthly and 2-weekly 1 year	LBP frequency	Two-step cluster		62% 38%	Severe Moderate	42%[1] Severe persistent 33%[1] Moderate persistent 25%[1] Severe fluctuating
Macedo (308) Primary + secondary care RCT SMS	2014	LBP	155	Monthly 1 year	LBP intensity	Hierarchial cluster		47% 25% 15% 13%	Recovering mild Persistent moderate Severe chronic Fluctuating
Lagersted-Olsen (317) Workers Observational SMS	2016	LBP	842	Monthly 1 year	LBP intensity	Factor analysis: Pain level and variation Visual pain mapping		34% 26% 22% 19%	Low intensity, low variation Low intensity, high variation High intensity, high variation High intensity, low variation

Cont. Table 1 Author Setting Design Measurement tool	Year	Pain area	Sample size (N)	Timeline/ Duration	Outcome measure	Analytical method		Trajectories identified
Dunn (240) Primary care Observational Questionnaire	2006	LBP	342	Monthly 6 months	LBP intensity	LCA	31% 30% 21% 13%	Persistent mild Recovering Severe chronic Fluctuating
Dunn (305) Primary care Observational Questionnaire	2013	LBP	155	Monthly 6 months	LBP intensity	LCA	37% 31% 21% 11%	Persistent mild No or occasional Persistent severe Fluctuating
Chen (318) Primary care Observational Questionnaire	2018	LBP	281	Monthly 6 months	LBP intensity	LCA[2]	47% 28% 21% 4%	Persistent mild No or occasional mild Persistent severe Fluctuating
Schuller (319) Primary care Observational Questionnaire	2021	LBP	1117	6-weekly 6 months	LBP intensity	LCGA	52% 29% 20%	High pain, strong improvement Mild pain, moderate improvement High pain, no improvement
Knecht (320) Primary care Observational Questionnaire	2017	LBP	722	0/1/3/6/12 months	LBP recurrence	Descriptives as categories	39% 21% 19% 13% 8%	Other (fluctuating or stable, but never NRS < 1) Recovery Slow recovery Recurrent Chronic (NRS ≥ 3.5)
Knecht (321) Primary care Observational Questionnaire	2020	Mid back	90	0/1 week, 1/3/6/12 months	Mid back intensity	Clustering 2 clusters 6 clusters	80% 20% 28% 20% 18% 14% 11% 10%	Rapid improvement Persistent moderate to severe Rapidly improvement, severe to mild/recovery Improvement from severe to mild/recovery Improvement from mild to mild/recovery Improvement from moderate Persistent severe Persistent severe, with exacerbation
Long-term follow-up								
Glette (322) General population Observational Questionnaire	2019	General MSK	1905	6-monthly 4 years	Pain intensity	LCA	31% 24% 22% 13% 11%	Fluctuating Persistent mild Persistent moderate Persistent severe Gradual improvement

Hebert (323) Schoolchildren Observational SMS	2022	Spinal	1556	Weekly 5.5 years	Spinal pain	LCGA	50% 28% 15% 7% 1%	No pain Rare Rare, increasing Moderate, increasing Early-onset, increasing
Picavet (306) General population Observational Questionnaire	2019	General MSK	3485	0/5/10/15 years	Pain intensity	Pre-defined patterns	32% 20% 19% 18% 11%	Never pain Persistent pain Development of pain Fluctuating pain Diminishing pain
Canizares (324) General population Observational Questionnaire	2019	LBP	12,782	Biannually 16 years	Pain	Group-based trajectory analysis	33% 28% 21% 18%	Occasional Developing Recovery Persistent
Aili (325) General population Observational Questionnaire	2021	Regional Wide-spread	1858	0/3/8/12/21 years	Chronic regional (CRP) or widespread (CWP) MSK pain	LCGA	57% 22% 10% 6% 5%	Typically no chronic pain Persistent regional, or CRP and NCP migration From CRP to CWP Persistent CWP No chronic to CRP or CWP

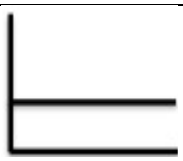
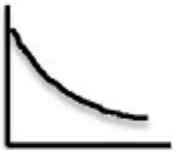
NP, Neck Pain; SMS, Short Message Service; RCT, Randomized Controlled Trial; LCMM, Latent Class Mixed Model; LBP, Low Back Pain; LCGA, Latent Class Growth Analysis; LCA, Latent Class Analysis; MSK, Musculoskeletal; CRP, Chronic Regional Pain; CWP, Chronic Widespread Pain

The proportion of patients belonging to the severe persistent pain trajectory ranged from 13% to 62% in all but one study (310), and between 20% and 54% of patients were classified as having mild persistent pain in all but three studies (177, 279, 311). Patterns described as recovery, recovering or improvement were identified in all but two studies (309, 311), with the proportion of patients ranging from 13% to 36%. The two studies without a recovery pattern differed on methodology; one cohort included patients with long-term back complaints (309) and the other was done in a secondary care setting (311). Five studies included an improvement pattern that was described as either rapid (12% to 41% of patients) or slow (12% to 14%) (177, 279, 310, 312), where all but one included a cohort with a large proportion of patients with recent onset pain (312). A fluctuating pattern was identified in all but two studies (310, 312), with a patient proportion ranging from 11% to 34%. Studies with weekly or fortnightly measures identified more patients with a fluctuating trajectory (25% to 34%) (279, 309, 311) compared to studies with monthly measures (11% to 13%) (177, 240, 305, 308, 311, 312, 318). Only one study identified an episodic pattern, classifying 29% of patients (279). The study duration (six months or one year) did not reveal any obvious differences in patterns or distributions.

The identified pain trajectories were also examined for association with background clinical and patient characteristics. Significant and clinically meaningful differences were found between the trajectories in all of the studies; trajectories characterized by persistent severe pain included patients that were most impacted by their pain regarding functional disability, psychosocial distress, and general health related factors, while patients in a mild or recovering trajectory were generally only mildly impacted by their pain (195). The differences were not only pain related, but most studies identified differences between patients in the trajectories on factors like functional disability, psychological status, history of low back pain, and general health or comorbidity (195). In addition, few studies found associations with age (309, 310), duration of prior episode (310), quality of life (309), or catastrophizing (240). The findings of the review indicated that the trajectory subgroups represent different patient profiles

The differences between the trajectory studies were concluded to most likely be due to methodological differences in exclusion criteria, measurement frequency, and analytical methods (195). However, the authors considered it unlikely that further data-driven studies would identify new patterns. Instead, they recommended trying to confirm the apparent shifting property of the fluctuating pattern in wider settings and assess patients' retrospective ability to recognize their own pain trajectory. Lastly, they emphasized the importance of using the same terminology and describe trajectories in terms of characteristics of the individual trajectory (195). As a step in that direction, the review proposed terminology and descriptions for the common trajectories for use in future studies, shown in Figure 2 below.

Figure 2 Principal trajectories with suggested labelling by Kongsted et al (195). Labels combine a descriptor of intensity, variability and change pattern. The suggested definitions are mainly based on interpretative consensus among the authors about commonly observed trajectories and therefore should be altered as evidence for other definitions emerge. (Reproduced with minor changes for print quality with permission https://creativecommons.org/licenses/by/4.0/legalcode)

Principal pattern	Terminology for labelling	Suggested definition
INTENSITY		
	*Severe pain* *Moderate pain* *Mild pain* *Minor pain/ Recovery*	**Mean scores 0-10 Numeric Rating Scale** **6 to 10** **4 to 5** **2 to 3** **0 to 1**
VARIABILITY		
	*Persistent pain*	**An individual's pain intensity stays within mean +/-1-point (0 to 10 NRS)** **Pain reported >4 days per week**
	*Fluctuating pain*	**Variation in pain intensity exceeds 2 points, without periods of no pain (0) lasting ≥1 month (250)**
	*Episodic pain* *Single episode*	**Experiencing more than one period of pain separated by periods with no pain (0) lasting ≥1 month**** **One period of LBP preceded and followed by periods with no pain (0) lasting ≥1 month**
Change pattern **(likely to be most relevant for clinical populations)**		
	*Rapidly improving pain*	**Marked decrease in pain intensity within 1 month**
	*Gradually improving pain*	**Marked decrease in pain intensity occurring gradually over more than 1 month**
	*Progressing pain*	**An overall pattern of increasing pain intensity**

*The term 'recovery' would be suitable for groups that initially present with pain. **Using the definition of episodes suggested by de Vet et al (250). NRS, Numeric Rating Scale; LBP, Low Back Pain

Concerning patients with acute low back pain, the studies from Downie et al (177) and Kongsted et al (279) revealed that most patients recovered (70% and 60%, respectively), either rapidly or gradually, and only a minority of patients experienced persistent severe pain (5% and 3%, respectively) (177, 279).

Similarly, a more recent study on patients with a first episode of acute low back pain reported recovery in 67% and persistent pain in 7% of patients (Wirth, 2017). More recent studies vary regarding methodology and setting (317, 319, 320, 326), and although few follow the proposed terminology, they have all identified trajectories that are similar to those described by Kongsted et al (195).

Neck pain trajectories

On searching the literature for this thesis, four studies on the clinical course of neck pain trajectories were found (68, 194, 314, 315). They varied on measurement frequency and follow-up duration, as well as sample size and setting. However, the studies identified generally similar pain trajectories that were either improvement/recovering, persistent, or fluctuating (Table 1).

The first study on neck pain trajectories was based on weekly pain intensity measures over one month in a physical therapy setting in the US (314). They identified two subgroups for pain intensity based on latent class growth analysis: slowly, but insignificantly, a worsening group (48%) and a more rapidly improving group (52%). Most patients included had a pain duration of between 3 weeks and 6 months (54%). They found no variables that could predict subgroup membership. The likelihood of identifying any patterns of change other than worsening or improvement was very low due to the small sample size and short follow-up period.

The first long-term study with frequent pain measures on neck pain patients was the study by Ailliet et al (68). In total, 153 neck pain patients, with or without radiation into an upper extremity, without having received chiropractic treatment the previous six months, were followed weekly for one year. Patients were asked about their pain intensity at the day of reporting on a 0-10 NRS. They defined a clinically meaningful improvement as a 30% change from the baseline measure, which is in line with recommendations for low back pain (327). Pain intensity was divided into three categories of mild (1-3 NRS), moderate (4-5 NRS) and severe (6-10 NRS) pain prior to analyses, based on cutoff recommendations (175, 211). Although their objective was to present data for the full year, issues surrounding the data-collection process resulted in large amounts of missing data. Therefore, trajectories were presented, based only on the first six months. They used latent class growth analysis (68), and revealed four classes: “recovering from mild baseline pain” (74%) with 30% reduction within first three weeks, “recovering from severe baseline pain” (16%) with 30% reduction of pain within first 6 weeks, “severe chronic” (7%), and “recovering from mild baseline pain with a flare-up” (3%). The last class contained four patients. Only a minority of the patients had complete recovery. Differences were found between the patients in “recovering from mild baseline pain” and those in “severe chronic” only, where the first group had lower number of patients with long-term pain and lower functional disability scores (NDI), and higher patient expectations. They concluded that most patients (90%) reported 30% improvement at the end of follow-up, regardless of pain intensity at baseline (68).

A study on 748 Swedish workers with neck and shoulder pain (315) showed similar results to Ailliet et al (68). However, their data were collected monthly with SMS over one year. They revealed six clusters of increasing pain intensity. Class 1 ("asymptomatic", 11%), Class 2 ("very low pain", 10%), and Class 3 ("low recovering pain", 18%) were similar to the "recovering from mild baseline pain" (78%) by Ailliet et al (68). In addition, they identified two classes with fluctuating pain (Class 4: "moderate fluctuating pain", 28% and Class 5: "strong fluctuating pain", 24%), and lastly persistent class (Class 6: "severe persistent pain"). Although they found overall significant differences in baseline characteristics between the six classes and thus defined the classes as being distinctly different, no between-class analyses were used/carried out. Considerable overlap was found between several classes, in particular between classes 1-3, but also between classes 5 and 6.

More recently, a study collected weekly pain data through SMS on neck pain patients in the general population, all invited to participate in the study through local newspapers in large public companies in Sweden (194). Their cohort consisted of 614 participants who responded to a mean of 48.4 (standard deviation 12.4) of the 53 weekly SMS. Inclusion criteria was a self-rated pain intensity of ≥2/10 and disability due to pain of ≥1/10 on NRS, and most patients had pain duration above 12 months at recruitment. In addition, the patients were randomly assigned to one of four different treatment groups. After analyzing the data with latent class mixed model, six clusters were identified. The clusters had a mean reported pain ranging from 5.0 (SD 1.4) to 7.3 (SD 1.4). The most common clusters were "small improvement" (42%), "moderate improvement" (24%), and "persistent" (22%). Less common were "large improvement" (7%), "slightly fluctuating" (3%), and "largely fluctuating" (2%). They categorized the two fluctuating and the persistent clusters as unfavorable (27%), and the three clusters with improvement as favorable (73%). Patients in the favorable clusters showed improvement in pain intensity between 2/10 and 5/10 during the first part of follow-up, visually estimated from the illustrated trajectories of the cluster mean pain intensity to be from 14 to 20 weeks, with little improvement after that. The three unfavorable clusters were strongly associated with higher pain intensity and having depressive symptoms at baseline. In addition, being female, younger, and having sudden onset of pain were associated with unfavorable clusters.

In summary, the four trajectory studies on neck pain vary greatly on cohorts and methodology. They describe similar trajectories in terms of recovery/improvement over time, as well as differences between patients with trajectories characterized by low pain/improvement and patients with trajectories of fluctuating and persistent pain. None of the studies identified an episodic pattern, despite two of them having collected data weekly over 6-12 months (68, 194). As all described the trajectories based on the subgroup's weekly/monthly mean pain, this could explain the lack of an episodic trajectory. Most of the studies found that patients in the trajectories differed on somatic and

psychosocial factors, but none of the trajectories were distinctly different. As with most trajectory studies, differences in methodology makes further comparison difficult.

Pain trajectories in general musculoskeletal conditions

Several studies have assessed pain trajectories in different musculoskeletal regions (63, 148, 153, 321, 322). Commonly, they identify only small differences between the pain trajectories and the musculoskeletal regions they assess. One study (322) identified several trajectories that were comparable to those described by Kongsted et al (195). The other studies identified persistent or improving patterns (63, 148, 153). In addition, higher scores on functional disability and psychosocial factors were generally associated with poorer outcome across all pain sites. Similarly, a recent Norwegian study on recovery trajectories for musculoskeletal pain patients in primary health care found a modest decrease in pain intensity overall across musculoskeletal sites (155). Nine measures of pain intensity over one year revealed similar patterns of improvement for each of the pain sites. However, when patients were divided into five phenotypes based on pain, symptoms, and patient characteristics (154) rather than diagnosis, a variation of pain patterns were found (155). Based on these results, they suggest focusing on general, rather than site specific, targeted treatment approaches and research (115, 140).

Only two studies published after the 'Trajectory Overview Group' article (195) have applied the group's recommended definitions and/or terminology to describe their trajectories (316, 328). In addition, large variations in methodology hamper the comparisons between studies.

1.3.2 Stability of trajectories over time

Traditionally, the course of pain was seen as a linear trajectory where an acute episode led to subacute episodes and progressed to a chronic pain condition. This view has probably influenced research on musculoskeletal pain for decades. By intervening in the subacute stage, persistent pain would be avoided for the vast majority of patients. However, as described so far in this thesis, the course of pain is much more complex, with a large variety of individual trajectories. To establish when and how to intervene effectively to prevent the patient from establishing a pain pattern that becomes persistent and probably be costly for both patient and society, it is important to investigate the stability of the trajectories over time. In 2006, Dunn et al studied low back pain trajectories over six months (240). They found that the trajectories matched well with the hypothesized pain trajectory for the period from 6 months to 1 year and hypothesized that the trajectories were stable over time. However, they did not repeat the trajectory analyses for the last 6 months of follow-up. Tamcan et al identified 1-year natural course trajectories of low back pain, as well as assessed the trajectories in shorter, quarterly periods (309). They found that most of the patients were allocated to the same trajectory throughout the 1-year follow-up. Conversely, patients allocated to the fluctuating trajectory, both in the first and the

subsequent quarterly periods, had the most unstable course of pain. Dunn et al repeated the assessment of the trajectories in the same cohort from 2006 and found that most patients remained in the same trajectory 7 years after (305). However, patients classified as fluctuating were less likely to have same classification during the 7-year follow-up period compared to patients with any of the other trajectories. Moreover, studies with single-point measures and several years between measurements show that most trajectories for low back pain are stable, perhaps even for as long as 15 years (306, 329-331). However, all studies show that a group of patients has pain that fluctuates over time. Musculoskeletal pain appears to be both long lasting and recurrent over a lifetime (306, 322, 324, 332-334), and patterns might even be established at an early age (335, 336). However, no studies have assessed the stability of neck pain trajectories over time.

1.3.3 Methodological considerations

There are various methodological approaches that can be used to identify subgroups for the clinical course of pain. Selection of the type of data collection and analysis may affect the number and type of trajectories found in longitudinal studies. The analytical methods vary in complexity, from the simplest type by visual inspection, to the more complex techniques that involve algorithmic analyses with advanced computer software. Below is a description of the different methodologies available for trajectory research, and how they might affect results.

Methods for collecting data

The term “Ecological Momentary Assessment” (EMA) has been used to describe the “repeated sampling of the subjects’ current behaviors and experiences in real time in the subjects’ natural environment” [2]. This was previously exclusive for the use of diaries. With mobile phones, sending and retrieving information repeatedly and as frequently as desired to large groups of people through text messages, this is possible. In Norway, 95-99% of the population owns a personal computer, mobile phone and/or a smartphone (337).

The traditional method for collection of patient-reported outcomes is paper questionnaires. This allows for long questions with multiple response options. There are also few limits on the number of questions or type of figures, illustrations, or scales with paper questionnaires, beyond patient fatigue with too many questions. Pain is generally measured before and after an intervention, as well as subsequent follow-ups. However, paper questionnaires are not suitable for frequent measures, as there are logistical challenges for both patient and researchers. Also, there are limited abilities for collecting data momentary or in the patient’s natural environment, as well as issues related to incomplete or back-filled diaries (299, 338).

As society is rapidly becoming more computer literate, and the majority of us own smartphones, tablets, and personal computers. Hence, collecting data through these methods are preferable to paper, post, or telephone calls. There is increasing evidence that data collected via electronic methods contain less errors than paper or telephone communication, and that electronic methods produce comparable results to the traditional methods like paper (339-342). Questionnaires can be sent in their entirety through an internet-based data-collection method (339, 340). Apps are readily available on smartphones and tablets, and are ideal for studies that require repeated and/or EMA data, as they fit both longer questions and responses and also scales requiring illustrations (343). Evidence shows that if questions are kept identical in the paper and electronic versions, and user-friendliness is maintained, no information is lost or results changed (344, 345). An alternative method for data collection has become available in the form of 'Short Message Service' (SMS). SMS monitoring fits EMA or other frequent measures perfectly, as the technology can collect data on the patient's present state with real world information (and not in a simulated or clinical setting) in real time (299, 341). The technology enables messages to be sent directly to patients, regardless of time, season, place, or setting (346). Furthermore, most people seem to always bring their phone with them, thus making measurements truly ecological, i.e., they take place in the patients' own environment. This may be important when context might influence the variable of interest. Also, the use of mobile phones minimizes seasonal interruption (such as holidays) of data collection (346). It is user friendly for patients, however the very oldest generation might struggle with responding to SMS. The questions are easily accessed for researchers as data can be retrieved and followed up during the data collection phase. There is no interviewer bias, questions can be answered quickly, and it is cheaper to use compared with paper questionnaires and diaries (341). Axén et al found an overall compliance of 090% in studies with up to two years follow-up with weekly measures, and response appears to be influence, only to a mild degree by the type of study (variables measured) rather than individual factors (347).

Timing of measurements

Previously, most studies on the course of pain were designed as prediction studies for an outcome from baseline to a set number of time-points, often set at 3, 6, and 12 months after inclusion (27, 31, 348). New technology permitted more frequent measures, and most trajectory studies now use either a monthly or weekly measurement frequency (Table 1). Axén et al explored the optimal measurement frequency for trajectory studies by comparing weekly and bimonthly measures (349). They found small changes in trajectory distribution between the two measurement frequencies for the first 18 weeks. However, the study by Kent et al found that monthly measures did not identify a fluctuating pattern, whereas fortnightly measurements did (Kent 2008). Axén et al also found that measurement periods of 8 and 13 weeks were too short to give an accurate prediction of trajectory development until 26 weeks (349). Furthermore, weekly recall corresponds well with daily measures of pain (350). It has been

emphasized that data collected repeatedly and very frequently requires close follow-up of patients' responses by researchers (68, 347).

Aiming to study acute pain trajectories, it is likely that weekly, daily, or even multiple measures during the day are necessary to be able to capture the temporal fluctuations of exacerbations and amelioration of pain (195, 288, 292, 296, 328, 349, 351, 352). However, this is not feasible for assessing the development of persistent pain over a lifetime, where studies to data have collected data monthly in periods separated by years (305), or used single measures with long recall separated by several years (306, 324, 325, 332).

Handling missing data

Longitudinal data involves repeated measures, which are likely to result in some missing data for various reasons (like responders' fatigue, seasonal issues like holidays, or technical issues). Some of the analytical methods for longitudinal data cannot handle missing data directly, which means that patients with even only one missing response risk exclusion to obtain appropriate data for analysis (complete case analysis) (353-357). Another option is imputation of data (filling in missing values) like single imputation, where one value for a missing element is filled in by another. A common example is mean substitution, where the missing value is replaced by the individual's mean score of the variable (358). Other analytical methods, like Latent class growth analysis, assume that data are missing at random and can handle missing data directly (353, 359). An example of missing not at random would be if patients with missing data differed significantly from patients without missing data. However, this is difficult to test in larger cohorts with frequent measures over time (360). All imputation methods increase the risk of bias, and for statistical analyses that do not handle missing data directly, it is therefore important to select the best suited imputation method (355, 361).

Analytical considerations in trajectory studies

As the knowledge on the highly individualized aspect of the pain experience grew (362), so did the need for analytical techniques with a more person-centered approach (240, 363-365). There are several valuable methodologies that can be used to monitor profile patterns over time (195, 304, 365-367). Identifying patterns of behavior, disease, or symptom cannot be done by a single observed variable (240). Rather, factors or characteristics are often combined to form groups, and thus, probably capture the more multi-dimensional aspect of most pain conditions. Following is a summary of important considerations and possibilities when conducting trajectory studies.

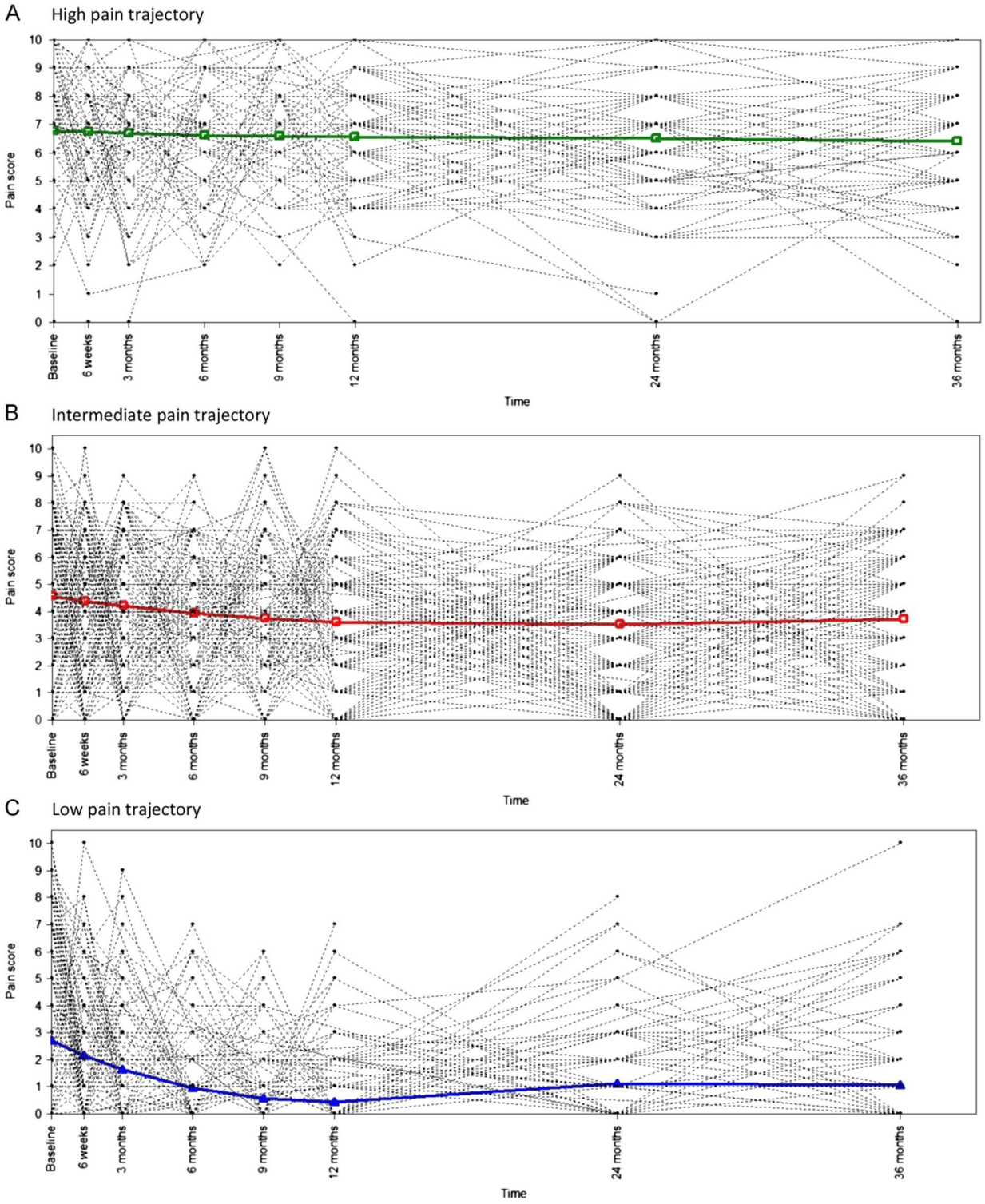
An accurate, but primitive, method in assessing the course of pain is through visual analyses. Displaying the individual trajectories graphically will enable visual identification of painful and pain-free episodes and duration of these. Fluctuations will also be easy to categorize, as will the size of variation and the trend of recovery or exacerbation over time. With definitions and criteria for subgroups decided a priori,

there are few restrictions on the detail of the course, or the number of subgroups examined. In a study with 78 courses of pain, this method has shown to have a substantial inter-observer reliability (kappa=0.7) between two observers (304). This method was assessed on a group of low back pain patients followed weekly for 18 weeks and found that visually described patterns could be derived from 215 patients (304). However, this is only feasible in studies with up to a few hundred participants, as any more than that would be very time-consuming.

Trajectory modelling focuses on the relationship between individuals, and classify them into distinct subgroups based on their individual patterns of response (359). These methods allow for a better understanding of intra- and inter-individual variability over time, which is lost with measures based on cohort means. There are several different types of clustering methods, factor analyses, and latent class analyses that are used in pain trajectory studies, and the subgroups are usually described and labelled based on the mean of the individual trajectories within each subgroup (195, 311, 317, 366, 368).

Also within subgroups, there will be large individual variations of timing and duration of episodes and fluctuations between the patients. The problem of superimposed individual trajectories combined to a group mean is inadequate to illustrate a particular subgroup classification, as emphasized by Kongsted and wo-workers (195) and illustrated by Enthoven et al (326) in Figure 3 below. This figure illustrates that although the subgroup mean trajectory is very smooth, the individual patients within each subgroup experience periods of exacerbations and improvements without a particular pattern over time. Therefore, it is still a challenge to know when the “window of opportunity” to target treatment occurs.

Figure 3 Plot of class means and individual back pain scores at follow-up in the three different trajectories. Pain measured at baseline, 6 weeks, and 3, 6, 9, 12, 24, and 36 months (326). (Reproduced with permission from Age and Ageing).



It would clearly be useful to be able to identify trajectory subgroups from descriptive definitions. These definitions could be easily applied to independent datasets or individual new patients and lead to researchers and clinicians using the same definitions of mutually exclusive subgroups across populations. For example, standardized definitions are needed to explore the prevalence of trajectory patterns in different populations or associations with types of intervention. In addition, defining

operationally specific and clearly described trajectory subgroups would be useful to assess whether the trajectory patterns are clinically useful indicators of relatively homogenous phenotypes. Lastly, it would be beneficial to provide a possible solution to remove the need for complex analytical software. Aiming to address these issues, Kongsted et al (328) assessed a set of pre-defined subgroups based on two of the principle patterns described by the 'Trajectory Overview Group'; intensity and variability (For definitions, see Figure 2) (195). The four patterns: ongoing, fluctuating, episodic, and single episode, were separated into four subgroups based on four pain intensity cutoffs: severe, moderate, mild, and minor, leaving sixteen subgroups in total. They found that the pre-defined subgroups could be readily applied to the low back pain cohort. The pre-defined subgroups also had a strong match with most of the five trajectories previously derived from latent class analysis on the same cohort (279) . More specifically, most patients were classified as either episodic (51%) or fluctuating (25%). Very few patients were classified as ongoing. Although not totally distinct, there were clear differences between the fluctuating and episodic low back pain patterns (328).

1.3.4 Classifying patients' clinical course by visual trajectories

Trajectory research through repeated measures is a very good way of capturing the temporal variation of pain (53, 195, 211, 225, 240, 278). Data-driven methods as described above have, through complex analyses, identified common trajectory patterns in different cohorts, populations, and conditions (68, 148, 195, 321). Patients can be classified into trajectories that are distinct and potentially meaningful clinically. The four main patterns of importance for low back pain: ongoing, fluctuating, episodic, and recovering, have been described in both text and graphically (195, 304, 328) (Figure 2). A good picture of the patients' development of pain can be formed by combining the identified trajectory with the patients' report of past pain history. However, following patients repetitively over time is arduous and a burden on patients. It is also time-consuming and expensive for use in research and requires comprehensive analytical skills.

Asking the patient to select an illustration that best describes their past clinical course of pain, however, has been suggested as a possible solution by the 'Trajectory Overview Group' (195). To assess how well such visual illustrations reflected the patients' actual pain trajectory, Dunn et al (369) assessed a single, self-report item questionnaire, "Visual Trajectories Questionnaire-Pain" (VTQ-Pain). The visual trajectories were based on the suggestions by Kongsted and colleagues and included eight different trajectory descriptions. They compared the VTQ-Pain response selected at 12 months to the patient allocation to statistically derived trajectories for the first 6-month data (305) as well as against constructs from the stages of pain model (370). They concluded that the VTQ-Pain had acceptable face, content, and construct validity (369). However, patients with persistent mild pain had a discordant hypothesized data-derived trajectory, and a proportion of patients selected a fluctuating visual trajectory when their pain in fact was not. Similarly, visual trajectory patterns were given to neck and

low back pain patients recruited in a chiropractic setting in the Netherlands assessing prognostic factors for predicting recovery (64). They included four patterns based on Dunn et al.'s latent class analysis trajectories (persistent mild, recovering, severe chronic, and fluctuating) (240) and two patterns based on clinical expertise of the authors (first time acute and episodic) (64). They found that patients selecting a fluctuating pattern had poorer outcome than those selecting a single episode pattern. However, the pain patterns were not significant predictors in the final model. Similar visual trajectories have been used to categorize patients when assessing pain threshold and spinal manipulation in low back patients (371, 372). Lastly, a visual trajectory questionnaire, the PainDETECT, includes four different visual pain trajectories; persistent pain with slight fluctuations or with pain attacks, and pain attacks with or without pain between them (373) and is widely used for neuropathic pain (167). However, no data on the selected visual trajectories is available for comparison.

In summary

The overall conclusion from research on the clinical course of pain, for neck pain in particular, is that comparisons between studies are difficult due to substantial methodological and definition heterogeneity. In addition, the methodological quality of studies is of varying quality (92, 130, 374). Attempts have been made to make more uniform definitions and terminology (195). Nonetheless, these definitions are still not fully implemented in research. Recently, a Delphi study including neck pain experts summarized views on the future agenda for neck pain research (290). Ranked as fifth out of fifteen research priorities was "Defining the natural or clinical course and the prognostic factors of neck pain". Furthermore, the new ICD-11 extension codes published in 2018 contained, for the first time, a more detailed description for pain that included the temporal aspect of chronic pain (227), describing it as including 'continuous' (always present), 'episodic recurrent' (recurrent attacks of pain with pain-free periods), or 'continuous pain attacks' (recurrent attacks described as exacerbations of underlying continuous pain). Combined, these definitions are a good reflection of the history of the research and the recent findings on the clinical course of pain and highlights the relevance of the topic of this thesis in the current research environment.

Aims of the thesis

Main aims

The overall aims of this research were twofold: First, to explore the clinical course of non-specific neck pain patients in Norwegian chiropractic practice in terms of SMS-based patterns and subgroups over 1 year. Second, to explore visual pain trajectories in non-specific neck pain patients using clinical course and patient characteristics.

Specific objectives

Paper I

The main aim of this paper was to investigate if SMS-based patterns and subgroups for low back pain were applicable to neck pain patients, if the patterns and subgroups differed in clinical and patient characteristics at baseline, as well as explore the robustness of the SMS-based subgroups.

Paper II

In this study, we examined to what extend patients shifted from one SMS-based pattern to another in periods of four quarters in the follow-up year and compared patient characteristics within stable and shifting trajectories.

Paper III

The aim of this study was to explore and describe self-reported visual trajectories in terms of prospectively reported clinical course and SMS-based pattern classification of neck pain.

2 Material and methods

2.1 Design

This thesis is based on data from a large prospective observational study that followed patients with neck pain treated at chiropractic clinics in Norway, over one year. Data on patients were collected weekly with SMS-Track® over 52 weeks, as well as questionnaires at baseline, at 4 weeks, 12 weeks and 1 year. Data used in this thesis were from the weekly SMS, and baseline and 1-year questionnaires.

SMS-Track®

SMS-Track® is a web-based software developed specifically for research purposes (375). The technology allows real-time data from many participants to be collected at frequent intervals and is particularly suited for response options of numbers or a single word. Furthermore, the actual questions can be delivered by SMS directly to participants regardless of time, season, or place. The software stores the collected information safely in a system-generated database directly available to the researchers in real time. The method has been shown to be both inexpensive and easy to use, with acceptable reliability (346). It has previously been used for digital collection of high-frequency data in clinical practice (68, 304, 315, 376), and has the possibility for very high response rate (194, 279, 304, 377). Notable disadvantages for use in data-collection for research is the limitation of 160 characters per SMS, and it is ill-suited for responses other than single numbers or single words.

2.2 Study setting and recruitment

Chiropractic recruitment

We invited all members of the Norwegian Chiropractic Association (NKF) by e-mail to participate in our study in June 2015. The study was also presented at conferences directed by the NKF. To ensure that all members of NKF received the invitation, we re-sent the e-mail twice: in August and in October 2015. In addition, all included chiropractor clinics received a package including information material for patients, detailed descriptions of the study and recruitment process, and contact details for the researchers. Chiropractors were also provided with study information suitable for posting on their websites. In addition to the written information, we visited chiropractors in clinics in the South-Eastern region of Norway and provided verbal information and instructions. For the chiropractors in other parts of Norway, this information was given by telephone. In total, 124 chiropractors from 71 different clinics agreed to participate and signed a written consent form. Of these, 12 chiropractors did not recruit any patients. The mean age of the participating chiropractors was 37 (standard deviation (SD) 8), with an

even gender distribution. Most chiropractors were educated at Anglo-European College of Chiropractic in the UK (n=56, 50%) and the University of Southern Denmark (n=26, 23%). The geographical spread of chiropractors allowed for patients to be recruited from both urban and rural areas of all four regions of Norway, however there was an overweight of patients in, and around, the region of Oslo. We asked each chiropractor to recruit 23 patients with neck pain during a period of two months. To ensure a cohort with an optimal representation of patients with neck pain presenting to chiropractic clinics in Norway, we asked the chiropractors to invite all consecutive patients with neck pain who fulfilled the inclusion criteria. According to the approval from the Regional Ethics Committee in the southeast Norway (March 2015, (2015/89)) we were allowed to register information about patients not invited to participate, with the following options for exclusion:

- Patient declined to participate
- Chiropractor forgot/did not have time to invite patient
- Patient did not fulfil inclusion criteria (presence of red flags, no mobile phone, lacking sufficient Norwegian language skills)
- Patient with dementia
- Patient has psychosocial issues that the chiropractor deems are too significant to justify adding invitation to participate to study

Fifty chiropractors returned this form at the end of their recruitment process, but few of the forms were completed according to instructions.

Pilot testing

Five chiropractors, three with and two without previous research experience were asked to read through all questionnaires and test the recruitment and data-collection procedure. In June 2015, these chiropractors were asked to recruit 3-5 patients with neck pain each resulting in a total of 17 patients. These patients were followed for three weeks with SMS-track®, as well as given the baseline questionnaire according to the instructions in the study procedure. A second questionnaire was sent by post after three weeks. We used the information from this pilot to check responses (for instance, if letters were used instead of numbers or missing answers). The chiropractors and patients were asked to give feedback on the study procedure, as well as on the content of the questionnaires in terms of potential misunderstandings regarding the questions and answer alternatives. Based on responses from this pilot, we did some modifications on the questionnaires and the procedure, to ensure they were easy to use and well understood. We used the same procedure for the SMS collection as described by Kongsted et al (328).

Participant selection

All participants were recruited between September 2015 and June 2016. All were treated for neck pain at the time of recruitment. Table 2 presents the inclusion and exclusion criteria.

Table 2 Inclusion and exclusion criteria for studies in this thesis

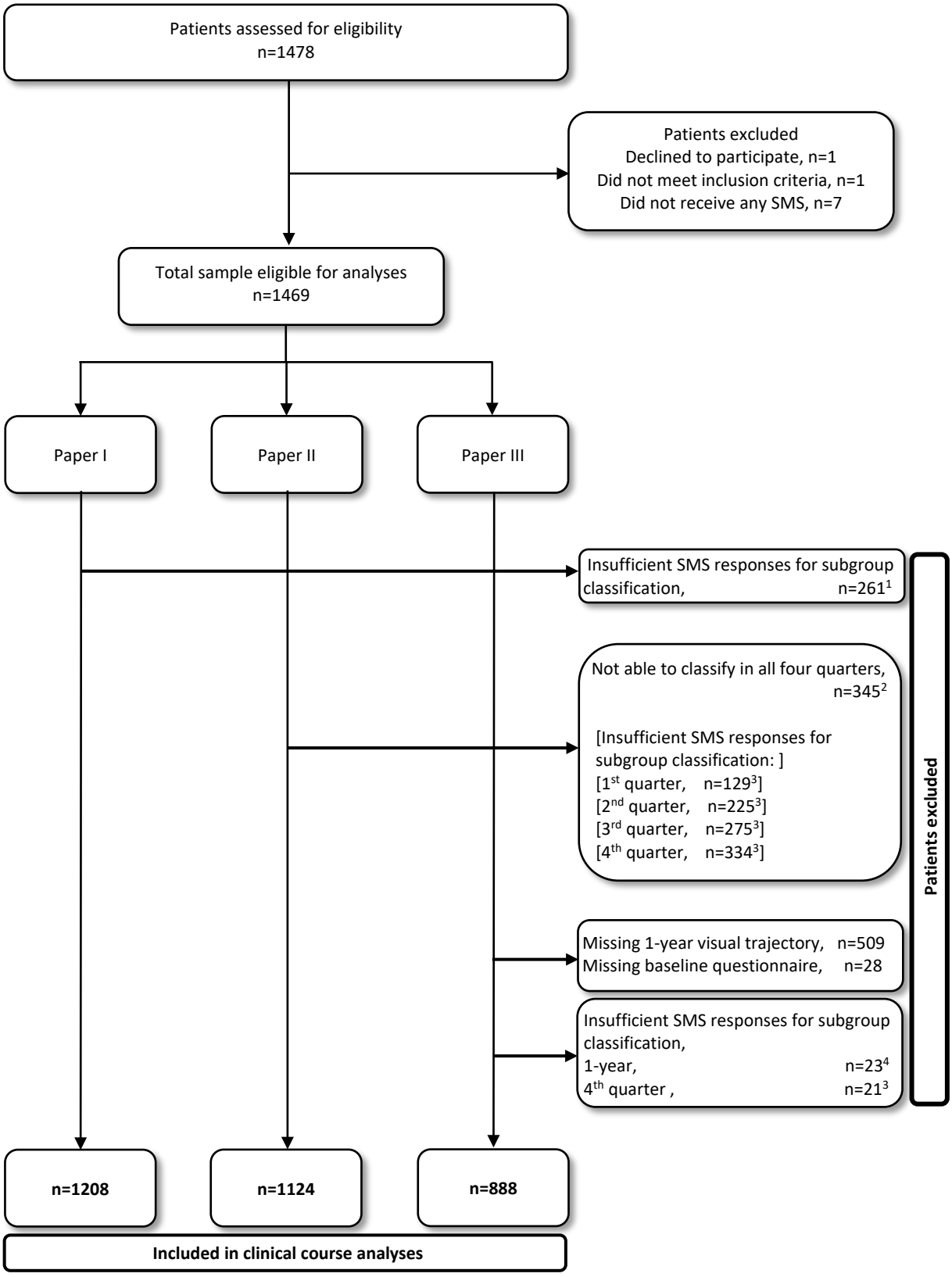
Inclusion criteria	Exclusion criteria
• 18 years or older • NP primary or secondary complaint regardless of pain intensity or duration • Received a neck ICD-10 diagnosis by the chiropractor either at inclusion or a previous consultation • Able to read and write Norwegian • Own mobile phone and able to receive and send SMS	• Systemic disorders • Fractures • Malignancies • Infections • Myelopathies • Vascular causes of neck pain • Known congenital malformations in the neck

NP, Neck pain; ICD-10, International Statistical Classification of Diseases and Related Health Problems

Our main aim was to ensure a cohort that potentially represented neck pain patients in chiropractic practice in Norway. Therefore, all patients with neck pain consulting the chiropractors could be invited to participate in the study. No restrictions concerning pain duration and time since last chiropractic consultation or other treatment were used. In other words, patients presenting to the chiropractor for the first time or already in a treatment course could be included. The pain could be a first episode of neck pain, or part of an episodic or persistent pain complaint.

In total, 1478 patients agreed to participate in the study. Of these, one later declined to participate, and one was excluded due to pathology as cause for the neck pain. For unknown reasons, 7 patients were not entered into the SMS-track® system. This was not noticed until week 34 of their follow-up, and they were therefore excluded from this study. Thus, the study sample for this thesis included 1469 patients. Figure 4 shows the patient flow for Papers I, II, and III.

Figure 4 Flow chart for the cohort and samples used in Papers I-III



[1]Patients responding on less than 20 out of 43 weekly SMS; [2]To be included in the analyses in Paper II, the patients needed enough SMS to be classified in all of the four quarters; [3]Patients with less than 6 out of 13 SMS responses; [4]Patients with less than 26 out of 52 SMS responses

2.3 Data collection

The recruiting chiropractor filled out the patient's contact details digitally through Nettskjema, an integrated net-based survey solution for collection of sensitive data, provided by "Services for sensitive data" (Tjenester for Sensitive Data, TSD) at the University of Oslo. The main researchers transferred the patient code with the corresponding mobile number manually into the SMS-Track® system, which in turn sent out the weekly short message services (SMS'). Every Sunday, at the same time and over a total of 52 weeks, the patients received 2-3 automated SMS with the following questions:

1) "How many days the last week has your neck been bothersome? Please answer with a number between 0 and 7".
2) How intense has your neck pain typically been the last week? 0= no bother, 10= worst bother imaginable.
3) How many days the last week has your neck limited your daily activities? Please answer with a number between 0 and 7.

If the answer to SMS 1) was 0, the patient did not receive SMS 2), but did receive SMS 3). The wording of the first two SMS were directly translated, by two of the researchers, from those used in the Kongsted study (328), and later discussed with the research group. These SMS-questions were well understood in the Pilot study. Responses on the SMS questions were stored in a data file at SMS-Track®, and non-responders could be identified and subsequently contacted using the subject identity list. An encrypted linkage key was used, linking the patient's ID number in the project and their personal identity. For patients who did not respond to, or stopped responding to the SMS', a reminder was automatically sent by SMS-Track® on the following Tuesday evening. Every Wednesday morning, the responses were checked by the researchers. Non-responders were subsequently called with a reminder to answer the SMS, and where necessary, informing them about painful periods with constant pain intensity as well as periods without any pain were important information to the study. On twelve occasions patients found difficulties with responding to the SMS, which resulted in a manual correction of data that were appropriately documented.

We used the term 'bother' for neck pain intensity anchors. Bothersome pain is a summary term across symptoms and diseases describing symptom severity that is acceptable to both patients and clinicians (310, 378-384). It has been proposed as a general measure for the impact of pain that is clinically relevant (253, 385, 386), and correlates well with pain intensity, functional disability, anxiety, depression, return to work, self-rated health, treatment outcome and satisfaction (379, 383, 387). The term has previously been suggested as a standard outcome for low back pain studies, however, and has not been validated it is not included in recommendations to date (210, 385, 388, 389). Instead, the term

bothersome is mostly used as inclusion criteria (371, 372, 390), or dichotomized as an outcome measure (yes/no) or days with bothersome pain (51, 52, 253, 391-395). One of the earliest trajectory studies with weekly SMS used 'bothersome days' as measure (310).

At recruitment, the patients could choose between paper or digital questionnaire. Patients who selected paper questionnaire were given the questionnaire at the end of the consultation, together with a pre-addressed and stamped envelope. They could fill in the questionnaire in the waiting room and return by post the closed envelope immediately or fill in the questionnaire at home and return by post. For patients selecting digital questionnaire, their e-mail address and patient code was transferred into Nettskjema manually, and the digital questionnaire was sent through e-mail. All non-responders to the questionnaire were given a reminder after 1 week; for patients selecting digital questionnaires, this was done automatically by Nettskjema. Further, reminders were given by telephone if no reply was obtained after 2 weeks. The same procedure was used at 1-year follow-up. Of the responders, 14% preferred paper questionnaire at baseline. Altogether, 11% (n=163) did not respond to the baseline questionnaire, and 34% (n=509) did not respond to the 1-year questionnaire. Sixty-five percent of patients (n=952) responded to both the baseline and the 1-year questionnaires. Treatment content and frequency was completely at the chiropractor's discretion, and the study was not designed to assess or explore treatment effect.

2.4 Measurements

Chiropractor-reported variables

All chiropractors completed five digital questionnaires (about the chiropractor, and patient data from recruitment consultation, and 4, 12, and 52 weeks after recruitment). Data concerning the chiropractor demographics and recruitment consultation were used in this thesis. The chiropractor filled out this questionnaire for each patient at the time of recruitment, after the patient had signed the written consent. The questionnaire included extensive information surrounding the clinical examination and findings, as well as treatment decisions. To explore the clinical course trajectories for patients recruited at different time- points in the treatment course, we asked the chiropractor about the consultation type for each patient: "Is this first consultation for the patient?" (Yes/No) (answer Yes was later defined as "First consultation"), and "If this is NOT the first consultation, please cross off the most appropriate response: 1) The patient is in a course of treatment for a specific episode of neck pain (later defined as "Follow up"), or 2) The patient has persistent neck complaints and receives treatment regularly or periodically due to pain/discomfort/stiffness in the neck" (later defined as "Maintenance care").

Patient-reported variables

Table 3 gives an overview of how the variables from the questionnaires, with items and responses, collected from baseline and 1-year questionnaires were used in Papers I-III.

Data collected at Baseline

The patients were asked about sociodemographic details regarding their age (years), gender (female, male), and physical activity (never, less than once a week, once a week, 2-3 times weekly, more than 3 times weekly). In addition, factors relating to their neck pain were collected, including duration of current neck pain episode (from item 1 on the Örebro Musculoskeletal Pain Screening Questionnaire, see below), previous episodes of neck pain (none, 1-3 times previously, more than 3 times previously, more or less chronic neck complaint), and duration of their neck pain history (less than one year, 1-5 years, 6-10 years, more than 10 years, as long as I can remember).

Pain intensity was measured on a 0-10 numeric rating scale (NRS), with anchors of 0=no pain and 10=the worst pain imaginable (396). Participants were asked the following question: "How would you grade your pain right now?", with the anchors 0= no pain and 10=as painful as it is possible to have (397). The NRS is among the most widely used patient reported outcomes for measuring pain in primary health care (398), being both simple to administrate and score. It is defined as a standard outcome measure for low back pain by the National Institutes of Health research task force (388), and has shown moderate to acceptable reliability and validity for use in neck pain patients (180, 399, 400).

We measured functional limitations and degree of neck disability using the Neck Disability Index (NDI) (401, 402). The NDI is the most commonly used patient-reported outcome measure for neck complaints in both clinic and research (403). Participants report their degree of pain and activity limitations the past week on 10 items: pain intensity, personal care, lifting, reading, presence of headache, concentration, working, driving, sleep, and leisure activities. The scores range from 1 (not affected) to 5 (worst possibly affected), giving a total sum-score of 0 (no impairment) to 50 (complete impairment) (401). More specifically, scores between 0–and 4 indicate no disability, 5–14 mild disability, 15–24 moderate disability, 25–34 severe disability and 35–50 complete disability (404). The index has been validated for disability and pain in acute and chronic conditions (404), and the Norwegian version has shown good test-retest reliability (405).

Psychological state and distress was measured by the Norwegian version of the Hopkins Symptom Check List (HSCL-10) (406), a questionnaire including ten items on depression, anxiety and somatization (407). It is scored on a four-category Likert scale from 1 (not at all) to 4 (extremely). A mean score is calculated. A Cronbach's alpha of 0.88 is demonstrated in a Norwegian population, and a mean value above the value of 1.85 as predictor for mental disorder (406). However, the level of 1.85 is not diagnostic of a psychological distress.

Psychosocial risk factors were measured at baseline with the Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ). ÖMPSQ is developed for early identification of yellow flags and patients at risk of developing work disability (measured as sickness absenteeism) due to pain (408, 409). The ÖMPSQ is one of the most widely used screening questionnaires in musculoskeletal research, and its reliability is demonstrated in several studies in both research and clinical settings (409-412). The 25-item ÖMPSQ has satisfactory psychometric properties, and can predict disability, long-term pain, and sick leave for patients with acute or subacute spinal pain (413-416). The short form, 10-item ÖMPSQ (ÖMPQ-10) (120) is based on the 25-item ÖMPSQ, and the correlation between the short and long form has been found acceptable (120). It covers two items from five concept areas: pain (items 1-2), self-perceived function (items 3-4), distress (items 5-6), return to work expectancy (items 7-8) and fear avoidance beliefs (items 9-10). The first item, duration of pain, has ten categories that range from 0 to 1 weeks and up to more than 1 year. The score is from 1-10. Items 2-10 are rated from 0-10 on a scale with extreme anchors (for instance, “no pain” to “pain as bad as could be” or “completely disagree” to “completely agree”), where items 3, 4 and 8 are inversely scored. The 10 item scores are added to a total score of 1 - 100 points. Scores of 1-50 points indicate low risk, and scores of 51 or higher indicate a high risk of future work disability (120).

We evaluated expectation of persistent pain in the future using a single question from the ÖMPQ-10: “In your view, how large is the risk that your current pain may become persistent?”, with a score from 0 (no risk) to 10 (very large risk) (120, 410).

General health was recorded using a single item VAS scale, asking the participant to rate their current general health on a scale from 0 (worst possible health) to 100 (best health imagined) (417, 418).

We measured concomitant musculoskeletal pain by the Nordic Pain Questionnaire (NPQ) (419). The NPQ contains a picture of a body marked with pain sites and names of body areas, ten in total, where patients report their pain distribution for the last seven days. We added the number of pain sites together for a sum score (0 = no other pain sites to 10 = pain in all ten sites), and also used the single item sites for low back pain and headache.

Data collected at 1-year follow-up

We collected data on pain history and symptoms, including pain duration of the current neck pain episode (<1 month) and neck pain history (>5 years). We also collected data on pain intensity measured as current pain on the NRS scale (0-10), functional disability (NDI) on a 0-50 scale, presence of radiating pain to the shoulder or elbow (Yes/No), and number of musculoskeletal pain sites the last seven days (NPQ) (from 0-10). We also collected data on general health status on a VAS 0-100 scale psychosocial risk factors for work disability (ÖMPQ-10) (0-100 scale), psychological state and distress (HSCL-10) (0-4), and expectation of future pain (0-10 scale) (described above).

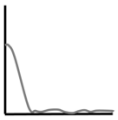
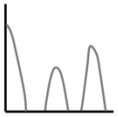
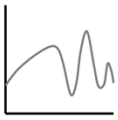
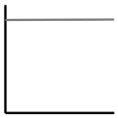
Table 3 Variables collected from questionnaires used in Papers I-III

Variable name	Categories/Scale	Paper I	Paper II	Paper III
Baseline				
Clinician-reported				
Consultation type	First-time | Follow-up | Maintenance care	x	x	x
Patient-reported				
Sociodemographic characteristics, history and symptoms				
Gender	Female/Male	x	x	x
Age	18-84 years	x	x	x
Physical activity	Yes/No			x
Duration of current neck pain episode	<1 month | 1-3 months | ≥ 3 months	x	x	
Previous episodes	First time | 1-2 times | ≥3 times	x		x
Neck pain history	>5 years, Yes/no		x	x
Pain intensity at time of recruitment	Numeric Rating Scale, 0-10 Scale	x	x	x
Functional Disability	Neck Disability Index, 0-50 Sum score	x	x	x[1]
Radiating pain to shoulder and/or elbow	Yes/No	x	x	
General health and MSK Comorbidity				
Low back pain	Yes/No	x	x	
Headache	Yes/No	x	x	
Number of MSK pain sites	Nordic Pain Questionnaire, 0-10 Sum score	x		
General health status	Visual Analogue Scale, 0-100 Scale	x	x	
Psychosocial and Expectations				
Psychosocial distress	Örebro screening questionnaire, 0-100 Sum score	x	x	x[1]
Psychological distress	Hopkins Symptom Checklist-10, 1-4 Sum score	x	x	x[1]
Recovery expectations	Örebro one single question, 0-10 Scale		x	x[1]
52-weeks				
Patient-reported				
Visual trajectory pattern past year	Single episode Episodic pain Mild ongoing pain Fluctuating pain Severe ongoing pain			x
Duration of current neck pain episode	<1 month, Yes/No			x
Neck pain history	>5 years, Yes/No			x
Pain intensity at time of reporting	Numeric Rating Scale, 0-10 Scale			X
Functional Disability	Neck Disability Index, 0-50 Sum score			X
Radiating pain to shoulder and/or elbow	Yes/No			X
General health and MSK Comorbidity				
Number of MSK pain sites	Nordic Pain Questionnaire, 0-10 Sum score			X
General health status	Visual Analogue Scale, 0-100 Scale			X
Psychosocial and Expectations				
Psychosocial risk factors	Örebro screening questionnaire, 0-100 Scale			X
Psychological state and distress	Hopkins Symptom Checklist-10, Scale 1-4			X
Recovery expectations	Örebro single question, 0-10 Scale			X

[1]As part of calculating mean change score from baseline to 1-year only.
MSK, musculoskeletal

We wanted to explore and describe self-reported visual trajectories in terms of prospectively reported clinical course and SMS-based pattern classification of neck pain. For this, patients were asked to choose one of five pictures best representing their past 1-year clinical course of pain: No neck pain or a single episode (hereafter 'single episode'), episodic, mild ongoing, fluctuating, or severe ongoing (Figure 5), with the following question: "Please tick off the description below that you think best represents how your neck pain has been the previous 12 months". This is a novel outcome used in three studies (369, 371, 420). One of these studies showed that the illustrations broadly resembled the most common pain trajectories for low back pain, using the variation patterns, intensity, and terminology suggested by the collaborative group of Kongsted et al (195). Added to the response options in our Visual trajectory pattern questionnaire were 'None of the above illustrated' and 'Do not know'.

Figure 5 Descriptions of the self-reported visual trajectories

	Visual trajectory	Illustration	Description
1)	Single episode		No neck pain or just a single episode of neck pain
2)	Episodic		Few episodes of neck pain separated by pain free periods
3)	Mild ongoing		Mild neck pain most of the time
4)	Fluctuating		Neck pain of varying intensity but never completely pain free
5)	Severe ongoing		Severe neck pain most of the time
6)			None of the above illustrated
			Do not know

2.4.1 SMS-based clinical course patterns and subgroups

Standardized terminology for the course of low back pain have been suggested by the 'Trajectory Overview Group' (195). They described pain variation patterns over time as ongoing, fluctuating, episodic, or single episode. Pain intensity was suggested with four categories: minor pain/recovery, mild pain, moderate pain, and severe pain. Aiming to establish useful definitions for classification into trajectory subgroups without the need for complex statistical analysis, Kongsted et al (328) generated

subgroups that are descriptive combinations of pain variability and pain intensity based on the suggested terminology by the 'Trajectory Overview Group' (195). A third trajectory domain, change patterns, was also described, which included rapidly or gradually improving pain and progressing pain. However, Kongsted et al initially wanted to assess the definitions on a period that is considered to be relatively stable (328). They therefore excluded the first 9 weeks of SMS measurement. The definitions were easy to apply to patients' observed data on low back pain and had a good match with trajectory patterns derived through latent class analysis (328). Below is a description of how the definitions used in Paper I were built up.

The variation patterns were divided into four patterns: ongoing, fluctuating, episodic, and single episode. Ongoing pain was defined as pain not deviating more than ±1 from the mean pain intensity value each week. In addition, patients should report more than 4 days with pain each week. For the fluctuating variation pattern, patients should have no pain-free period lasting four weeks or longer. Also, patients needed at least one deviation of pain that was larger than ±1 from the mean pain intensity value. They used the definition of an episode from de Vet et al (250), where an episode of low back pain is defined as a period of pain lasting 24hrs or longer, with a minimum of four weeks without pain immediately before and after the painful period. This definition has since been supported in a modified Delphi approach (263), and tested on a low back pain cohort (253). No restrictions were set for the number or duration of episodes. The single episode variation pattern was defined as having only one single episode of pain lasting 1-2 weeks during the study period. The single episode could not be at the beginning or the end of the study period, as the duration of an episode prior to the start of a study or after the end of a study is uncertain. Each variation pattern was then split into four pain intensity categories:

Pain intensity category	*Mean scores 0-10 on NRS*
Severe	6-10
Moderate	4-5
Mild	2-3
Minor/Recovery	0-1

These pain intensity categories are in line with previously suggested cutoff values for pain (175, 213, 215).

Ongoing and Fluctuating patterns were split into subgroups based on the **mean** intensity, while Episodic and Single episode patterns were based on the **maximum** intensity. Patients rating pain intensity to zero each week were defined by the researchers as "Recovery" and were classified as "Minor ongoing" subgroup. This left 16 subgroup possibilities for classification (Figure 6).

Figure 6 Operational definitions used for the defined trajectories in the study by Kongsted et al (328)

Table 2 Operational definitions used for the previously defined trajectory subgroups

Subgroup label	Intensity	Variation
Severe ongoing pain	Mean intensity > = 6	Intensity stays within +/− 1 of mean value >4 days with LBP per week
Moderate ongoing pain	Mean intensity > = 4 and <6	Intensity stays within +/− 1 of mean value >4 days with LBP per week
Mild ongoing pain	Mean intensity > = 2 and <4	Intensity stays within +/− 1 of mean value >4 days with LBP per week
Minor ongoing pain/ recovery	Mean intensity <2	Stays within +/− 1 of mean value AND - no pain-free 4-weeks periods *or* - always pain = 0
Severe fluctuating pain	Mean intensity > = 6	Difference between mean and minimum or maximum value exceeds 1 No pain-free 4-weeks periods
Moderate fluctuating pain	Mean intensity > = 4 and <6	Difference between mean and minimum or maximum value exceeds 1 No pain-free 4-weeks periods
Mild fluctuating pain	Mean intensity > = 2 and <4	Difference between mean and minimum or maximum value exceeds 1 No pain-free 4-weeks periods
Minor fluctuating pain	Mean intensity <2	Difference between mean and minimum or maximum value exceeds 1 No pain-free 4-weeks periods
Severe episodic pain	Max intensity > = 6	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.
Moderate episodic pain	Max intensity > = 4 and <6	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.
Mild episodic pain	Max intensity > = 2 and <4	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.
Minor episodic pain	Max intensity <2	Pain-free periods of min. 4 weeks in a row, but not always pain = 0. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.
Severe single episode	Max intensity > = 6	One episode lasting 1–2 weeks (which are not the first or the last week of measurement)
Moderate single episode	Max intensity > = 4 and <6	One episode lasting 1–2 weeks (which are not the first or the last week of measurement)
Mild single episode	Max intensity > = 2 and <4	One episode lasting 1–2 weeks (which are not the first or the last week of measurement)
Minor single episode	Max intensity <2	One episode lasting 1–2 weeks (which are not the first or the last week of measurement)

2.5 Outcome measures

2.5.1 Neck pain intensity

We based our patterns and subgroups on weekly measures of typical pain intensity during the last week (0-10). This outcome included 52 separate measures.

2.5.2 Defined patterns and subgroups

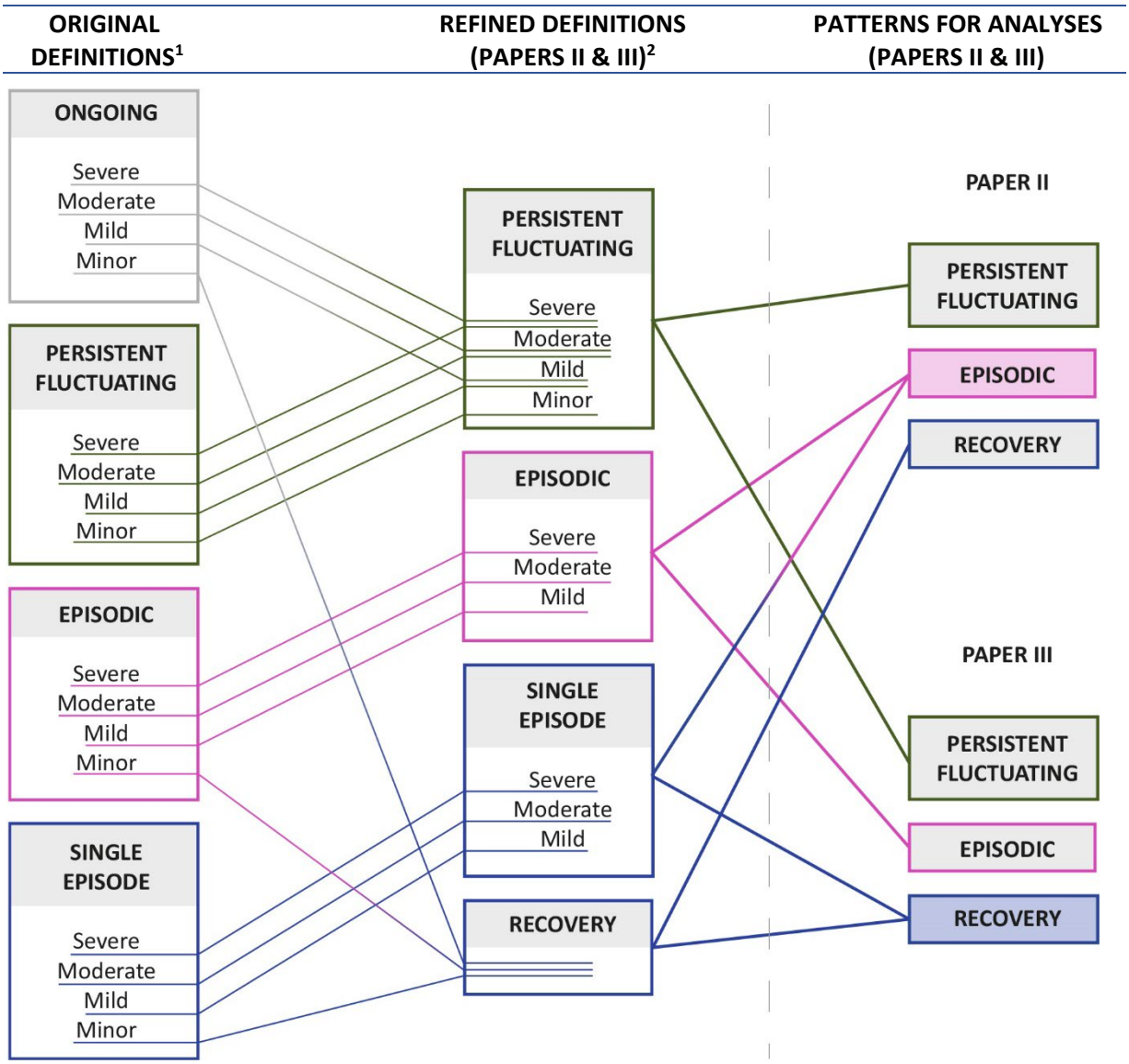
The classification into patterns and subgroups as described above was used as a composite outcome measure for this thesis. We used these definitions, either in their original form by Kongsted et al (328) or as a modified version, in the three articles as described below.

As a first step in exploring the clinical course of neck pain, we investigated if SMS-based patterns and subgroups from low back pain trajectory studies could be applied to neck pain patients. We therefore replicated all data handling and descriptive definitions of patterns and subgroups as done in the study by Kongsted et al as described above (328). The coding used in our study was in explicit accordance with their procedures. We followed their protocol for SMS-Track® procedure regarding both the wording of the SMS questions (see section 2.3, p.39) and time-schedule for the SMS' and follow-up for missing responses. Furthermore, we also excluded the first 9 weeks of study to be able to compare the results. We modified the nomenclature of the fluctuating variation pattern from the original study to 'persistent fluctuating' to improve the understanding between the persistent fluctuating and episodic patterns. This left us with a study period of 43 weeks and 16 subgroups.

Modification of definitions

To explore the stability of the SMS-based patterns and subgroups over time, we needed to reduce the number of subgroups. In Paper I, we found that all patients classified as Minor ongoing were, in fact, completely pain free. Also, only two patients were classified in one of the other 3 ongoing subgroups (mild, moderate, and severe), and very few patients were classified as single episode. Additionally, patients in the Minor ongoing, episodic, and single episode subgroups shared similar demographic, functional, and psychological characteristics, and patients were only negligibly affected by their pain. Moreover, patients' pain intensity in these Minor subgroups was rarely reported above what is considered clinically significant (<2 on NRS) (421, 422). The low back pain study by Kongsted et al had similar findings (328), suggesting that persistent pain is rarely completely steady concerning pain intensity, and that fluctuating pain scored below 2 on numeric rating scale can be considered a state of recovery. Based on this, we combined the ongoing and persistent fluctuating patterns into one pattern called 'persistent fluctuating', defined as a clinical course of pain without a pain-free period lasting four weeks or longer. We combined the subgroups of Minor ongoing, episodic, and single episode to a new pattern called recovery and included patients with a **maximum** pain intensity <2. In Paper I, we also found that patients in the Minor persistent fluctuating subgroup differed significantly from the patients in the Minor subgroups of the other three patterns in terms of higher pain intensity and frequency, functional disability, and psychological distress, and we therefore kept it as a separate subgroup. This left us with 4 patterns: persistent fluctuating, episodic, single episode, and recovery, divided into 11 subgroups: severe, moderate, mild, and minor for persistent fluctuating pattern; severe, moderate, and mild for episodic and single episode patterns; and recovery. Figure 7 below illustrates the modification of the definitions from Paper I to Paper II, as well as the pattern combinations used for analyses in Paper II and Paper III.

Figure 7 Original and refined definitions of the SMS-based subgroups and patterns used in Papers I-III



[1]Defintions by Kongsted et al (328); [2]Refined definitions after findings in Paper I (423)

Assessing the stability of trajectories

Research have identified common trajectories for musculoskeletal pain (68, 148, 195), and suggestions that low back pain trajectories appear to be stable over time (305). However, frequent data collection over one year has yielded more diverse and detailed pain trajectories, indicating that patients differ regarding fluctuating and episodic patterns and degrees of pain (279). We hypothesized prior to our data collection that frequent measures would show an improvement in pain symptoms in the initial phase after recruitment. This improvement was expected in the total cohort, regardless of consultation type. Moreover, we expected a steeper improvement for first consultation patients compared to patients presenting for maintenance care. We also hypothesized that patients with fluctuating pain could experience periods of exacerbations or improvement of different durations, and that patients with episodic pain could experience episodes of pain that varied in both duration and time of

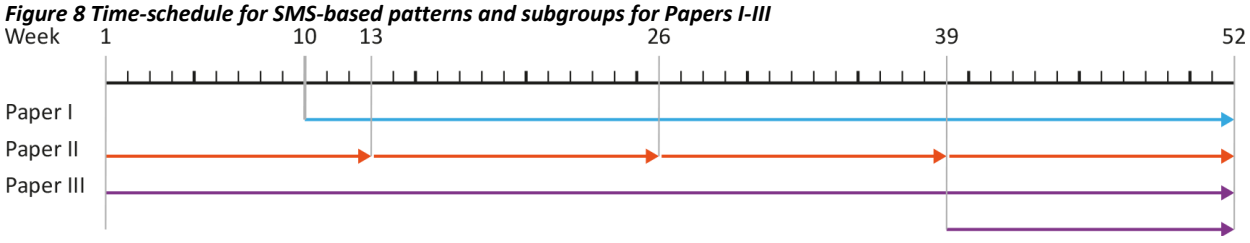
occurrence. Thus, we wanted to explore how the definitions fit when data were collected over shorter periods. Previous neck pain studies have shown that an initial episode can last anything from three to 20 weeks (68, 194, 233). We therefore settled on a period of 13 weeks, leaving four quarters for the assessment of stability from one quarter to the next over one year (hereafter '1st quarter', '2nd quarter', etc.).

Our next aim was to explore the stability of the trajectories. We had already reduced the number of subgroups to 11, but this number still gave too many possibilities for shifts. Results from Paper I showed that the low number of patients in the single episode pattern hampered the comparison with other patterns. In addition, patients classified as Severe, Moderate and Mild episodic where slightly more bothered than patients in the Minor ongoing, episodic, and single episode subgroups. Since having one single episode of pain within one quarter is probably different from having no pain, we decided to combine the single episode pattern with the episodic pattern. This left us with three variation patterns for the analysis of stability: persistent, episodic, and recovery. Nevertheless, we still had 81 possible shifts of trajectories over four quarters. From the Sankey diagrams used to assess the stability we found that the shifts were similar between the last three quarters. We therefore defined patients classified with a different pattern or a similar pattern in the 1st and 4th quarter as having a shifting or a stable trajectory pattern, respectively. This left us with three possible patterns for analyses:

Trajectory pattern	*Shift 1st to 4th quarter*
Stable	• Persistent to Persistent • Episodic to Episodic • Recovery to Recovery
Shifting - improved	• Persistent to Episodic • Persistent to Recovery • Episodic to Recovery
Shifting - worse	• Recovery to Persistent • Recovery to Episodic • Episodic to Persistent

Below is an illustration of which weekly SMS-based follow-up periods are used in the three different papers (Figure 8).

Figure 8 Time-schedule for SMS-based patterns and subgroups for Papers I-III



Exploring the clinical course of the visual trajectories

In Paper III, the aim was to explore and describe the five self-reported visual trajectories from the Visual trajectory pattern questionnaire in terms of prospectively reported clinical course and SMS-based pattern classifications of neck pain. In order to best explore the five visual trajectories and their classified defined pattern, we needed two adjustments on the SMS-based patterns. As the visual trajectories represented the patient's recollection of their previous 1-year course of pain, we combined the SMS-based single episode pattern with the Recovery pattern, called "Single episode/Recovery". There were two reasons for this. First, as the SMS classification period was 52 weeks, and not 13 weeks (as used in Paper II), one single episode of 1-2 weeks within a full year could be considered as a state of recovery. Second, the single episode visual trajectory illustrates a short, single episode of pain, with the descriptive text of "No neck pain or just a single episode of neck pain". As this was very similar to the combination of the two defined patterns, single episode and recovery, we combined the two patterns for parts of Paper III.

We classified the participants into patterns and subgroups for the complete follow-up year. To explore the possible role of recall bias on the selection of 1-year retrospective visual trajectory, we also classified the participants into patterns and subgroups for the 4th Quarter.

2.6 Statistical analysis

All data were analyzed using STATA/SE 15 and 16 (STATA Corp, College Stations, TX, USA).

Sample size

This study aimed to explore and identify the clinical course of neck pain. Previous low back pain and neck pain studies show that trajectory groups are not equal in size ((68, 194, 195), and the smallest group could contain less than 1% of the patients. We wanted to describe subgroups with minimum 10 patients to be able to make comparisons between the subgroups. With a dropout of 20%, we aimed for 1000 patients. Additionally, this study was part of a larger project that also investigated prognostic factors related to neck pain and planned to use 11 possible variables. Using the "rule of thumb" for prognostic models with 10 events per candidate variable is required (=1100 patients) (424) and possible 20% drop-out, we determined a sample size of 1320 patients to be sufficient for the prognostic part of this study.

Descriptive data

We reported descriptive data as means and standard deviations (SD) for normally distributed data, medians and interquartile ranges (IQR) for non-normally distributed data, and count and frequency for categorical data. Normal distribution for each measure was visualized using histograms, density plots

and QQ-plots, as well as visual inspection for skewness and data shape and tested with the Shapiro-Wilks test. Pain intensity used in Paper I and all variables used in Paper III were not normally distributed, while the rest of the variables presented were.

A p-value was set at 5% for Papers I and II.

Missing data and imputation

We handled missing values on the weekly pain intensity data as follows: Patients who responded 0 to the first SMS regarding number of days with neck pain, did not receive the SMS regarding pain intensity the past week. For these patients, the pain intensity was then automatically recorded as missing, for this week, by the SMS-Track® system. We later recoded these missing score as zero on pain intensity. In addition, answers other than numbers were replaced with the correct number; for example, the response “four days” was recoded as “4”. All other responses were recorded as missing.

Further, missing values on the weekly pain intensity measures were imputed in three stages, illustrated with examples in Figure 9:

A. We replaced missing responses in the first week of the study period by the equivalent values in the following week if these were not missing. Similarly, missing responses in the last week of the study period were replaced by the values reported in the week prior to the last week of the study period.
B. We replaced one-week and two-week missing gaps between weeks with the same pain intensity, with that same value.
C. We categorized as missing and subsequently excluded from the analysis patients who after steps 1 and 2 had:
    - Paper I: Less than 20 complete responses out of 43
    - Paper II: Less than 6 completed responses out of 13 for each quarter
    - Paper III: Less than 26 complete responses out of 52

Figure 9 Illustration of how imputation was performed when SMS responses were missing

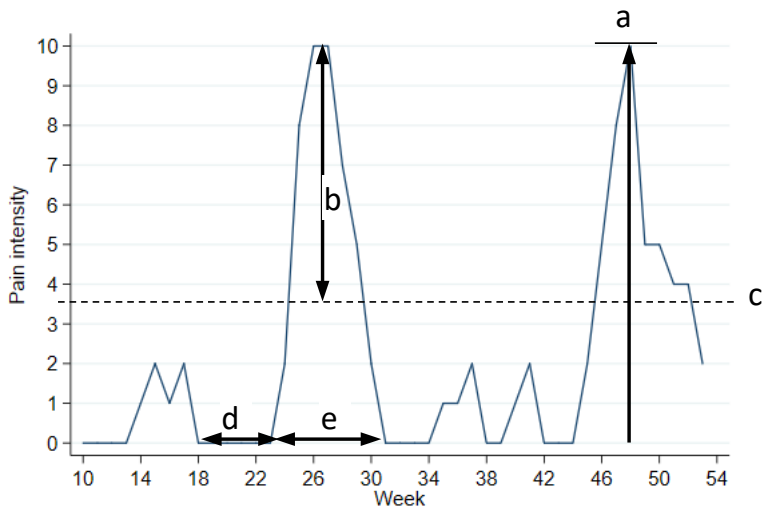
Imputation method		Week 1	2	3	4	5	6	7	8	9
A.	Original	.	3	4	.	4	4	1	1	.
	Imputated	3	3	4	.	4	4	1	1	1
B.	Original	.	3	4	.	4	4	1	1	.
	Imputated	.	3	4	4	4	4	1	1	.
After imputation		3	3	4	4	4	4	1	1	1
Study		Start								End

A and B: For imputation method, see descriptions above; numbers indicate responses on a 0-10 NRS, for a hypothetical duration of 9 weeks

Necessary data handling for clinical course details and subgrouping

To be able to develop the clinical course for the patients, we needed to calculate the weekly mean pain intensity (c) and the number of days with pain for the 52 weeks, identify maximum (a) and minimum pain intensity, number of days with and without pain, duration of pain free periods, and identify number of pain-free weeks in a row of four weeks or more (d). In addition, we calculated the size of fluctuations from the weekly mean pain intensity (b), the duration and frequency of pain-free and painful (e) weeks, the proportion of the weeks that were pain-free and in the four pain intensity categories (minor, mild, moderate and severe), and lastly, the standard deviation (SD) of the mean of the participant's weekly pain intensity (hereafter 'intensity variation'). Figure 10 illustrates an individual trajectory, with examples of the different clinical course calculations described above.

Figure 10 Visual illustration of an individual pain trajectory demonstrating the different definition criteria



a: max pain intensity; b: fluctuation size; c: mean pain intensity level; d: pain-free duration ≥4 weeks; e: painful episode duration

Comparing patterns, subgroups, and visual trajectories

The distribution into subgroups, patterns and visual trajectories were presented and compared using frequency tables and stacked bar graphs. We present the stability of the patterns visually using Sankey diagrams, flow diagrams where the width of the arrows is proportional to the flow rate. It allows us to show complex processes visually, giving emphasis on the size and direction of flows within a system. Sankey diagrams are especially useful to track dynamic changes and interpret trends over more than one interval, where the traditional use of multiple cross-tabulation matrices is more inefficient. In this study, the Sankey diagrams show the flow of patients from one pattern in one quarter, to the same or a different pattern in the next quarter. The columns represent the proportion of patients in the respective patterns in each quarter. The width of an arrow is equal to the frequency of patients shifting from one into another pattern. Shifts between subgroups and the four quarters were presented as frequency tables and assessed visually. To describe the distribution of patients in the SMS-based patterns and subgroups we used multiple cross-tabulation matrices, as using Sankey diagrams cannot accommodate all the possible shifting patterns using 11 subgroups over four quarters.

Differences in baseline categorical data between subgroups or patterns were analyzed using the chi-square test, or Fisher's exact test when appropriate.

Paper I

For categorical data, we used Dunn's post-hoc pairwise comparison test (425) and Bonferroni-Holm correction (426) for comparisons between patterns. For the comparison of continuous baseline data between subgroups of the same intensity level in the Persistent fluctuating and Episodic patterns (such as Moderate Persistent fluctuating vs Moderate Episodic), we used the Student's paired *t*-test. In addition, the one-way analysis of variance (ANOVA) with Bonferroni post-hoc pairwise comparison test was used for evaluation of continuous baseline data between the four patterns.

Robustness

We also assessed the robustness of the definitions used for subgrouping. We included patients regardless of the time in their treatment plan (first consultation, follow-up, or maintenance care), meaning there was no restriction of when treatment first started. This was a deliberate choice, as we aimed for a cohort that represented all possible clinical courses of neck pain in chiropractic practice. To assess if this broad inclusion criteria would result in a subgroup distribution that differed between patients without treatment and those that already had received treatment for their neck pain, we compared the distribution of patients recruited at first-time consultation to the whole cohort. Furthermore, we also explored the influence of inclusion criteria for the subgroup analyses by changing the criteria from a minimum of 20 SMS responses to a minimum of 10 in the 43-week follow-up. Thirdly, we reduced the Episodic definition of 4-weeks to 2-weeks pain-free period and repeated the Student's

paired *t*-test comparing the characteristics of patients in the Persistent fluctuating and Episodic subgroups. A priori, the definitions were considered robust if the distribution or characteristics as described above did not change significantly. Lastly, we explored the weekly number of days with neck pain and the neck pain intensity in each week following a pain-free period lasting one week or longer. More intense pain in the first weeks after a 4-week or longer pain-free period compared to shorter pain-free periods, could indicate a definite break for a new episode of pain. This in turn could lend empirical support to the threshold of four pain-free weeks to mark the separation between episodes (250, 263).

Paper II

We used one-way analysis of variance (ANOVA) to compare the differences in functional status (NDI), emotional stress (HSCL-10), psychological risk factors (Örebro screening questionnaire), and pain intensity between patients in stable and shifting trajectory patterns. For all analyses of shifts we performed pairwise comparisons with Bonferroni corrections. As a sensitivity analysis, the same analyses were performed with the definition of shift changed from 1st to 4th quarter to 3rd to 4th quarter.

Paper III

To improve the understanding of visual trajectories, we aimed to explore and describe the self-reported visual trajectories, both in terms of the patients' clinical course from their weekly SMS measurements and their SMS-based classified pattern and subgroup. There are uncertainties regarding minimal important change (MIC) and how it is measured (427), and there are few instruments that have been tested for cutoff values for change or improvement. We therefore decided to measure patients' change in functional disability (NDI), psychological distress (HSCL-10), psychological risk factors (ÖMPQ-10), and recovery expectations by subtracting the 1-year scores from the baseline scores for each patient. Patients with a change score equal to or higher than the 80th percentile score for the cohort, were defined as having a positive change.

2.7 Ethical aspects

The study protocol was approved by the Regional Ethics Committee in the southeast Norway (March 2015, (2015/89)).

The three studies in this thesis were conducted in accordance with the Helsinki Declaration (428). Possible negative effects of frequent measures of pain intensity over time has previously been assessed and found not to affect pain intensity or pain control (429). More recent studies have supported this (430, 431). Also, frequent SMS-tracking is an accepted method in both time-series studies and treatment monitoring. Hence, the weekly measures over 1 year were not considered to cause any harm to participants.

Participating chiropractors were given written and verbal information regarding the study, as well as their role as recruiter. All patients were informed verbally of the study by the recruiting chiropractor and subsequently by member of the research team. Patients were also given extensive written information about the project. This included clear instructions that participation was voluntary, they had the right to withdraw from the study at any time, and that participation or a subsequent withdrawal did not influence decisions surrounding their care. The latter was fully left to the discretion of their treating chiropractor or their own decision. Patients gave their written consent before inclusion.

A proper safeguard and handling of the thesis data was prepared in the line of research ethics. All sensitive data was stored and analyzed in "Services for sensitive data" (Tjenester for Sensitive Data, TSD), a secure environment provided by the University Center for Information Technology at the University of Oslo, in compliance with the Norwegian Personal Data Act (Personopplysningsloven) and the Norwegian Health Research Act (Helseforskningsloven). The digital questionnaire (Nettskjema) used to collect data for this thesis is an integrated solution provided by TSD for the collection of sensitive data. The SMS-Track® used to collect the weekly SMS data stored the incoming data in a server at their location. Data can only be accessed through a unique login, and transfer of data from the server is encrypted.

3 Results

The total study sample included 1469 patients. They had an average age of 44 (SD 13) years, and 962 (74%) were women. Most patients reported pain duration at baseline of one month or longer (n=990, 78%), and 256 (18%) were recruited at their first consultation with the chiropractor. The average pain intensity at baseline was 4.2 (2.3), and the average functional disability was 12 (7) on NDI. Table 4 gives an overview of the characteristics of the total study sample, as well as the cohorts used in Papers I-III and the excluded cohort for Paper III.

Table 4 Characteristics and clinical findings of the thesis cohort, patients included in Papers I-III and patients excluded from analyses for Paper III

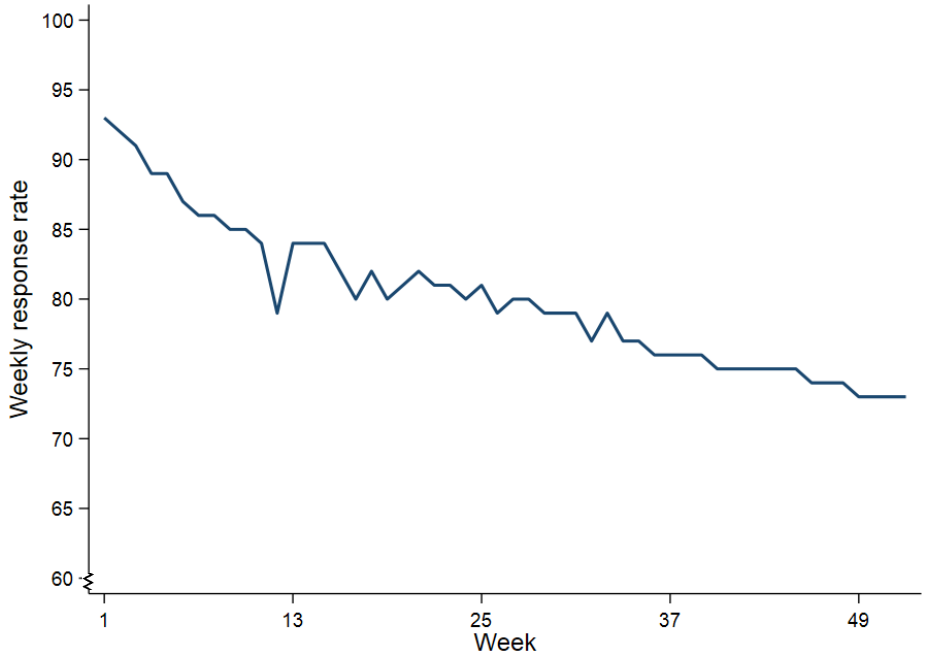
Variable name	Thesis cohort	Paper I[1]	Paper II[1]	Paper III[1]	Excluded cohort[2]
Baseline	n=1469	n=1206	n=1124	n=888	n=418
Clinician-reported					
Consultation type, (%)					
First consultation	256 (18)	186 (17)	179 (16)	135 (16)	101 (18)
Follow-up consultation	436 (31)	340 (29)	321 (29)	256 (30)	179 (30)
Maintenance care plan	727 (51)	630 (54)	592 (54)	473 (55)	290 (52)
Patient-reported					
Sociodemographic characteristics, history and symptoms					
Gender female, (%)	962 (74)	847 (74)	792 (74)	655 (74)	307 (73)
Age, Mean (SD) [range 18-85]	44 (13)	44 (13)	45 (14)	45 (14)	43 (13)
Physical activity, ≥2 times weekly, (%)	901 (69)	859 (76)	735 (68)	613 (69)	288 (69)
Duration of current neck pain episode, (%)					
<1 month	298 (23)	263 (23)	242 (23)	197 (22)	101 (25)
1-3 months	189 (15)	161 (14)	168 (14)	135 (15)	54 (13)
>3 months	801 (62)	710 (63)	660 (63)	553 (62)	248 (62)
Number of previous episodes, (%)					
0	186 (14)	161 (14)	150 (14)	118 (13)	62 (14)
1-2	220 (17)	197 (17)	184 (17)	148 (17)	72 (17)
≥3	897 (69)	791 (69)	740 (69)	620 (70)	281 (69)
Neck pain history ≥5 years, (%)	720 (67)	676 (68)	597 (68)	534 (69)	229 (67)
Pain intensity[3], (NRS 0-10) Mean (SD)	4.2 (2.3)	4.1 (2.3)	4.0 (2.2)	4.1 (2.3)	4.3 (2.4)
Function Disability, NDI (0-50) Mean (SD)	12 (7)	12 (7)	12 (7)	12 (7)	12 (7)
Radiating pain to shoulder and/or elbow, (%)	980 (76)	859 (76)	804 (76)	671 (76)	309 (77)
General health and MSK Comorbidity					
Low back pain, n (%)	687 (54)	602 (53)	566 (54)	470 (53)	217 (54)
Headache, n (%)	932 (73)	810 (72)	762 (72)	638 (72)	294 (73)
Number of MSK pain sites, NPQ 0-10 Mean (SD)	4.1 (2.5)	4.4 (2.3)	4.4 (2.3)	4.7 (2.1)	4.3 (2.4)
General health status, VAS 0-100 Mean (SD)	71 (20)	71 (19)	71 (19)	71 (19)	70 (20)
Psychosocial and Expectations					
Psychosocial screening, ÖMPQ (0-100) Mean (SD)	35 (19)	39 (16)	38 (17)	40 (15)	37 (19)
Psychological distress, HSCL-10 (1-4) Mean (SD)	1.6 (0.5)	1.6 (0.5)	1.7 (0.5)	1.6 (0.5)	1.6 (0.5)
Recovery expectations[4], (1-4) Mean (SD)	5.8 (3.1)	5.8 (3.1)	5.8 (3.1)	5.8 (3.1)	5.9 (3.3)
52-weeks					
Patient-reported					
Visual trajectory pattern past year, (%)					
Single episode	141 (15)			121 (14)	12 (16)
Episodic	342 (36)			331 (37)	20 (27)
Mild ongoing	91 (9)			81 (9)	9 (12)
Fluctuating	345 (36)			315 (36)	27 (36)
Severe ongoing	17 (2)			14 (2)	3 (4)
Neither/Unsure	27 (3)			22 (2)	4 (5)

[1]Patients responding to baseline questionnaire;[2]Patients with baseline questionnaire data excluded for Paper III;[3]At time of measurement; [4]Recovery expectations from Item 7 of the Örebro Musculoskeletal Pain Questionnaire.

SD, Standard Deviation; NP, Neck pain; NRS, Numeric rating scale; NDI, Neck Disability Index; ÖMPQ-10, Örebro Musculoskeletal Pain Questionnaire short form; HSCL-10, Hopkins Symptom Checklist-10.

The weekly response rate for the total study sample is shown in Figure 11 (1-year weekly response rate of total study sample). A total of 68 (%) responded to all 52 SMS in the 1-year follow-up.

Figure 11 1-year weekly response rate (%) of the total study sample (n=1469)



All patients included for analyses in Papers I-III could be classified into a subgroup, apart from Paper I, where two patients did not fit any subgroup definition. These two patients never reported pain that deviated more than ±1 of their mean pain intensity, and therefore did not qualify as having a persistent fluctuating pattern. However, they reported some weeks with less than 4 days (out of 7) of pain and could therefore not be classified as having an ongoing pattern. The distribution into patterns and subgroups for the five study periods in Papers I-III is shown in Table 5 below.

Table 5 Distribution into patterns and subgroups in Papers I-III

	Thesis	Paper I	Paper II				Paper III
Study period	**1 year follow-up n=1213**	Weeks 10-52	1st quarter	2nd quarter	3rd quarter	4th quarter	Weeks 1-52
Classified pattern		n=1206	n=1340	n=1244	n=1194	n=1135	n=888
Ongoing		***51 (4)***					
Severe	-	1 (<1)	-	-	-	-	-
Moderate	-	1 (<1)	-	-	-	-	-
Mild	-	0 (0)	-	-	-	-	-
Minor	-	49 (4)	-	-	-	-	-
Persistent fluctuating	**585 (48)**	***582 (48)***	***999 (75)***	***808 (65)***	***758 (63)***	***713 (63)***	***436 (49)***
Severe	53 (4)	54 (5)	76 (6)	56 (5)	65 (5)	74 (7)	39 (4)
Moderate	200 (16)	185 (15)	292 (22)	213 (17)	197 (17)	186 (16)	147 (17)
Mild	301 (25)	298 (25)	492 (37)	394 (32)	357 (30)	322 (28)	223 (25)
Minor	31 (3)	45 (4)	139 (10)	145 (12)	139 (12)	131 (12)	27 (3)
Episodic	**586 (48)**	***547 (45)***	***274 (21)***	***238 (19)***	***213 (18)***	***194 (17)***	***426 (48)***
Severe	359 (27)	276 (23)	93 (7)	68 (6)	59 (5)	49 (4)	264 (30)
Moderate	163 (13)	174 (14)	97 (7)	79 (6)	74 (6)	82 (7)	119 (13)
Mild	64 (5)	88 (7)	88 (7)	91 (7)	80 (7)	63 (6)	43 (5)
Minor	-	9 (1)	-	-	-	-	-
Single episode	**16 (1)**	***26 (2)***	***14 (1)***	***41 (4)***	***67 (6)***	***60 (5)***	***15 (2)***
Severe	3 (<1)	5 (<1)	3 (<1)	8 (1)	7 (1)	14 (1)	2 (<1)
Moderate	2 (<1)	11 (1)	5 (<1)	16 (1)	21 (2)	15 (1)	0 (0)
Mild	11 (1)	7 (1)	6 (1)	28 (2)	39 (3)	31 (3)	9 (1)
Minor	-	3 (<1)	-	-	-	-	-
Recovery	**26 (2)**	-	***49 (4)***	***146 (12)***	***156 (13)***	***168 (15)***	***15 (2)***

Summary of results

The results are described in detail in paper I, II, an III. Below is a (short) summary of the main results.

When classifying patients into SMS-based patterns and subgroups in the last 43 weeks of the 1-year follow-up, the majority of patients were classified as Persistent fluctuating (48%) or Episodic (45%). The most common subgroups were Mild persistent fluctuating (including 25% of the participants), with mean pain intensity of 3.4 (SD 0.6) and mean of 130 (SD 66) days with pain in total, and Severe episodic (including 23% of the participants), with mean pain intensity of 3.9 (SD 1.0) and mean of 58 (SD 50) days with pain in total. The 4% classified as Minor ongoing all reported no pain (NRS=0) on each SMS response in the 43-week study period. Patients classified as Persistent fluctuating had smaller, but more frequent, fluctuations than patients classified as Episodic.

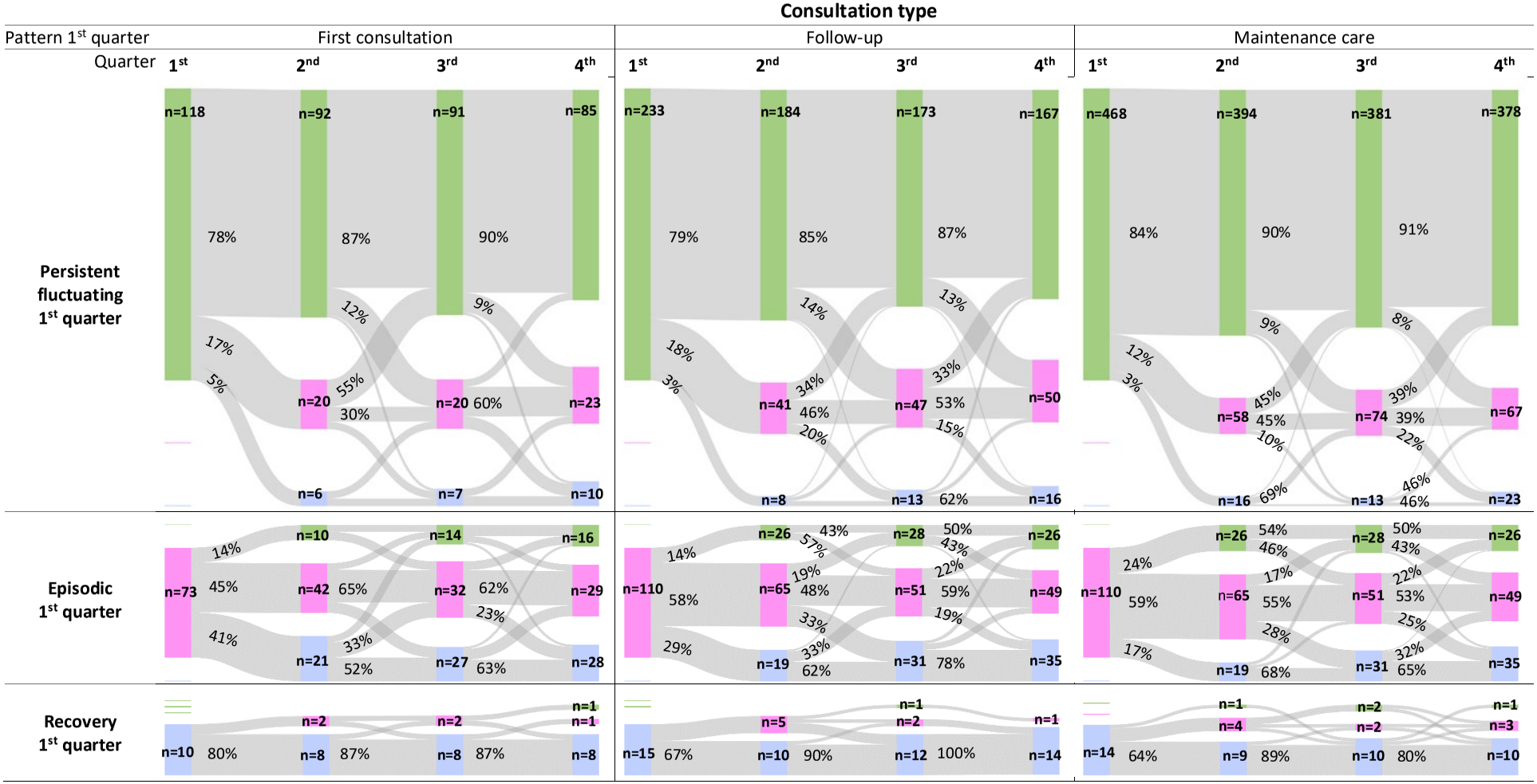
There was an overall decrease in patients' functional disability and psychological distress from the Severe through to the Minor subgroups within the Persistent fluctuating and Episodic patterns. In addition, patients classified as Persistent fluctuating scored significantly lower on general health (VAS 66/100), higher on all clinical factors including pain intensity (median 5, IQR 3-6), and had more previous pain episodes and concomitant low back pain and headache than patients in any of the three other patterns ($p \geq 0.006$). There were no gender differences between patients classified as Episodic and

Persistent fluctuating, nor any differences in the proportion of patients with pain duration >1 month prior to recruitment and recruited at first consultation.

A slightly lower percentage of patients recruited at their first consultation were classified as persistent fluctuating (41%) compared to the whole cohort (48%). Fourteen percent of patients classified as Persistent fluctuating would have been classified as Episodic if the criteria for Episodic pattern had been changed from 4-week to 2-week pain-free period. We found only small differences in pain intensity and number of days with pain in the first week following an increasing pain-free period. In addition, 42 more patients could have been included in the analyses if the inclusion criteria had been reduced from ≥20 to ≥10 SMS responses, however this resulted in only minimal changes in distribution.

Close to 80% (n=1124) of the total study sample were classified in an SMS-based pattern in all four quarters. The frequency of patients with Persistent fluctuating pattern reduced gradually from 75% to 65% from first through to fourth quarter. The frequency of the Episodic and Single episode patterns remained stable with approximately 20% and 5% of the patients, respectively, while the Recovery pattern increased from 4% to 11% from first to second quarter and up to 15% in the last quarter. Close to 70% of patients were in a stable trajectory, where eighty-two percent (648) were in a stable persistent fluctuating pattern, and 13% (104) and 4% (33) were in stable episodic and recovery patterns, respectively. However, most patients shifted between subgroups (intensity levels) within their respective patterns. The most common shifts were from the Minor Persistent fluctuating subgroup to the Severe or Moderate Episodic subgroups. After the first quarter, most of the patients in Persistent fluctuating and Recovery patterns remained in their pattern from one quarter to the next (82-90% for Persistent and 68-90% for Recovery). More shifts occurred in the patients with an Episodic pattern in the first quarter, where only half of the patients remained stable in an Episodic pattern from one quarter to the next, but no further trends were found. Similar shifting trends were found when patients were separated based on consultation type (first consultation, follow-up, and maintenance care). There were only minimal differences in shifts and stable distributions between patients in the three consultation types (Figure 12).

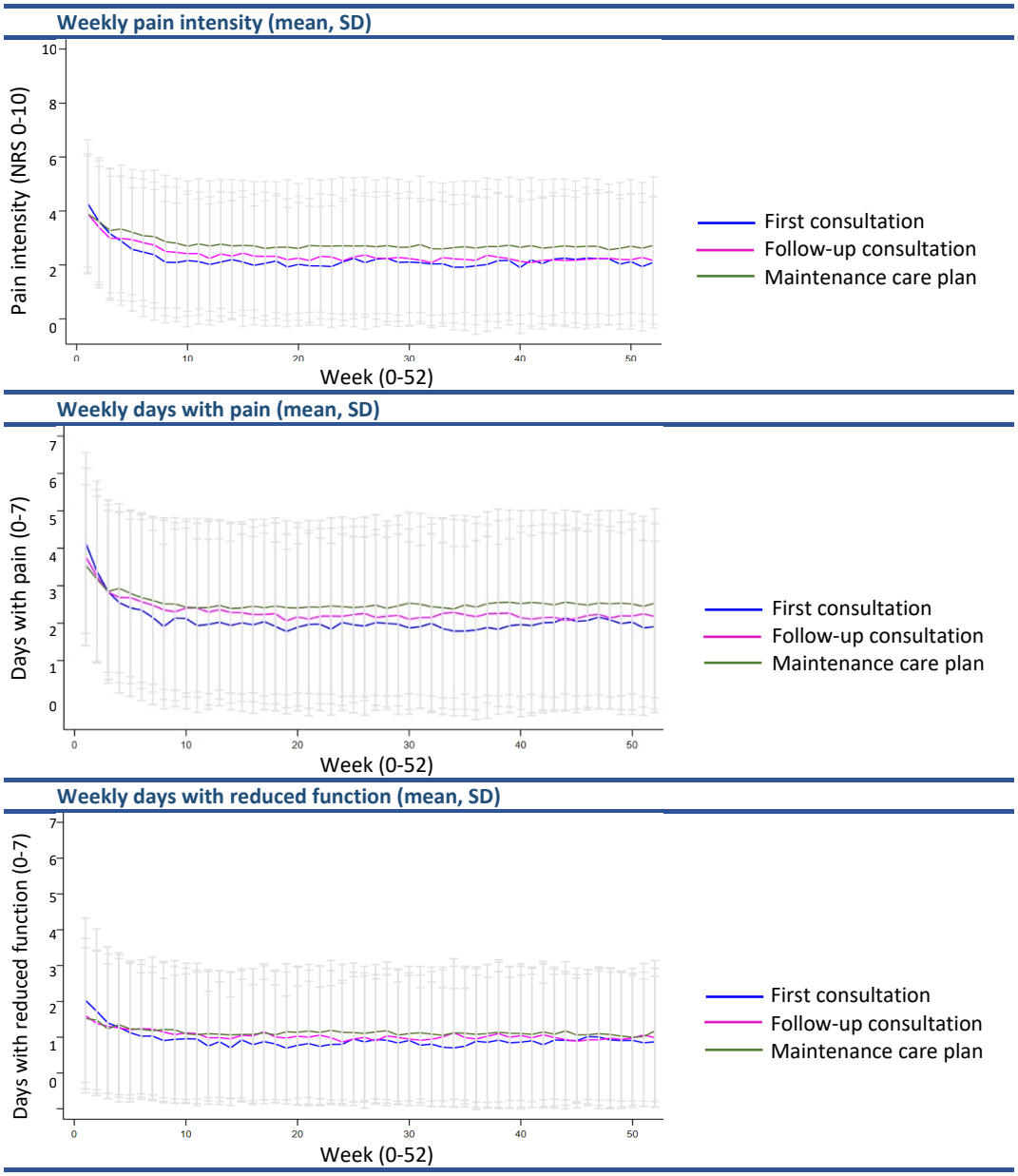
Figure 12 Sankey diagram illustrating the proportion shifting from 1st through to 4th quarter, in persistent fluctuating, episodic (episodic and single episode) and recovery patterns in the three consultation types: First consultation, Follow-up, and Maintenance care.



The height of the columns reflects the number of patients in each quarter. The percentage reflects the proportion of patients from one quarter to the next. For instance, 41% of patients classified as episodic in 1st quarter shifted to recovery pattern in 2nd quarter, and among these 33% shifted back to episodic and 52% remained in recovery pattern 3rd quarter. ***Shift with n<8 is not presented with percentage for flow***

Patients with a stable persistent fluctuating pattern had a neck pain history of longer duration and scored worse on baseline variables than patients with a shifting persistent fluctuating pattern. For the other shifting and stable patterns, only minimal differences in clinical and health related factors were identified. There were only negligible differences in the weekly mean pain intensity, weekly days with pain, and weekly days with daily activities affected due to neck pain between the three consultation types for the 1-year follow-up (Figure 13). Patients in all three consultation types had an initial decrease in pain intensity and days with pain and activity limitation in the first 2-4 weeks of follow-up.

Figure 13 -Weekly mean pain intensity, days with pain, and days with reduced function by consultation type

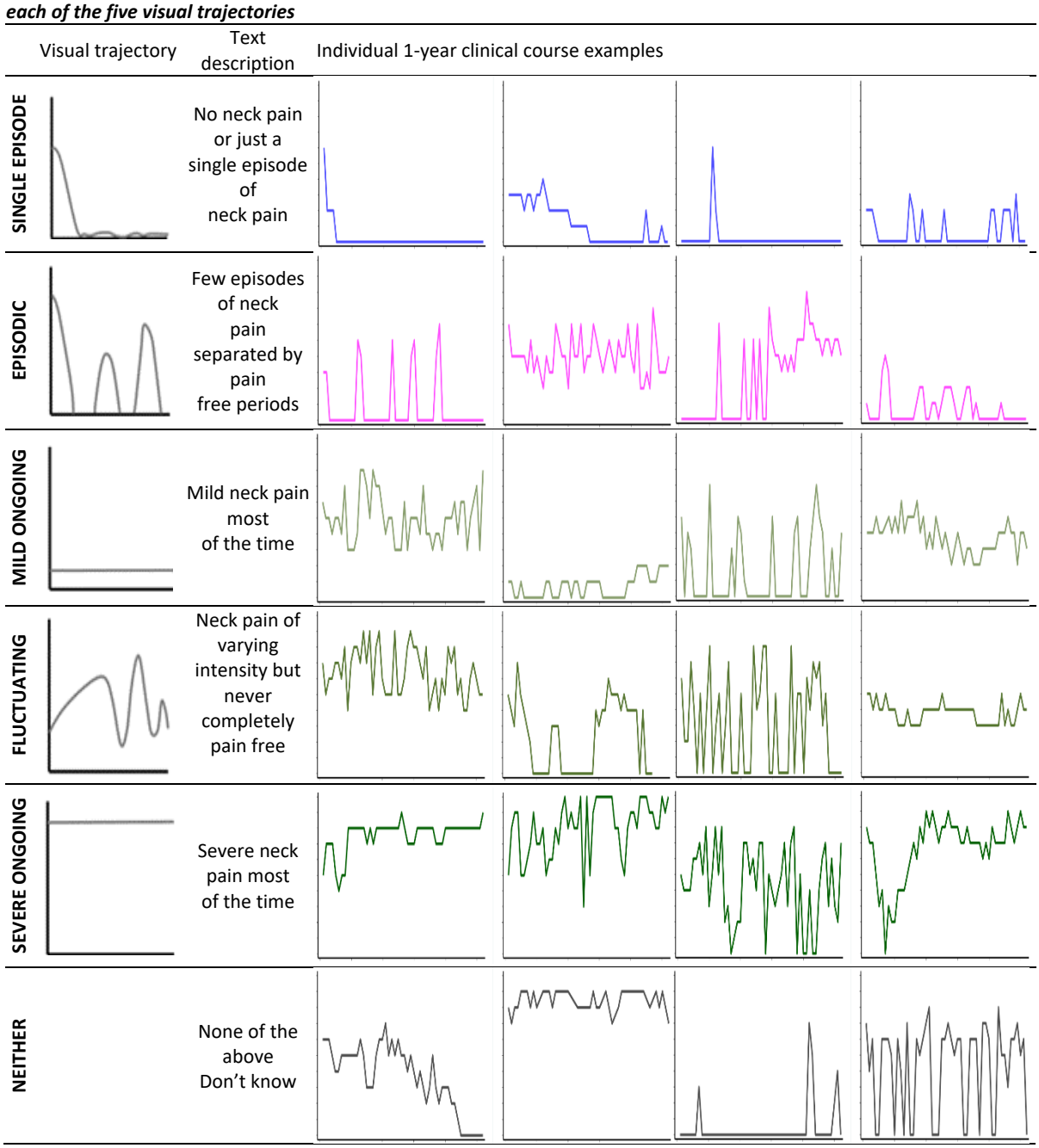


Bars indicate standard deviation (SD)

There was a slight increase in the number of patients classified as episodic (49% vs 45%) when patients were classified for the whole 1-year follow-up compared to the last 43 weeks, and the number of patients that were completely pain-free were reduced (2% versus 4%).

The most commonly selected self-reported visual trajectories were Episodic (37%), Fluctuating (36%) and Single episode (14%). Nine and two percent selected the Minor and Severe ongoing visual trajectories, respectively, while 2% selected “None of the above”/”Don’t know” option. Based on SMS data, the majority of patients were classified as Episodic (49%) or Persistent fluctuating (48%).

Figure 14 Description of the self-reported visual trajectories and examples of 1-year individual SMS-based clinical course for each of the five visual trajectories

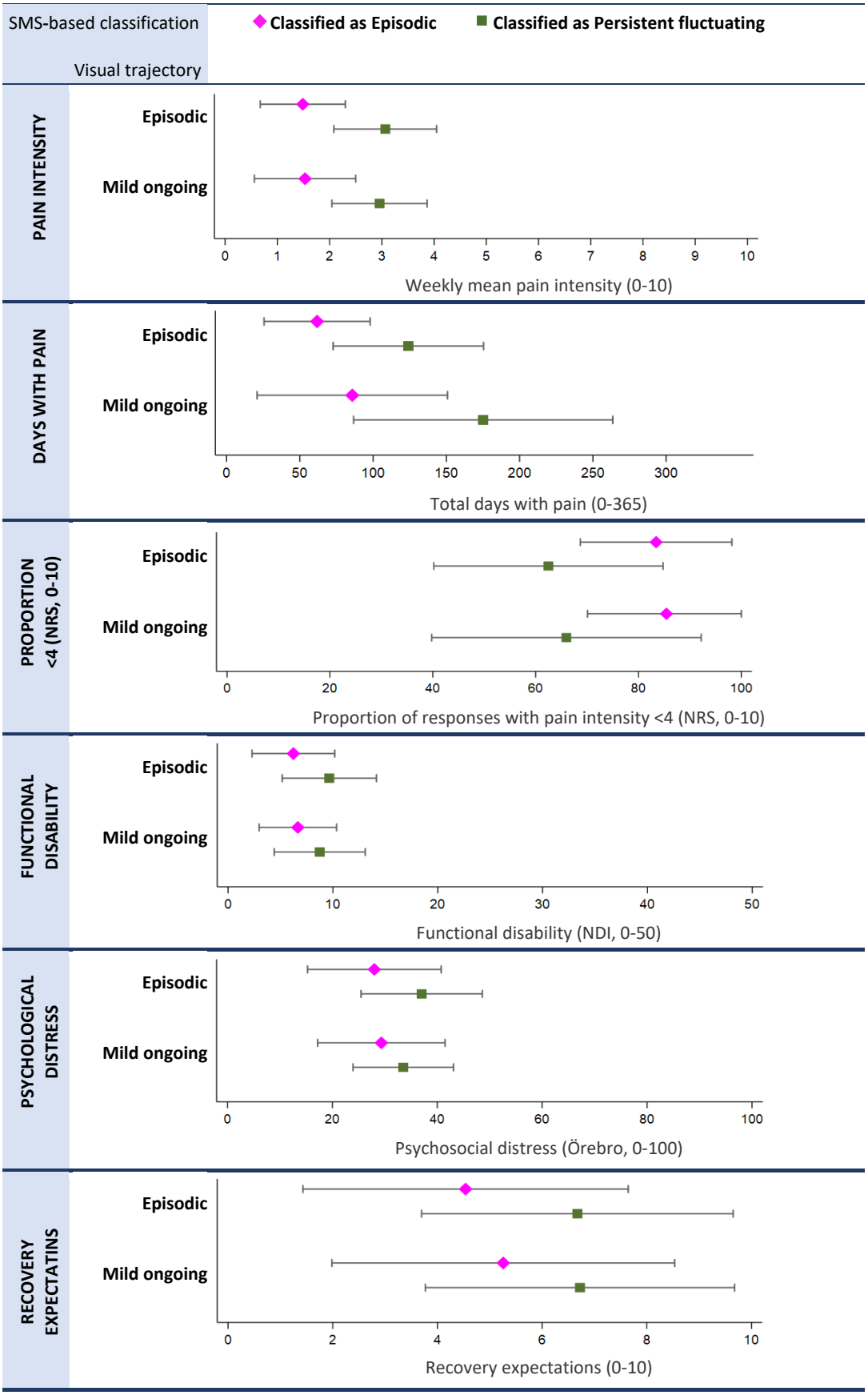


There was a large variation in the individual pain trajectories among patients selecting each of the five visual trajectories, as seen in Figure 14. The visual trajectories generally resembled well the clinical course descriptors and SMS-based classification within each visual trajectory on group levels, with clear differences in patients' weekly mean pain intensity between the five visual trajectories apart from episodic and mild ongoing. The majority of patients selecting the Mild ongoing, Fluctuating or Severe ongoing visual trajectories were classified as Persistent fluctuating based on SMS data (57%, 80%, and 100%, respectively), and 68% of patients selecting Episodic visual trajectory were classified as Episodic. There was also an increase in severity of symptoms, functional disability, psychosocial and psychological distress from patients selecting Single episode through to Severe ongoing visual trajectory.

Patients selecting the Episodic and Mild ongoing visual trajectories, on the other hand, had a clinical course characterized by frequent pain episodes of mostly minor or mild pain and similar weekly mean pain intensity on a group level. The patients also resembled each other closely on all baseline and 1-year data. As illustrated by Figure 15, patients classified as persistent fluctuating reported more pain, less pain-free weeks, and were more bothered by their pain than the patients classified as episodic, regardless of selected visual trajectory.

When we compared the visual trajectory selection to the classification based on SMS data from the last quarter only, there was a general improvement in the resemblance between the selected visual trajectory and the classified pattern compared to using the whole follow-up year. There was a marked increase in patients selecting Single episode visual trajectory and classified as Single episode/Recovery based on SMS (from 19% to 64%), but a decrease in patients selecting Episodic visual trajectory and classified as Episodic (from 68% to 30%). Of the patients selecting Single episode visual trajectory, 43% were classified as Single episode/Recovery the last quarter. In addition, all patients classified as Single episode/Recovery for the full year (18%), had their single episode of pain the last quarter of follow-up.

Figure 15 Characteristics of patients selecting Episodic and Mild ongoing visual trajectory, stratified by SMS-based classification as episodic or persistent fluctuating pattern



NRS, Numeric Rating Scale; NDI, Neck Disability Index

4 General discussion

Summary of key findings

Understanding the clinical course of pain is essential in order to be able to predict the future progression of a symptom or condition and enable appropriate and cost-effective interventions. From a clinical point of view, having insight in the clinical course of pain allows for better communication between patients and health personnel. This is the first study on the clinical course of neck pain where treatment-seeking individuals are followed weekly for one year, and as far as we know the largest cohort of this kind to date.

The focus of this thesis can be divided into three stages. The first stage involved data collection and handling. The second stage involved the methodological choices in applying trajectory patterns and subgroup definitions to our neck pain cohort and assessing if the trajectory patterns were stable over time. The third stage involved a descriptive study on what the visual trajectory pattern questionnaire represents in terms of patients' clinical course of neck pain.

The definitions used in this thesis were based on recommendations for future research on low back pain (195), and later operationalized for a low back pain cohort (328). We found that the defined patterns and subgroups were readily applicable to neck pain patients, but that the original definitions would benefit from refinement. Most patients were classified in a persistent fluctuating or episodic pattern. Having pain-free periods during the year relates to a more benign condition regarding distress and activity limitation compared to pain that is more persistent. Furthermore, steady, ongoing pain was almost non-existing. Most patients classified as persistent fluctuating in the first quarter, remained in this pattern throughout the year. Very few patients experienced only a single, short episode of pain during one quarter, and painful episodes could last longer than one quarter. Therefore, a shorter measurement period (i.e., three months) led to more patients being classified as persistent fluctuating than for the full year. The visual trajectories reflected the past 1-year clinical course characteristics on a group level. However, it is uncertain if the visual trajectories in their current form are an adequate substitute for the 1-year clinical course of neck pain on an individual level.

The most central aspects of each study are discussed in the scientific papers. The thesis' discussion will concentrate on some of the important methodological considerations, followed by comparison and discussion of the main findings against current knowledge on the field.

4.1 Discussion on methodological issues

4.1.1 Participants and study samples

In this thesis, we study patients with neck pain, treated by chiropractors in Norway. Approximately 700 chiropractors were working in Norwegian primary health care at the start of this project, and approximately 16% of patients with neck pain seek chiropractic care (24). All four health regions in Norway were represented in our cohort, with 125 chiropractors from 71 clinics volunteering to recruit patients. However, not all chiropractors agreed to participate, and an overweight of the clinics were situated in urban areas. The most common reason for not participating was logistical and/or familial time restrictions. Still, the participating chiropractors were comparable in characteristics and they generally report similar use of chiropractic techniques in treatment compared to a survey of Norwegian chiropractors from 2011 (36). Furthermore, most chiropractors recruited similar number of patients.

It has been discussed which patients should be included in studies on the clinical course of pain. Previous trajectory studies show large variation on pain duration for the patients included (195), and most of the studies exclude patients already in a treatment course (68, 328, 432). Furthermore, it has been argued that it is best to include patients that either experience their very first episode or are at the start of a new pain episode (an inception cohort (31, 433)). However, we wanted to ensure that all possible pain trajectories present in chiropractic patients with neck pain were represented. Therefore, we asked the chiropractors to include every patient with neck pain independent of treatment prior to inclusion. This broad inclusion criterion allowed for a wide specter of patients and gave us the opportunity to study clinical course in the broadest context. The variation within the cohort is therefore likely to be representative for patients seen in clinical practice, and also provides external validity. Hence, we believe that our broad inclusion criteria are a strength and not a limitation in this thesis. We have otherwise used similar inclusion criteria as previous neck pain studies (60, 68, 154, 432, 434).

The characteristics of the patients in our cohort are similar to previously described chiropractic patients in Norway (435). Previous studies on patients with back and neck pain have generally found that patients in general practice (GP) and physiotherapy care experience higher overall burdens, report longer pain duration, and have lower expectations of positive outcome than patients in chiropractic care (247, 436-442). However, the differences between patients in different clinical settings, are usually small and the measured differences seem often to be below clinical relevance (437, 438). Furthermore, results from recent studies comparing patients in chiropractic versus GP and physiotherapy care add to the question whether they might not be so different. In a Swedish study, the chiropractic patients reported more pain and worse psychosocial factors than patients in GP and physiotherapy practice (443). In addition, a Norwegian study found that older patients with widespread pain (considered more complex) were more likely to seek chiropractic than GP or physiotherapy care (440). The patients

included in our cohort were comparable on patient characteristics with patients in previous neck pain studies in primary care and with the general population (63, 68, 194, 314, 315, 432, 444, 445).

The participating chiropractors were instructed to invite all neck pain patients for participation. We neither have information about the total number of patients not invited, nor any detail information of those who declined to participate. To limit, or at least document, the possibility of selection bias by the chiropractors, we asked them to report the number not willing to participate and reason for the patients not invited to participate or declined participation. We received this information from 50 chiropractors (40%) on 378 patients. The most reported reasons for not inviting a patient were 'the patient does not wish to participate' and 'chiropractor forgot or did not have time to ask'. Another reason for declining participation could be the request for weekly SMS follow-ups. Very few chiropractors reported 'does not own a mobile phone' or 'does not read/write Norwegian' as cause for patients' non-participation. Since we have this information from only 40% of the chiropractors, these data represent only trends.

Eighty percent of the recruited participants reported to already be in a treatment course when included to the study. We expected this number to be lower and cannot exclude that some patients presenting at first consultation were not invited.

We excluded patients who responded to less than 50% of the weekly SMS' from the analyses. Moreover, since we used different measurement periods for the three papers in the thesis, the samples sizes differed somewhat between papers

For Paper I, 17% percent of the cohort was excluded from analyses, which is almost similar to what Kongsted et al reported in their study on low back pain (13%) (328).

In Paper II, we examined the stability of the SMS-based patterns and excluded patients (23%) with too little data for classification in all four quarters (ranging from 9% in first quarter to 23% in fourth quarter).

For paper III, we excluded patients without response to the Visual trajectory pattern questionnaire and the baseline questionnaire (37%). In addition, patients with less than 26 of SMS responses for the full year and 7 of the SMS responses in the last quarter were excluded. In total, 40% were excluded for the analyses in Paper III. This is comparable with what Dunn et al reported in their VTQ-P study on low back pain (40%)(369).

4.1.2 Study design

We based our protocol and methodology mainly on the description and experiences from three trajectory studies on low back and neck pain patients (68, 279, 310). We used a prospective, cohort design and followed patients with neck pain with weekly SMS over one year. A prospective observational study with frequent measures is the best way to identify the clinical or natural history of a disease or symptom (433, 446). In addition, a well-planned and executed prospective observational study design limits bias (446). We performed a pilot study prior to the main data-collection to optimize our protocol. We did some minor changes in the wording of the introductory letter based on the feedback in the pilot study and minor alterations on the described inclusion procedure for the chiropractors. Minor alterations in these two areas were implemented in the protocol prior to onset of data-collection. We think that our 1-year follow-up with weekly SMS measures, collecting data on both the number of days with pain and the intensity of pain, increases the likelihood of capturing even a rare and/or short-term event (like a very short episode or flare-up of pain) occurring during the study period. Weekly questions could of course be bothersome and might have led to missing data. However, little responders' fatigue has been found in studies with weekly measures and recall bias is reported to be minimal (192, 234, 301, 350, 429, 447, 448). In fact, studies using frequent health measures have found that, rather than triggering more negative feelings and/or pain, the frequent measures appear to reduce the reports of depressive symptoms and pain intensity (392, 430, 449). Hence, we do not believe that the weekly measures themselves have had a notable effect on the pattern or subgroup classification.

Loss to follow-up are common in longitudinal cohort studies, and reported to be due to both the duration and frequency of measurements in the follow-up period (450). Moreover, it may lead to missing data that can influence the interpretation of results (357, 446, 450-452). To minimize missing data, we supervised the responses closely according to protocol (see Material and Methods section 2.3, p.39). We contacted non-responders with a reminder at specific times set a priori. When appropriate, we gave them an explanation regarding the importance of responding even in periods without any pain.

The 82% response rate of the weekly SMS measures in our study is high. It is markedly higher than in the study from Ailliet et al over 26 weeks (55%) (68) and similar to the 26-week follow-up study from Axén et al (82.5%) (453). Still, it is lower than the studies from Kongsted et al and Pico-Espinosa et al, both with 92% response rate (194, 279). Most patients in our study reported the cause for missing to respond as forgetfulness or being on holiday. We expected that some of the missing responses could be because the patients have become pain-free during follow-up and, consequently, stopped answering the weekly SMS. This indicates that most data are missing at random (356, 360). A possible explanation for the difference between the response rate in our study and the study from Pico-Espinosa et al (194) could be methodological. They included an intervention and their participants generally reported more

pain each week. These two factors are previously suggested to result in a stronger attachment to the study, and thus a closer adherence to SMS-responses (360). We compared patient characteristics and clinical data between participants and non-responders using two-sample *t*-test and chi-square test to explore possible bias in our data. There were only marginal differences between the two groups, and it is therefore unlikely that the missing data were an important source of bias.

All patients in our cohort were treated by chiropractors during parts of our follow-up period. The content of treatment and the treatment plan was completely at the chiropractor's discretion, without any influence from the research team. Since we did not collect data about the details of the individual treatments, we do not know whether treatment have influenced our results. Nevertheless, we think that our cohort gives a good picture of patients with neck pain treated by chiropractors in Norway.

4.1.3 Instruments used

We used questionnaires to collect information about the patients' demographical, clinical, and general health data at baseline and 1-year follow-up. To minimize responders fatigue, we used short-versions where possible (HSCL-10 (406) and Örebro screening questionnaire (120)). Most of our patients wanted electronic questionnaires on e-mail. Electronic questionnaires may have some weaknesses. For the Visual trajectory pattern questionnaire, the patients were asked to choose one of five drawings of pain trajectories that best represented their clinical course the previous year. Ideally, the patients could have been given the option to draw their own pain trajectory if none of the illustrations in the questionnaire represented their clinical course. However, the technology hampered this, and we therefore inserted the additional two answer possibilities "None of the above" and "Don't know". Only 2% of patients selected these options. However, we cannot exclude that if a self-made drawing option were made possible could have yielded additional illustrations of pain trajectories, but this could also have resulted in an added complexity with analyses. Sixty-five percent of the patients answered the Visual trajectory pattern questionnaire at the 1-year follow-up. This is well within the reported range of data missing at random (40-95%), and is unlikely to cause bias (357). Furthermore, the most common response for non-reply was that patients considered the questionnaire to be too time-consuming or that they no longer had neck pain.

We used responses on SMS to collect weekly data on pain intensity. This has previously been reported to be an optimal method to capture remissions and exacerbations of the clinical course of pain (195, 279, 291, 308, 310, 311, 315-317, 323, 347). According to Statistics Norway, more than 97% of Norwegians had access to a mobile phone in 2015 (337). Hence, there is no indication that this data collection method has excluded patients from participation. Collecting data with SMS does have some limitations, such as the number of words is restricted, and the answer alternatives are limited to be

single words or numbers. However, as we were asking about pain intensity, using a numeric rating scale (NRS) for response, and number of pain days, the SMS system was ideally suited for our purposes.

The Numeric Rating Scale

We used the 11-point numeric rating scale (0-10, NRS) to measure the weekly pain on SMS, as it is easy to use and accepted as a proxy for subjective pain (236). It is also a universally applied tool to quantify pain intensity (174, 398, 454), and the most commonly used instrument for pain registration in trajectory studies (68, 194, 195). A criticism of the NRS is that it is not able to capture the multiple dimensions of the pain experience (165, 275, 277, 455). However, multidimensional pain questionnaires are not suited for weekly SMS collection, with word and response restrictions. Hence, such instruments would have required a different form of data-collection. Nevertheless, the construct validity of the pain NRS is still not completely resolved (454, 456, 457). Several studies, however, indicate that the NRS has acceptable psychometric validity and reliability (179, 456, 458) and is considered superior to other tools of measuring pain intensity (179, 180, 399, 454, 459). Given our aims and type of collection method, the unidimensional pain NRS is still the most appropriate measurement tool to date (458).

The NRS is most used with the end anchors "no pain" for 0, and "worst possible pain" for 10. We used "no bother" (Norwegian 'plage') and "worst imaginable bother" for the anchors of the NRS (question: "How intense has your neck pain typically been the last week? 0= no bother, 10= worst imaginable bother"). The reason for using bother instead of pain was primarily based on the study from Axén et al, where they used 'days with bothersome low back' as basis for their trajectories (310). The term 'bothersome' has been thought to represent more than just pain intensity levels (211, 253, 379, 382, 385, 460), and there may be an increased risk of non-differential subgroup misclassifications. As far as the we know, only one study has used the 11-point NRS scale with 'bothersome' pain (461). They found that in patients with whiplash-related neck pain, the 11-point NRS for 'bothersomeness' had similar internal and external responsiveness compared to the 11-point NRS for pain intensity. However, they did not compare the two scales head-to-head regarding pain intensity, nor did they provide any details on the anchors used for each end of the scale. Dunn et al. (379) have shown that 'bothersome' correlates well with a composite pain intensity measure (the mean of 11-point NRS of pain right now, worst, least, and average pain during the last 2 weeks) when using a 5-point scale for 'bothersomeness' with anchors from 'not at all' to 'extremely'. The term 'bothersomeness' identified patients with the highest category of pain and disability with a sensitivity of 81% and specificity of 61% (379).

To assess if the wording of 'bother' in the NRS anchors differed from the word 'pain', we compared the SMS scoring of weeks 12 and 52 against the scoring on the item number 2 from the Örebro screening questionnaire ("How much pain have you had the last week? 0=no pain, 10= worst imaginable pain") (120) and found that differences are unlikely to be significant (Spearman's rank coefficient of 0.71).

Consequently, we consider that the use of 'bother' instead of 'pain' did not have a noteworthy influence on the subgroup distribution and should not limit our ability to compare our findings with other studies. The selected wording for the anchors in the data-collection, however, were unfortunate, and the word 'pain' should have been used. Considering the issues discussed above, we have referred to 'bother' as 'pain intensity' for this thesis.

It has been discussed how to ask about pain in different studies. Should we ask for typical pain, average pain, or worst pain, and what is best? We do not have any answer to this but realize that different wordings are likely to influence the answers and complicate the process of comparing results between studies. Moreover, no consensus seems to exist (283, 301, 462), and trajectory studies have asked for 'average' pain over a specified time period (194, 308), 'current' (68, 240, 305, 318, 321), 'typical' (328) and 'peak'/'worst' (240, 305, 314, 315, 317, 318) as basis for trajectory analysis. Combining different pain scores seem to have shown some potential in increasing both sensitivity and reliability of pain outcome measures (178, 463), and is hypothesized to be a better index for the variability of pain (162, 234). We found three trajectory studies that have used pain as a composite score operationalized as the total mean value of three measures: least and usual pain over the past two weeks, and current pain (240, 305, 318). However, it has previously been proposed that in studies with large sample sizes, like our study, and using weekly measures, individual intensity ratings are likely to have sufficient psychometric strength (456). Taken together, we cannot conclude whether the use of 'typical' in our study has led to a different clinical course than if we had used other indices of pain. This should be explored further in future studies.

4.1.4 SMS-based pattern and subgroup definitions

Originally, we planned to investigate the clinical course using LCA in the present study (240, 464). Until 2015, most trajectory studies were on low back pain (195). Hence, the protocol for our data-collection on neck pain patients was set up to suit that type of analysis. However, at the end of our data-collection period, Ailliet et al published a trajectory study on neck pain patients (68). This study supported previous reported similarities between the course of neck and low back pain (63, 69, 71-74). Furthermore, before we started our data analysis, a group of researchers with extensive experience in trajectory research, the 'Trajectory Overview Group', published a review paper on low back pain trajectory studies: "What have we learned from ten years of trajectory research in low back pain?" (2016) (195). They identified trajectory patterns that were consistent across statistical methods, cohorts, and over time. The patterns also represented patients with different clinical and patient characteristics across health parameters. Three common pain domains were found: variation, intensity, and speed of improvement. The pain variation patterns included persistent, fluctuating, episodic, and single episode. The researchers concluded that it was unlikely that further studies with statistical

methods like cluster analysis, factor analysis, or latent class type analyses (LCA) (hereafter 'complex analysis') would yield new trajectories. Instead, they recommended future studies investigate (195):

a) If the identified patterns could be found in new cohorts and in other musculoskeletal regions
b) If the patterns were stable over time
c) The length of the follow-up period needed to predict the future trajectory after first onset of an episode
d) How to provide standardized ways to measure trajectories to improve comparisons between cohorts and settings
e) Patients' ability to retrospectively identify their trajectory pattern

In response to d), a Danish study by Kongsted et al had already operationalized two of the pain domains (variability and intensity) into 16 subgroups and found that these matched well with LCA-derived trajectory patterns (328).

In compliance with these recommendations, we decided to change our planned analyses and to include points a), b), and c) for the aim of this thesis. The last point, e), was already part of our original aims. As a first step, we wanted to investigate if the definitions developed for the Danish low back pain study (328) fit our neck pain cohort. As these definitions were based on weekly measures for one year, our selected methodology for data-collection was ideal.

Consequently, for Paper I, we deliberatively mirrored statistical approaches regarding definitions of subgroups and the follow-up period of 43 weeks from the Danish study, to achieve maximal possibility for comparison between the two studies. However, we changed the name of the fluctuating pattern from the original study to 'persistent fluctuating' based on reviewer comments for Paper I. We agreed that adding 'persistent' to fluctuating would result in a better distinction between the fluctuating and episodic pattern, as 'fluctuating' alone is frequently used to describe variations in pain. We believed that this change did not deviate substantially from the original terminology and decided to use the new name 'persistent fluctuating' throughout the three papers. The same reviewer also recommended changing 'episodic' to 'occasional episodic' for similar reasons. However, as we believed 'occasional' implied a certain number of episodes, we decided to keep the original terminology 'episodic'.

Our findings in Paper I indicated that the definitions could also benefit from refinement of some of the patterns and subgroups. These were in line with the results from the Danish low back pain study (328). We therefore reduced the number of subgroups from 16 to 11 for Papers II and III. In addition, the minor subgroups of ongoing, episodic, and single episode patterns resembled each other on most clinical and patient characteristics and were combined into one pattern called 'recovery'. Lastly, as all

but two patients with persistent pain experienced fluctuations, the ongoing pattern was superfluous and therefore removed.

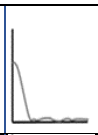
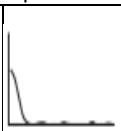
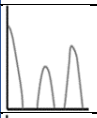
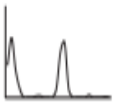
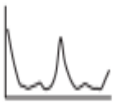
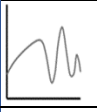
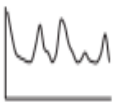
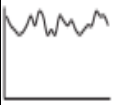
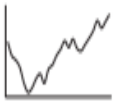
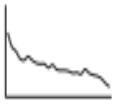
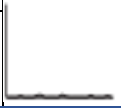
We also wanted to explore the stability of the defined patterns over time (point b) in the recommendations from the review paper mentioned above). The definitions of the subgroups are broad, and most patients are therefore likely to have a clinical course that fits a pattern. However, this could indicate that there might be too much room for change within a pattern. Consequently, this opens up for the possibility that a patient might have clinically significant change in their pain trajectory for a period, yet still fulfil the 1-year pattern classification criteria. It was uncertain if the definitions represented a definite pain pattern or were simply a reflection of a phase or transition to a different course of pain. We used data from each of the four quarters separately and performed the same subgroup classification. This method is similar to a low back pain study using complex analyses (309). We defined a pattern to be stable if the patient had the same classification in the first and fourth quarter. We selected this method, as using all four quarters would have yielded too many shifting options for evaluation. We also illustrated the flow of patients from one quarter to another by using a Sankey diagram, a method which has also been used in a very recent study on shifts of visual trajectories in a low back pain cohort (465). However, both methods have their limitations. First, although Sankey diagrams give a good overview of trends, individual shifts cannot be illustrated due to the numerous possible shifting patterns identified in our cohort. Second, our method assumes that having the same pattern in the first and fourth quarter (stable), equals having the same pattern in all four quarters. We found that as many as 89% (n=655) of patients classified as 'stable' in actuality stayed in the same pattern in all four quarters, and the majority of the remaining patients had only one shift, and this was to a neighboring pattern. Lastly, we found no differences in clinical and patient characteristics between patients "correctly classified" compared to those "misclassified" as having a stable trajectory. We therefore think that this is an acceptable method to assess the stability of a trajectory.

4.1.5 Visual trajectory pattern questionnaire

At the 1-year follow-up, patients were asked to select an illustration that best represented their clinical course for the previous year. No validated questionnaire for visual trajectories existed at the time of data-collection. We used the illustrations of five pain trajectories (single episode, episodic, mild ongoing, fluctuating, and severe ongoing) identified in previous low back pain studies (240, 279, 309-311), and called the Visual trajectory pattern questionnaire (Figure 16). A descriptive text accompanied each illustration to help patients in the selection and to avoid misinterpretation. None of the participants in the pilot study reported any difficulties with the questionnaire. In addition, we included the two answer alternatives, "None of the above" and "Don't know". These options were selected by

only 2% of the cohort, indicating that the illustrations were likely both representative of the cohort's pain trajectories and well understood by the patients. Moreover, there was a trend of increased pain, functional disability, and psychological distress from patients selecting the Single episode visual trajectory to those selecting the Severe ongoing. This demonstrates that the Visual trajectory pattern questionnaire may represent different aspects of the pain experience, which has also been found with the same questionnaire given at baseline (466). A similar questionnaire with eight illustrations, the "Visual Trajectories Questionnaire – Pain" (VTQ-P), was developed by Dunn et al (369), based on previous results from monthly measures over six months (240). The VTQ-P is validated for low back pain patients in general practice (369). Dunn et al reported that participants found the questionnaire easy to understand and answer, showing that the VTQ-P had good face validity (369). For most participants, their latent class trajectory classification from the first six months of their 1-year follow-up matched their selected VTQ-P. Hence, the illustrations demonstrated acceptable criterion validity. In addition, they established construct validity against parameters supported by "The stages of pain model" (370), a pain model for chronic low back pain that includes regional pain, concomitant pain, and cognitive and emotional status. The construct validity of the VTQ-P is supported in a later study (without the worsening and improving illustrations included), that found that participants selecting the persistent type trajectories had significantly higher pain intensity and anxiety at baseline, compared to patients selecting the episodic type trajectories (371).

Figure 16 – Comparison and participant distribution (%) of three visual trajectory questionnaires developed for neck and/or low back pain

The Visual trajectory pattern questionnaire used in our study			**The Visual trajectories questionnaire for pain by Dunn et al (369)[1]**		
"Please tick off the description below that you think best represents how your neck pain has been **the previous 12 months"**			"Below are some descriptions of how some people's **back pain can change over time**, with pictures to show how their pain might go up or down. Please look at these and cross the box next to the one option that you think comes closest to how your pain has been over **the last year**"		
1) *14%*		***Single episode*** No neck pain or just a single episode of neck pain	**a)** *3%*		A single episode with no other major episodes of back pain
2) *37%*		***Episodic*** Few episodes of neck pain separated by pain free periods	**b)** *31%*		A few episodes of back pain, with mostly pain-free periods in between
3) *9%*		***Mild ongoing*** Mild neck pain most of the time	**c)** *22%*		Some back pain most of the time, and a few episodes of severe pain
4) *36%*		***Fluctuating*** Neck pain of varying intensity but never completely pain free	**d)** *18%*		Pain that goes up and down all the time, with episodes of severe back pain
5) *2%*		***Severe ongoing*** Severe neck pain most of the time	**e)** *3%*		Severe back pain all or nearly all of the time
6) *2%*		None of the above Don't know	**f)** *2%*		Back pain that has got gradually worse
			g) *4%*		Back pain that has improved gradually
			h) *16%*		No back pain, or only the odd day with mild pain

[1,2]Reproduced with minor modifications with permission from [1]The Journal of Pain

The VTQ-P by Dunn et al (369) included 8 visual trajectories compared to 5 in our study (Figure 16). The main difference between the two questionnaires is that Dunn et al have two trajectories f) and g) that describe worsening and improving pain, respectively. These trajectories are not in our model. However, only 6% of the patients in their low back pain cohort selected these two trajectories. Other studies on the course of neck pain have identified improving trajectories (68, 194, 315). We therefore cannot exclude the possibility that using the Visual trajectory pattern questionnaire without these options may have resulted in a bias toward patients selecting the Single episode trajectory in our study. However, there are similarities between the two questionnaires. The picture 1) ('No neck pain or just a single episode of neck pain'), showing a Single episode in the Visual trajectory pattern questionnaire used in our study, is comparable to trajectories a) and h) by Dunn et al (369). Visual trajectories 2) and b) both describe episodes of pain separated by pain-free periods, and 5) and e) describe persistent severe pain for both questionnaires. However, the persistent severe trajectory e) by Dunn et al illustrates mild

fluctuations, while our illustration shows a steady, horizontal line. The fluctuating trajectory 4) in our study, seem to be a combination of c) (more mild pain) and d) (more severe pain) by Dunn et al. Most of the participants in our cohort selected a visual trajectory that we found was similar to their 1-year SMS-based subgroup classification. This is in accordance with the patients in the VTQ-P study (369). As the two visual trajectory questionnaires are built on similar data-driven trajectories and show many similarities both in distribution and patient characteristics in each visual trajectory, it is likely that the methodological qualities found in the VTQ-P by Dunn et al (369) are relevant for the questionnaire used in this thesis.

4.2 Discussion of the main findings

4.2.1 The clinical course of pain

The definitions based on low back trajectories fit well with our cohort of neck pain patients. Furthermore, our assessment of the definitions' robustness to change yielded similar results as the Danish low back pain cohort (328). Most of our neck pain patients (93%) presented with either a fluctuating or an episodic pain trajectory, when we analyzed the last 43 weeks like Kongsted et al (328). This is higher than results from the Danish study (76%). These differences in distribution could have several explanations, such as the patients included, time of recruitment, and clinical settings. Both studies included patients from chiropractic care, but with pain in different parts of the spine. Previous studies have found that patients visiting chiropractic clinics in Norway and Denmark are comparable on psychosocial risk factors such as depression, fear avoidance, and catastrophizing (435, 467). Interestingly, the subgroup distribution in our cohort more closely resembled the Danish GP sample than the sample of chiropractic patients (328). This could be due to our inclusion criteria being more comparable to their GP sample concerning previous treatment. By including patients already in a treatment program, the proportion of patients with long-lasting pain was likely increased in our study, and possibly resulted in more patients with a persistent fluctuating pattern. When we repeated the analyses, including only first consultation patients, the pattern distribution between the Danish chiropractic sample and our neck pain cohort were more similar. Nevertheless, concerning the level of pain intensity, weekly pain days, and total number of days with pain, there were no differences found between the cohorts, which supports the previous evidence of similarities between patients with pain in the two spinal regions (63, 68, 69).

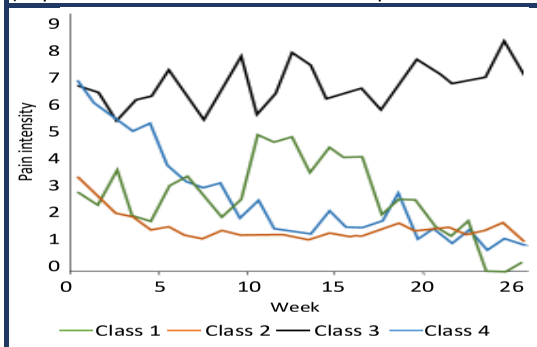
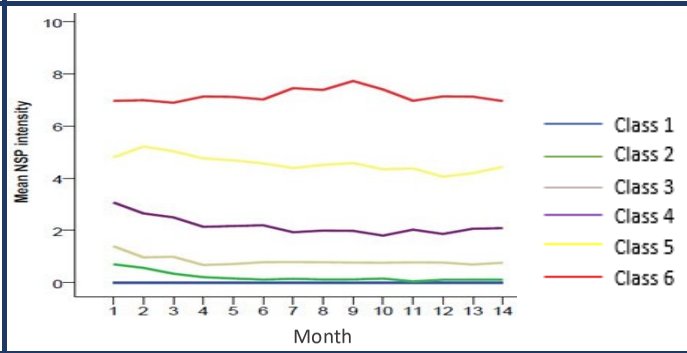
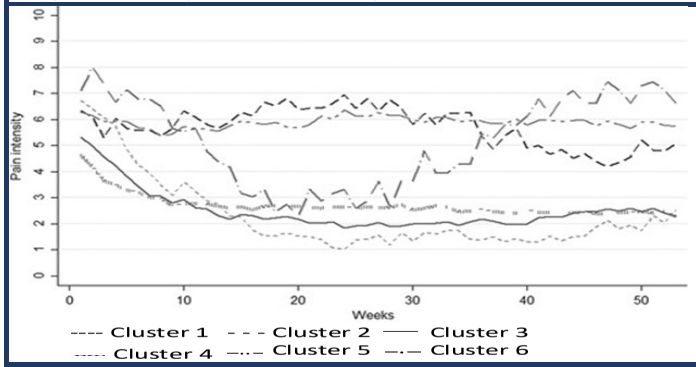
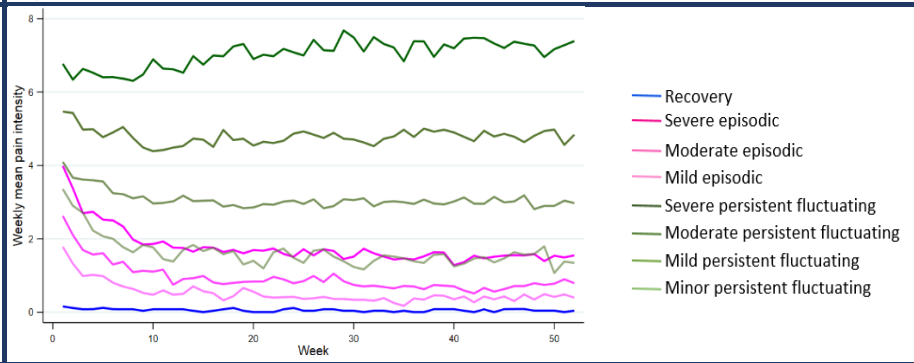
When we used the total number of weeks (52) instead of the last 43, only small changes in the pattern distribution were found. This might indicate that having a period without treatment before patients are included into cohort studies is of less importance. This could imply that inclusion of patients into studies can be easier and counteract the underpowering common in pain trials that include subgrouping (294,

468). However, we recommend registering patients' last treatment and details regarding treatment plan for future studies to be able to examine this further.

Most of our patients reported either episodic (48%) or persistently fluctuating (48%) pain, and 10% of the cohort had mean pain intensity below 2 on an 11-point NRS throughout the year. Interestingly, patients with persistent, steady pain were almost non-existent in this cohort. In addition, we found that the patients in the different patterns differed on functional and health-related factors. This supports the results of other studies where trajectories identified in spinal pain include patients that are statistically different on several aspects (68, 194, 195, 315, 317, 319-321). Moreover, in accordance with these previous studies, we found a large variation between the patients within each pattern. This resulted in an overlap in patient scores between the patterns. In other words, the trajectories include patients with a degree of heterogeneity, and do not represent patients that are distinctly different. Hence, the identified trajectories seem to have some uncertainties for use in both research and clinically.

Our 1-year results differ somewhat from other neck and low back pain trajectory studies. The proportion of patients with a fluctuating trajectory in other studies ranges from 4-35% (68, 194, 195, 315, 317, 319-321), and only one study has identified an episodic trajectory (29%) (279).

Figure 17 – Weekly or monthly mean intensity by identified trajectories of three four long-term frequent measurements studies on the course of neck pain (68, 194, 315) and our study

Four trajectories of neck pain over 26 weeks. Data came from 153 patients with neck pain presenting to chiropractors in Belgium and the Netherlands, in 2010-2011 (68). (Reproduced with modifications with permission from European Journal of Pain)	Six identified trajectories of 748 neck-shoulder pain patients sorted by pain intensity based on a 6-class latent class growth model (315) (Reproduced with permission from Scandinavian Journal of Work, Environment and Health, https://www.creativecommons.org/licences/by/4.0/)
	
Class 1: recovering from mild baseline pain with a flare up (3%); Class 2: recovering from mild baseline pain (74%); Class 3: severe-chronic (7 %); Class 4: recovering from severe baseline pain (16%)	Class 1: asymptomatic (11%), Class 2: very low pain (10%), Class 3: low recovering pain (18%), Class 4: moderate recovering pain (28%), Class 5: strong fluctuating pain (24%), Class 6: severe persistent (9%).
Mean pain intensity over time by clusters generated with latent class mixed modeling analysis (194) (Reproduced with the permission from The Clinical Journal of Pain)	Weekly group mean pain intensity of our cohort over 1 year by subgroups generated with defined trajectories in this thesis[1]
	
Cluster 1: "slightly fluctuating" (3%, n=21); cluster 2: "small improvement" (42%, n=260); Cluster 3: "moderate improvement" (24%, n=148); Cluster 4: "large improvement" (7%, n=41); Cluster 5: "persistent" (22%, n=138); Cluster 6: "largely fluctuating" (2%, n=9).	Subgroups: Recovery (2%); Episodic: Severe (30%); Moderate (13%); Mild (5%); Persistent fluctuating: Severe (4%); Moderate (17%); Mild (25%); Minor (3%). [1]Single episode subgroups are not presented, as patients only have one episode of pain lasting 1-2 weeks, and the episode could be at any point during the 1-year follow-up.

NSP, Non-specific neck Pain. [a] Single episode subgroups are not presented, as patients only have one episode of pain lasting 1-2 weeks, and the episode could be at any point during the 1 year follow-up. Figures are reproduced with minor modifications with the permission from: [1] European Journal of Pain, [2] Scandinavian Journal of Work, Environment and Health, https://www.creativecommons.org/licences/by/4.0/, [3] The Clinical Journal of Pain,

Figure 17 illustrates the trajectories found in the three neck pain trajectory studies compared to the weekly subgroup mean in our study (68, 194, 315). For further comparison with our results, these studies are of most interest (68, 194, 315), however, these differ somewhat regarding methodology and results. The main difference is that the majority (90%) of the patients in the study by Ailliet were classified as recovering from mild or severe baseline pain (68). This large proportion could be explained by the study's much lower response rate, and a follow-up period of only 6 months. Our study included fewer patients with a moderate or severe persistent fluctuating trajectory than two of the other neck pain studies (194, 315), but comparable to many low and mid-back pain studies (240, 279, 305, 318, 319, 321). The study by Pico-Espinosa included non-treatment seeking individuals and is most similar to our study with regards to trajectory distribution (194). Only Hallman et al (315) identified a trajectory comparable in intensity level to our 'recovery' pattern. The larger proportion in the study by Hallman et al compared to our cohort in this trajectory (11% vs 2%, respectively), could be explained by their monthly measures and non-clinical cohort of workers with and without pain. Our cohort was otherwise generally similar on baseline characteristics to the other neck pain trajectory studies, as well as for other spinal pain studies (68, 194, 195, 315, 317, 319-321).

When exploring the distribution of patients in trajectories in each of the four quarters of the 1-year follow-up, we found that most patients were in the same trajectory pattern from one quarter to the next. However, patients with an episodic pattern in the first quarter shifted pattern more frequently between quarters. Patients classified as persistent fluctuating in the first quarter tended to stay (>80%) in this pattern, but they shifted between subgroups (intensity) within the same pattern. Conversely, patients with an episodic pattern in the first quarter shifted to the persistent fluctuating or recovery patterns equally. These findings are in accordance with results from a study on low back pain patients by Tamcan et al (309). They found that most patients with a persistent pattern had the same trajectory from one quarter to the next (58-94%), with a mild decrease in intensity from first to second quarter. The fluctuating trajectory, however, was considered unstable. In contrast to our results, the Tamcan study did not identify an episodic trajectory. They described the fluctuating pattern as having a range of pain intensity from "intense" to "minimal", but they neither defined these anchors nor whether "minimal" included pain-free weeks (309). Patients in this fluctuating trajectory reported a very low mean pain after week 13 (<1 on a 0-6 NRS), as well as functional disability and psychological distress levels that was between the moderate persistent and mild persistent trajectories. Hence, we can hypothesize that this trajectory resembles the episodic pattern definition used in our study. Our findings of stability are also supported by a very recent study on low back pain patients, where patients generally did not transition between very different self-reported visual pain trajectories given at baseline and 1 year (465).

Interestingly, our findings of pattern stability were independent of consultation type (first consultation, follow-up, and maintenance care), suggesting that previous pain history and duration is of less importance for the stability of pain over one year in patients with neck pain treated by chiropractors in Norway. It has previously been questioned when patients establish their clinical course (195, 278, 305, 469). Studies have found that spinal pain is common from childhood through to adolescence (323, 470), but it is still uncertain whether this pain pattern tracks into adulthood (336, 471, 472). However, three previous studies on adults have found trends in stability similar to our findings. Lemeunier et al (330) followed 40/41-year-olds over 8 years, and found that patients mostly displayed the same pain patterns over time. Dunn et al showed that patients' pain and disability for each identified trajectory pattern of the last six months matched well with the same characteristics of the first 6 months of a 1-year follow-up (240). In addition, most patients were allocated to the same pattern in a new 6-month follow-up period 7 years later (305). This indicates that, from adulthood, trajectories appear to be stable over several years. However, as with the findings by Tamcan et al (309), the fluctuating trajectory found in the study by Dunn et al was not stable over time (305). One could speculate that, rather than being considered as unstable patterns, the fluctuation trajectory found by Tamcan and Dunn and the episodic pattern in our study simply reflect the large variability in the duration of episodes and fluctuations.

Most trajectory studies have also found that, regardless of previous pain duration or treatment, the period after recruitment is usually characterized by improvement (68, 194, 195, 473, 474). Unfortunately, the defined trajectories used in our study did not include a "changing pattern" (195) (see Material and Methods section 2.4.1, p. 54-56), which limits further comparison. Nevertheless, we found that the cohort had a general improvement in the first 2-4 weeks (see Figure 13, Results section, p.61). We also found an increase in patients classified as recovered from first to second quarter, as well as a general trend of patients shifting to a subgroup with milder pain intensity within the same patterns from one quarter to the next. The similar quarterly trend was also found in the study by Tamcan et al (309), where no improving pattern was described. These results point towards a general improvement in a short period after recruitment.

Using pain duration, previous pain history, and information about recruitment at first contact or in a treatment course (consultation type) we assessed the influence of previous pain duration and consultation type on the clinical course of pain. Surprisingly, only small differences were reported on pain duration at baseline, regardless of consultation type. However, while not significant, patients recruited at their first consultation reported somewhat higher pain intensity and functional disability score at baseline compared to patients in a maintenance care plan. Patients already in a treatment plan or preventative care are not expected to have the same improvement as patients included with a new episode (475). We therefore hypothesized that patients presenting at first consultation would distribute differently into subgroups than patients recruited at follow-up or in preventive care. Although we found

frequent individual variations within each consultation type, we still expected to see a significantly higher pain intensity at baseline combined with a more rapid recovery in patients included at first consultation. We also expected that patients in a maintenance care plan would have a more stable trajectory than the rest of the cohort. However, this was not confirmed by our result (see Figures 12 and Figure 13, p. 61 and 62, respectively). In fact, we found only small differences in the 1-year course of pain intensity, days with pain, and days with restricted daily activities between the three consultation types in the first quarter of follow-up. Furthermore, we have previously found that consultation type had no interaction with other factors when tested in a prediction model (93).

The different results in our study compared with other trajectory studies are probably due to the use of fixed definitions that specifically focus on fluctuations and pain-free periods (episodes) (328), and not because our cohort is substantially different. Although the Danish low back study found that the operationalized definitions matched well with the LCA-derived trajectories (328), their study is the only trajectory study identifying an episodic trajectory (279). Our findings support the suggestion given by the 'Trajectory Overview Group' that the description and terminology of the trajectories identified by complex analysis is subjective (195). This can be the reason for other studies' lack of descriptions of an episodic trajectory. The output from complex analysis does not give as a set of factors describing the clinical course (i.e., frequency and size of pain-free episodes or fluctuations in pain intensity). Rather, the participants are assigned a probability of belonging to groups that are based on a latent (but unspecified) pattern found through the analyses (464). It is up to the study's research group to find common clinical course factors that represent each latent class (trajectory). Hence, there is an aspect of subjectivity in deciding on distinct factors for a particular clinical course trajectory, the selected cutoffs for each trajectory, as well as how they are subsequently defined (terminology). As a result, definitions, descriptions, and terminology vary greatly between studies (68, 194, 195, 306, 314, 315, 321, 476).

4.2.2 Visual trajectories – what do they represent in terms of the clinical course of pain?

The primary interests for subgrouping patients and develop trajectories have focused on identifying groups that may respond to specific treatments or interventions, as well as an intent to improve treatment (115, 125, 128, 140). There is little support for "one cure fits all", and by subgrouping patients the intention is to identify factors that may aid in more effective treatment and/or improved outcome. Visual trajectories are pictures meant to illustrate the clinical course of pain and can easily be used in clinical practice.

Little is known about the methodological quality for visual trajectories, and we wanted to explore if patients were able to identify their own retrospective pain trajectory through a questionnaire given at the 1-year follow-up. Patients primarily identified their past clinical course of pain as episodic (37%), fluctuating (36%), and single episode (14%) based on the Visual trajectory pattern questionnaire used in

this thesis. In addition, we found a gradually increasing severity regarding functional disability, pain intensity, and psychosocial factors from single episode to severe ongoing visual trajectories. Our findings were, with only a few exceptions, comparable to the study by Dunn et al using the VTQ-P on a low back pain cohort in general practice (369). However, both studies illustrate that there are substantial individual variations within each visual trajectory. In addition, the overlap of clinical and psychosocial factors between patients selecting different visual trajectories may indicate that the visual trajectory questionnaires seem, in their current form, to be more likely to represent phenotypes than being representations of transitional phases.

Thirty-eight percent of the patients in our cohort selected a fluctuating or severe ongoing visual trajectory. Their clinical courses were characterized by moderate or severe pain intensity cutoffs (≥4 NRS) in most weeks, and they had few to no pain-free weeks. They also had large fluctuations in pain throughout the year and very low expectations of recovery. Moreover, most of the patients selecting the fluctuating or severe ongoing visual trajectory had an SMS-based classification as persistent fluctuating (80% and 100%, respectively). Similarly, this congruency was 62% and 77% in the study by Dunn (369). These results demonstrate that two visual trajectories reflect the patients' actual clinical course to a very large extent, and that patients recognize this pattern to a satisfactory degree. In a mixed method study, Hestbaek et al used telephone interviews to determine the patients' self-reported retrospective clinical course over 1-year (316). They compared these responses with visual interpretation of the patients' weekly SMS responses, classifying patients according to the operationalized patterns for the Danish low back study (328). In contrast to our results, the most common disagreements identified between the patients SMS-based pattern and their described past trajectory was with the categorizations were related to the fluctuating pattern. An explanation for the incongruency could be that only four patients in their study described a fluctuating trajectory. It has been emphasized that it is important to patients that health care providers understand and accept that their pain fluctuations are real, and that the unpredictability accompanying such fluctuating pain is difficult to handle (282). Furthermore, patients also stated that it is important that the treatment addresses these fluctuations, which are described as unique and not necessarily follow a pattern. Hence, this emphasizes the importance of identifying fluctuating patterns in spinal pain.

For the visual trajectories that indicate a milder course of pain (single episode, episodic, and mild ongoing), we found less similarities between the patients' selected visual trajectories and their detailed clinical course. The patients selecting the single episode reported mostly minor to no pain and were only negligibly affected by their pain. However, they had frequent but generally mild pain of short duration throughout the year, findings that are in line with the studies by Dunn et al (369) and Hestbaek et al (316). Most patients in the study by Dunn et al were observed to have a statistically derived trajectory of 'no or occasional mild pain' (73% and 86%, respectively). In contrast, only 18% of the

patients in our study were classified with a single episode based on the SMS', and all reported their single episode in the last quarter, suggesting that recall bias could be involved (191, 477-479). These findings indicate that the SMS-based single episode pattern might be better defined as 'no or occasional mild pain', rather than "One single episode or flare-up lasting 1-2 weeks" used in our study (328).

Interestingly, our results show only negligible differences between consultation types (first consultation, follow-up, and maintenance care) regarding the selection of visual trajectories. In addition, of the patients recruited at first consultation, only 19% selected the single episode visual trajectory.

We found only minimal difference in functional disability and psychosocial risk factors between patients selecting the episodic and mild ongoing visual trajectories. Both trajectories represented patients with mostly minor or mild pain, with variations in degrees and durations of pain-free periods and pain exacerbations. In addition, there was a poorer relationship with the patients' SMS-based classification compared to the fluctuating and severe ongoing visual trajectories. Our findings, which are largely in line with the studies by Dunn et al (369) and Hestbaek et al (316), indicate that pain that is episodic or mildly persistent, in particular, is difficult for patients to categorize and describe. One likely explanation is that mild pain and short pain episodes are difficult to remember, evaluate, and/or report retrospectively (161, 162, 193, 301, 480). Moreover, evidence indicate that the duration of periods of high and low degrees of pain, represent different elements of the pain experience (162, 481, 482). The duration of pain periods is also noted as important by patients, and more important than the pain intensity itself (301, 483). Hence, several shorter episodes of pain are likely to be less memorable. This could explain why patients selecting the single episode visual trajectory had a clinical course characterized by several mild episodes. However, review papers show that there is little agreement on how well people remember pain (307, 484, 485), and that the recall of pain is related to much more than the pain intensity and duration alone (229, 486).

Pain is a subjective and highly personal experience that is formed by a myriad of factors unique to each individual. In fact, pain impacts, and is profoundly influenced by, a range of psychological (185, 487, 488), social (160, 184), cognitive (489), functional (162), genetic (490, 491) and lifestyle factors (492), reflecting the biopsychosocial view of pain (76, 493). Pain is also influenced by the patient's expectations regarding the future pain intensity or treatment outcome (494-497). As a result, patients can react very different to the same pain stimulus (498, 499), which can directly influence the reporting of pain.

The selection of visual trajectory is likely influenced by affective dimensions of pain (unpleasantness) (165, 480). As described by Price and Harkins (500): "when thinking about listening to music, pain intensity can be thought of as the volume of the music, and pain unpleasantness can be likened to how much one likes or dislikes the music". In other words, a certain pain intensity can be interpreted as

being of high importance in one setting, and therefore more memorable (484, 501, 502), while in a different setting or mental state it can be considered of low importance. The individual interpretation and experience of pain combined with the importance of the experienced pain is therefore likely to influence the patient's description of the pain and selection of a retrospective pain trajectory. This is also illustrated in results from recent studies on low back pain flares, showing that a flare is not necessarily the same as an increase in pain intensity, and vice versa (287-289, 291, 292).

It is also important to consider that the data used to describe patients pain trajectories and clinical course characteristics in our study are based on pain intensity measured on a pain scale. These single measures of pain have been shown to be just as vulnerable to influence by the factors mentioned above as the selection of visual trajectories (274, 275, 296, 455, 503), and the interpretation of the results can therefore be difficult. However, the SMS-based classifications used in our study appear to give a good indication of the temporal aspects of pain. The visual trajectories, on the other hand, appear to not only represent the patients' clinical course of pain. Rather, they likely give an indication to what degree the patient has experienced is at an acceptable or tolerable level or not (277, 504). It has been suggested to use descriptions like 'no worse than mild pain' instead of 'no pain' or 'mild pain', since the latter two are cutoffs that patients might struggle with (216-219). This might be more suitable descriptions of the definitions for the SMS-based patterns as well as for the visual trajectories.

Given the small differences found between neck, mid-back, and low back pain, our study can add to the debate regarding how to subgroup and treat patients' spinal pain (70, 113, 505). Should patients be treated according to spinal regions (diagnosis), or are the similarities between the regions such that patients with low back, mid-back, and neck pain can be treated as one? Recent studies have advocated that focusing on musculoskeletal regions as one entity rather than separate entities will improve patient-centered care (70, 505). Nevertheless, both lumping patients into one spinal group and splitting into diagnosis carries with it advantages and risks. Merging spinal regions into one group runs the risk of clustering important pathoanatomic, genetic, or psychosocial factors that might be distinct for the specific spinal region. Still, as with previous studies (68, 194, 195, 315), the clinical course patterns and subgroups in our study did not represent patients that were distinctly different. On the other hand, splitting patients into complex classification systems based on diagnosis might be one reason for the discrepancy between the treatment effect reported in studies and what clinicians themselves report (155). Also, important similarities between regions can easily be missed (506). Our findings strengthen the evidence for the resemblances found in the clinical course of pain between the three spinal regions (63, 69, 73, 148, 153). In addition, patients with spinal pain share similar risk and prognostic factors (146-152) and the spinal regions are frequently comorbid (142-145). They also share approaches for assessment and management (38, 39, 140, 141). As the primary goal of treatment is to achieve optimal

care for the individual patient, lumping patients with spinal pain might reveal subgroups that respond better to care (39, 505, 507).

5 Clinical implications and future considerations

This thesis has furthered the insight into classifying and describing pain trajectories and subgrouping of neck pain patients. Our study has identified issues on the fluctuating and episodic nature of neck pain as well as the difficulty differentiating mild pain from recovery. Subgrouping was primarily introduced with purpose to improve treatment and thereby prevent pain to become chronic. However, it is still debated whether subgrouping patients is useful or not in clinical and/or research settings (128, 508, 509). Our findings indicate that subgrouping based on the course of pain can be useful as part in the puzzle to prevent chronic pain conditions and improve low treatment effect, as well as developing more targeted treatment. Results from this thesis can be useful both in clinical practice and future research in several ways, as described below.

Clinical implications

Knowledge about common pain trajectories found in neck pain patients, may be helpful for clinicians in patient management and communication. Although our findings have added to this knowledge, it still remains to develop treatments and/or treatment plans for the different subgroups, which is an important next step in future studies. Nevertheless, recognizing the large variation in pain intensity and duration over time, and that full recovery is rare, is important to consider when clinicians plan treatment of patients with neck pain. Furthermore, as psychological and social factors appear to be equal, or perhaps even more significant to the pain experience compared to physical factors (167, 480, 510). Informing patients that persistent and recurrent pain is common can help patients understand that their neck pain is legitimate and recognized. Furthermore, providing insight regarding the clinical course of neck pain and using the visual trajectories can help focus the dialogue and language used by clinicians. The visual trajectories may also serve as a tool to increase the patient involvement in decisions regarding prognosis and intervention. This may also help patients learn to better handle the fluctuating, and often unpredictable, nature of pain.

Future considerations

The results from this thesis support previous studies in that the clinical course of pain are similar in neck and low back pain patients (63, 68). This may indicate that the research and clinical experience on prognosis and interventions can be transferred between spinal regions and may be helpful in development of better treatment options for patients. It may also be unnecessary to split spinal pain into different regions in future studies. As a result, recruitment of patients into studies can be easier

and this can potentially increase sample size. However, whether lumping or splitting spinal pain is the best way forward needs to be studied further.

Our findings on the fluctuating and episodic nature of pain indicate that outcomes in future studies should include the temporal aspect of pain. Avoiding doing this may result in participants being wrongly included in or excluded from clinical studies. It may also introduce error in treatment effect sizes, as participants may be misclassified. One option is to explore the usefulness of the visual trajectory pattern questionnaire instead of simple pain intensity or duration as inclusion criterium and could be an important next step in subgroup research.

Additional studies on the ideal frequency and follow-up period, in order to identify the most representative clinical course for the actual research purpose, is needed. Using Apps rather than SMS' introduces the possibility for data on more comprehensive pain constructs. A composite score from a combination of pain domains can offer a more extensive assessment of the clinical course of pain (160, 511, 512). One possible benefit might be that the complexity of pain is better captured. This may enable the exploration of concurrent or temporally lagged relationships between pain intensity and connected pain-constructs (like psychological factors, fear avoidance or catastrophizing, or activity limitations). Furthermore, it may reveal factors that can be targeted with interventions and/or advices, which could be of great clinical benefit. Still, there is little agreement regarding which dimensions to include or combine, nor on the selection of measurement tools and cutoff points. This needs to be studied further.

Our results indicate that the terminology, the operationalized subgroups, and the visual trajectory pattern questionnaire would probably benefit from further refinement. Additional investigation is needed to determine if all four pain intensity levels are necessary, and whether the single episode pattern is clinically relevant. The patients' selected visual trajectory, in particular the single episode visual trajectory, most closely resembled the patients' clinical course the last quarter compared to the full year. Therefore, the role of recall bias on the pain experience, and in particular on the selection of visual trajectories, needs further study. Furthermore, the vast majority of patients, treated by chiropractors for non-specific neck pain, do not recover from their neck pain during a 1-year follow-up. It would be of interest to investigate closer the meaning of 'recovered' and 'pain-free' in terms of defining and determining the clinical course. Moreover, development and testing of alternative terminology to 'recovered' or 'pain-free' need to be investigated further, as these terms appear to be interpreted differently between individuals.

Previously, studies have reported that maintenance chiropractic care reduces the number of days with pain in one year, as well as being a cost-effective treatment plan (49, 51, 52). However, little is known whether and eventually how treatment can alter patient's pain trajectory. One may hypothesize that

interventions may reduce the frequency and duration of pain episodes. Intervention may also result in a reduction in pain intensity for patients with persistent fluctuating pain. A time-series analysis assessing pain intensity in the periods immediately before and after each treatment might shed light on this and serve as basis for future studies in development of treatments tailored to the different pain trajectories. Furthermore, the relationship, if any, between patients' pain trajectory and treatment response needs to be investigated. This may open for possibilities of trajectories as treatment effect modifiers.

There is an increase in research aiming at identifying phenotypes from prognostic studies (93, 154), with intention to provide tools for stratifying patients for treatment types and treatment frequency. It would be of interest to study if there is a relationship between phenotypes, based on clinical and patient characteristics measured at baseline, and pain trajectories, and whether phenotypes can predict future pain trajectories. In addition, future studies should assess the usefulness of introducing pain trajectories, ideally with visual trajectories, to phenotype and stratification development, by adding the patients' clinical course to the model. Using that knowledge to develop interventions specifically targeted to those findings would be of great benefit in clinical practice.

Lastly, the individual variability found in common pain trajectories; should future discussions continue to focus on, and try to, resolve this variability? This would probably give more, and smaller, subgroups. However, as found in this thesis, a higher number of subgroups might not increase in the relevance and applicability for either research or clinic. This leaves us with the question: is this simply a variability that we have to live with?

6 Conclusion

Our results challenge the concept 'chronic pain' and provide insights into how individual patients report their clinical course of neck pain, both prospectively and retrospectively. We found that neck pain patients in chiropractic practice reported pain that was mainly either persistent fluctuating or episodic in nature. Patients with persistent fluctuating pain reported a more stable course of pain. They were also most affected by their pain, both in terms of reduced function and increased psychological distress. In addition, these patients selected a visual trajectory after 1 year that largely resembled the details of their reported weekly pain, as well as their SMS-based classified pattern. In contrast, patients classified as having an episodic pain trajectory reported large variations in duration of both painful and pain-free periods. These patients also appeared to have more difficulties identifying their pain the past year based on the visual trajectory questionnaire. Surprisingly, steady, persistent pain and long-term recovery was almost non-existent in this cohort followed over one year.

Standardized definitions of subgroups, based on low back patients, fit readily to our cohort of neck pain patients in chiropractic practice. Moreover, the distributions and patient characteristics for the two

cohorts were generally similar. Our results support previous findings that pain trajectories appear to represent patients that differ in characteristics on several health domains. Further, the selection of visual trajectories generally reflected patients' SMS-based subgroup classification and previous clinical course on a group level. Our findings lend support to previous suggestions that neck and low back pain share the same pain trajectories, as well as similar baseline characteristics associated with the various pain trajectories.

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Neck pain patterns and subgrouping based on weekly SMS-derived trajectories

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Abstract

Background: Neck and low back pain represent dynamic conditions that change over time, often with an initial improvement after the onset of a new episode, followed by flare-ups or variations in intensity. Pain trajectories were previously defined based on longitudinal studies of temporal patterns and pain intensity of individuals with low back pain. In this study, we aimed to 1) investigate if the defined patterns and subgroups for low back pain were applicable to neck pain patients in chiropractic practice, 2) explore the robustness of the defined patterns, and 3) investigate if patients within the various patterns differ concerning characteristics and clinical findings.

Methods: Prospective cohort study including 1208 neck pain patients from chiropractic practice. Patients responded to weekly SMS-questions about pain intensity and frequency over 43 weeks. We categorized individual responses into four main patterns based on number of days with pain and variations in pain intensity, and subdivided each into four subgroups based on pain intensity, resulting in 16 trajectory subgroups. We compared baseline characteristics and clinical findings between patterns and between Persistent fluctuating and Episodic subgroups.

Results: All but two patients could be classified into one of the 16 subgroups, with 94% in the Persistent fluctuating or Episodic patterns. In the largest subgroup, "Mild Persistent fluctuating" (25%), mean (SD) pain intensity was 3.4 (0.6) and mean days with pain 130. Patients grouped as "Moderate Episodic" (24%) reported a mean pain intensity of 2.7 (0.6) and 39 days with pain. Eight of the 16 subgroups each contained less than 1% of the cohort. Patients in the Persistent fluctuating pattern scored higher than the other patterns in terms of reduced function and psychosocial factors.

Conclusions: The same subgroups seem to fit neck and low back pain patients, with pain that typically persists and varies in intensity or is episodic. Patients in a Persistent fluctuating pattern are more bothered by their pain than those in other patterns. The low back pain definitions can be used on patients with neck pain, but with the majority of patients classified into 8 subgroups, there seems to be a redundancy in the original model.

Keywords: Neck pain, Clinical course, Subgroup, Longitudinal, Episodes, Fluctuations, Chiropractic, Back pain

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Background

Neck pain (NP) and low back pain (LBP) are costly, common, and among the health conditions with the highest impact on disability across the world [1]. Evidence on the clinical course of spinal pain challenges the common understanding of spinal pain defined as acute, sub-acute or chronic conditions [2], and being categorized as recovered or non-recovered [3, 4]. Instead, spinal pain seems to represent dynamic conditions that change over time. In reality, the clinical course is mostly characterized by an initial improvement after the onset of a new episode, followed by flare-ups or more persistent patterns of variations in intensity or episodes [5–8].

In a review paper, a collaborative group of LBP researchers concluded that trajectory studies on LBP are numerous and have identified similar trajectory patterns [2]. From a theoretical standpoint, it is difficult to see that future studies will uncover considerable changes in existing trajectories. However, facilitating common terminology and categorization criteria for the patterns and subgroups will help promote consistency in the field of subgroup research. Also, there is a need for assessments on the number of classes that are clinically useful and recognizable. The collaborative group advised that focus should be on subgroups constructed on a combination of pain variation patterns, pain intensity, and speed of improvement based on previously identified trajectories [2]. To further investigate the usefulness of these variation patterns, it was also recommended to test whether the findings on LBP are similar across cohorts and conditions.

Kongsted and coworkers defined 16 subgroups based on two of the suggested constructs: pain variability and pain intensity, by outlining 4 standardized definitions of variation patterns (Ongoing, Fluctuating, Episodic and Single episode) [9]. These 4 patterns were further separated into 16 subgroups based on pain intensity levels (Severe, Moderate, Mild and Minor), and subsequently applied to a Danish cohort with LBP [9]. Classifications of patients using these definitions matched well with latent class analysis-derived trajectory patterns from the same cohort.

The definitions have so far only been applied to LBP patients. There are only two clinical course studies on NP for comparison [6, 10]. This limits the possibility of producing similar collaborative definitions as for LBP. However, previous studies show similarities between the clinical course of NP and LBP [5, 6, 11]. In addition, patients with NP and LBP have several similarities in psychosocial prognostic factors and comorbidities, clinical guidelines for best practice, and lack of specific pathoanatomic causality [11–14]. While the models for clinical management of musculoskeletal complaints to date have mainly been condition specific, there have recently been calls for management based on characteristics within the biopsychosocial model regardless of pain condition [14–17]. Studies have also demonstrated that patients with trajectories of NP display similar on most health-related factors as for LBP [5, 6]. Thus, as a next step in subgroup development it is important to examine how well the definitions based on LBP will fit in a NP cohort, and if the group of patients in the patterns differ with regards to clinical characteristics.

The objectives of this study were to 1) investigate if the defined patterns and subgroups for LBP are applicable to NP patients in chiropractic practice, 2) explore the robustness of the defined subgroups, and 3) investigate if the patients in the defined patterns or subgroups differ with respect to baseline characteristics and clinical findings.

Methods

Study design and setting

This study was part of a prospective, observational study on patients with NP in chiropractic care setting. Members of the Norwegian Chiropractic Association were invited to participate in the recruitment of patients. We asked seventy-two chiropractors geographically spread in Norway to invite all consecutive patients with NP from September 2015 until June 2016 to participate in the study. The chiropractors gave interested patients written and verbal information about the study. Patients that accepted to participate signed a written consent. The study was approved by The Norwegian Regional Committees for Medical and Health Research Ethics (2015/89).

We invited patients aged 18 years or more presenting with, or already in a treatment course for, a bothersome neck as a primary or secondary complaint with or without radiating arm pain to participate. They were eligible for inclusion regardless of pain duration and time since last chiropractic treatment. Patients had to possess and be able to operate a mobile phone and have basic Norwegian reading and writing skills. They were not included if serious pathology was suspected (inflammatory or pathological cause, fracture, or radiating pain requiring acute surgery). All patients received standard chiropractic care at the discretion of the chiropractor, unaffected by inclusion in the study.

Data collection

Patients completed a self-administered questionnaire at baseline, 4, 12, and at 52 weeks, either on paper or digitally. The present study used questionnaire data from baseline. Additional descriptions of recruitment of the cohort, the procedures and the questionnaires have been published previously [18, 19]. A researcher (PI or BLM) or an assistant contacted the patients by telephone to provide further information regarding the study

procedures. Once a week, at the same day and time over a 52-week period, the patients received 2–3 automated short message services (SMS) with the following questions (Additional file 1): "How many days the last week has your neck been bothersome? Please answer with a number between 0 and 7" (hereafter 'paindays'). If the answer to the first SMS was 0, question 2 was not sent. If the answer was between 1 and 7, the patient received a second SMS "How intense has your neck pain typically been the last week? 0= no bother, 10= worst bother imaginable" (hereafter 'pain intensity'). A third SMS was sent to all patients "How many days the last week has your neck limited your daily activities? Please answer with a number between 0 and 7." If the patient failed to answer the weekly SMS, they received a reminder after 2 days. The patient received a verbal reminder by telephone should they miss answering two consecutive weekly SMS.

Patient reported baseline variables

Baseline questionnaire (Additional file 2) included age, gender, education level (Primary school, High school, University/higher education ≤4 years, University/higher education > 4 years), as well as paid employment (yes/no), on sick-leave (yes/no), and daily dysfunction ("In your usual daily activities, how much trouble do you have from your neck complaints?" score ranging from 0 = no trouble to 10 = maximal trouble) [20]. Pain intensity was reported as "pain right now" on an 11-point numerical rating scale (NRS, 0–10, where 0 = no pain and 10 = as painful as it is possible to be) [21]. Disability was measured by the Neck Disability Index (NDI) (0 = no impairment to 50 = complete impairment) [22]. The 10 question version of Örebro Musculoskeletal Pain Questionnaire (ÖMPQ) was used for psychosocial screening (0–100), where a higher score is associated with higher risk [23]. General health status was measured on a 0–100 point VAS scale [24], and psychological state and distress was calculated as an average score on the Hopkins Symptom Checklist (HSCL-10) (scores from 1 = not bothered at all, to 4 = very much bothered) [25]. We used a cut-off value above 1.85, which has been proposed for the presence of psychological distress in a Norwegian population [26]. Concomitant musculoskeletal pain was reported by the Nordic Pain Questionnaire (NPQ) [27] and used as follows: Headache (yes/no), low back pain (yes/no), and number of pain sites ≥3 out of 10 (yes/no). Additionally, information regarding pain duration of current NP (0–2 weeks, 2–4 weeks, 1–3 months, 3–6 months, 6 months–1 year, > 1 year), first-time consultation with chiropractor (yes/no), acute onset of pain (yes/no), previous episodes (0, 1–2, and ≥ 3) was collected.

Data handling

We replicated all data handling, descriptive definitions of subgroups, protocol and coding described below in accordance with the procedures in the Danish LBP cohort [9]. First, we calculated the mean pain intensity and mean paindays from the weekly SMS across the 43 weeks for each patient. This formed the basis for defining the clinical course and the subsequent subgrouping. We subsequently calculated the number of weeks and frequency with deviations of ±1 from the mean pain intensity, as well as the duration and frequency of pain-free weeks. To ensure the best possible comparison between the two studies and the possibility to analyze patterns during the more stable period, we excluded data collected in the first 9 weeks as in the Danish study. Hence, the study period was 43 weeks from week 10 to week 52 in the follow-up.

We imputated missing values on the weekly pain intensity measures in three stages as follows: [1] we replaced missing responses in week 10 (the first week included in the present study) by the equivalent values in week 11 if these were not missing, and similarly, missing responses in week 52 were replaced by the values reported in week 51, [2] we replaced one-week and two-week gaps between weeks with the same pain intensity, with that same value [3]; we excluded from the analysis and categorized patients who after steps 1 and 2 had less than 20 complete responses out of 43 as missing .

Categorization into patterns and subgroups

Details of the definitions of patterns and subgroups are shown in Table 1. We modified the nomenclature of the Fluctuating pattern from the original study to improve the understanding. This resulted in four main patterns based on temporal pain variation (hereafter 'pattern'): Ongoing, Persistent fluctuating, Episodic, and Single episode. Ongoing pattern was the only pattern where the actual number of days with pain per week was defined. Further, patients in the Ongoing pattern should have a variation in pain intensity not exceeding ±1 from the mean value each week. In the Persistent fluctuating pattern, patients should have no pain-free periods of four weeks or more, and variation from the mean pain had to exceed ±1. Patients in the Episodic pain pattern should have pain-free periods of minimum four consecutive weeks between periods with pain. The latter definition was based on previously suggested definitions by de Vet et al., where an episode of LBP is defined as a period of pain lasting more than 24 h, preceded and followed by at least four pain free weeks. Patients with a Single episode could have only one episode lasting 1–2 weeks during the study period. In the present study, the single episode was defined as a short flare-up anywhere during the study period (i.e. after week 9). In addition, the Single

Table 1 Definitions of 4 the main patterns and 16 predefined trajectory subgroups used for analysis as presented in Kongsted et al. [9]

Pattern	Subgroup label	Variation Days	Variation Intensity	Intensity level
ONGOING	1. Severe	> 4 days with NP each week	Intensity stays within +/− 1 of mean value	Mean intensity ≥6
	2. Moderate	> 4 days with NP each week	Intensity stays within +/− 1 of mean value	Mean intensity ≥4 and < 6
	3. Mild	> 4 days with NP each week	Intensity stays within +/− 1 of mean value	Mean intensity ≥2 and < 4
	4. Minor/ recovery	- no pain-free 4-weeks periods *or* - always pain = 0 (recovered)	Intensity stays within +/− 1 of mean value	Mean intensity < 2
PERSISTENT FLUCTUATING	5. Severe	No pain-free 4-weeks periods	Difference between mean and min or max value exceeds 1	Mean intensity ≥6
	6. Moderate	No pain-free 4-weeks periods	Difference between mean and min or max value exceeds 1	Mean intensity ≥4 and < 6
	7. Mild	No pain-free 4-weeks periods	Difference between mean and min or max value exceeds 1	Mean intensity ≥2 and < 4
	8. Minor	No pain-free 4-weeks periods	Difference between mean and min or max value exceeds 1	Mean intensity < 2
EPISODIC	9. Severe	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.		Max intensity ≥6
	10. Moderate	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.		Max intensity ≥4 and < 6
	11. Mild	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.		Max intensity ≥2 and < 4
	12. Minor	Pain-free periods of min. 4 weeks in a row, but not always pain = 0. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.		Max intensity < 2
SINGLE EPISODE	13. Severe	One single episode or flare-up lasting 1–2 weeks (which are not the first or the last week of measurement)		Max intensity ≥6
	14. Moderate	One single episode or flare-up lasting 1–2 weeks (which are not the first or the last week of measurement)		Max intensity ≥4 and < 6
	15. Mild	One single episode or flare-up lasting 1–2 weeks (which are not the first or the last week of measurement)		Max intensity ≥2 and < 4
	16. Minor	One single episode or flare-up lasting 1–2 weeks (which are not the first or the last week of measurement)		Max intensity < 2

episode could not be at the beginning or the end of the study period, as the duration of the episode prior to week 10 or after week 52 would be uncertain.

We split each of the four main patterns into 4 subgroups based on mean (Ongoing and Persistent fluctuating patterns) or maximum (Episodic and Single episode patterns) pain intensity across the 43 weeks: Severe (pain intensity ≥6), Moderate (4 ≤ pain intensity < 6), Mild (2 ≤ pain intensity < 4), and Minor (pain intensity < 2). As Ongoing and Persistent fluctuating patterns are characterized by few or no pain-free weeks, we divided them into intensity subgroups based on deviation from mean pain intensity, with Persistent fluctuating displaying larger variation. In contrast, Episodic and Single episode patterns are characterized by pain episode(s) between pain-free periods, where the highest maximum pain of the episode(s) would better describe the severity of the episode(s) reported during the study period. This resulted in 16 different subgroups in total, and we classified the patients into one of these. The "Minor Ongoing/recovered" subgroup also contained patients that scored zero on pain intensity every week. In addition, we repeated the procedure and classified only the patients recruited at first-time consultation into the same subgroups. We did the latter to assess if these patients distributed differently into the subgroups compared to the whole cohort.

To describe how the pain differed between the subgroups we also calculated mean pain intensity and mean paindays across only the weeks when pain was present, as well as the total number of days and weeks with pain in each subgroup. In addition, we calculated and described the frequency and size of the absolute deviation from the mean pain and the duration and frequency of pain-free periods for the Persistent fluctuating and Episodic patterns.

Statistical analysis

Descriptive analyses are presented as means with standard deviations (SD) and medians with interquartile range (IQR) or range, for normal and not normal distributed continuous variables, respectively. Categorical data are presented with frequencies and percentages. In addition to the description of the characteristics of the patients in the four main patterns, we made a further distinction between the patients in the eight Persistent fluctuating and Episodic subgroups. We used Chi-square test and Fisher exact test to compare baseline data between patters and subgroups for categorical data. Furthermore, we used Dunn's post-hoc pairwise comparison test [28] and Bonferroni-Holm correction [29] for comparisons between the four patterns. T-tests were used for the comparison of continuous baseline data between the subgroups with the same intensity level (such as between Severe Persistent fluctuating and Severe Episodic) within the Persistent fluctuating and Episodic patterns. We also used ANOVA with Bonferroni post-hoc pairwise comparison tests for evaluation of continuous baseline data between the four patterns. For all comparisons, $p < 0.05$ was considered statistically significant (two-sided).

Robustness to inclusion criteria and pattern definitions

We also made a separate analysis for the patients recruited at first-time consultation to examine if they distributed differently from the cohort, and to assess if our inclusion criteria influenced possible differences in distribution. We did similarly with the inclusion criteria, where we changed the criteria from a minimum of 20 to 10 answers out of 43 SMS. In addition, we repeated the t-test analyses comparing the characteristics of Persistent fluctuating and Episodic subgroups after reducing the Episodic definition of pain-free duration between NP episodes from 4-weeks to 2-weeks, as the subgroups differed only on duration of pain-free periods. We considered the patterns to be robust if the distribution did not change appreciably with inclusion of only the first-time consultation patients.

All analyses were carried out using STATA 16 (StataCorp, Texas, USA).

Results

A total of 1478 patients consented to participate. One patient withdrew the consent, one was excluded due to being diagnosed with severe pathology after seven weeks of participation, and seven patients did not receive any SMS for unknown reasons. Two-hundred and sixty-one (18%) patients responded to less than 20 SMS follow-ups, and we excluded them from the analyses (the excluded cohort) (Fig. 1). Thus, 1208 patients were available for subgroup analyses. Baseline questionnaires were available from 1150 of these (the study cohort) and from 163 of the excluded cohort.

The patients in the study cohort had a mean (SD) age of 44 [15] years and 74% were female (Table 2). The majority of the patients had experienced NP periods previously and were in an ongoing treatment course. The most common comorbidities were headache, radiating pain to upper extremity, and LBP.

The patients in the excluded cohort were younger and slightly more severely affected in terms of disability (NDI) and scored higher on psychosocial screening (Örebro). They did not differ substantially on other parameters (Table 2).

There was an overall high response rate (81–84%), and 55% ($n = 663$) completed all SMS-answers. Eleven percent ($n = 135$) had no pain-free weeks throughout the study period, and 25% ($n = 301$) had no pain-free period lasting more than one week.

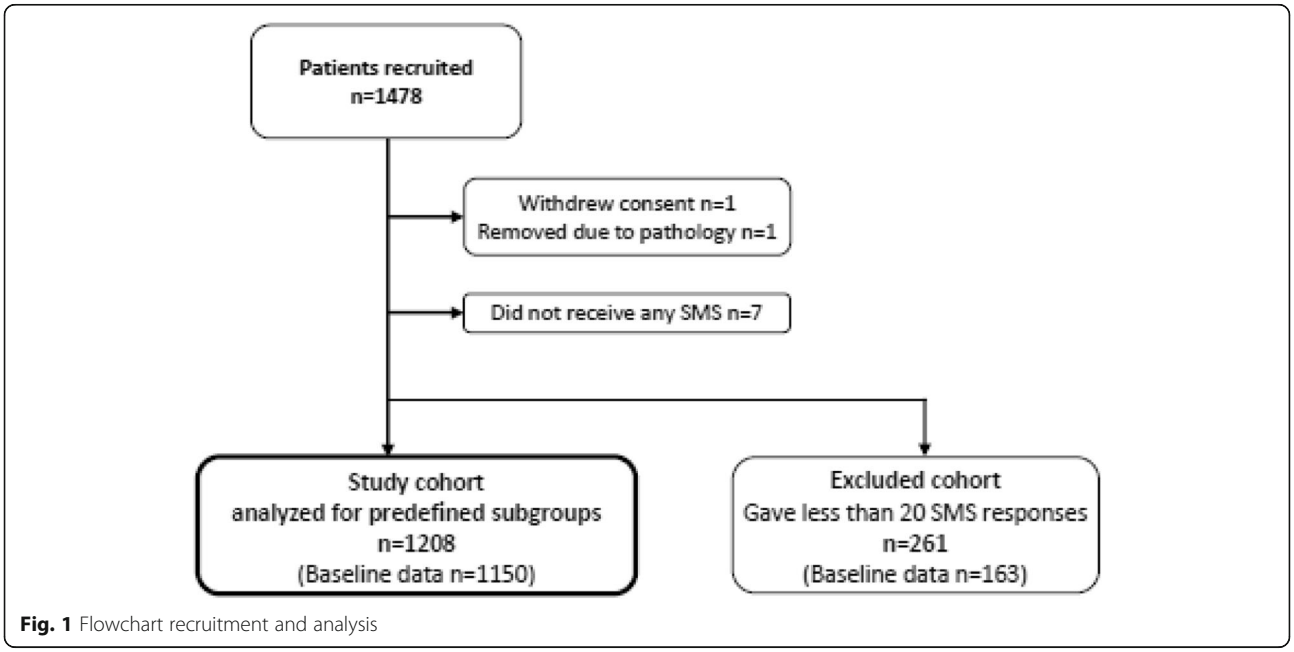

Fig. 1 Flowchart recruitment and analysis

Table 2 Characteristics and clinical findings of patients at baseline

Characteristics	Study cohort *n* = 1150		Excluded cohort *n* = 163	
	n (%)	Mean (SD)	n (%)	Mean (SD)
Age Mean (SD) [range 18–85]		44 (13)		41 (14)
Females	847 (74)		121 (75)	
Radiating pain	859 (76)		127 (79)	
Headache	810 (72)		126 (78)	
Concomitant low back pain	602 (53)		91 (56)	
Number of previous NP episodes				
0	161 (14)		25 (15)	
1–2	197 (17)		24 (15)	
≥3	791 (69)		113 (70)	
First-time consultation with chiropractor	186 (17)		35 (23)	
Duration of NP				
< 1 month	263 (23)		35 (21)	
1–3 months	161 (14)		30 (19)	
> 3 months	710 (63)		97 (60)	
Baseline intensity of NP (NRS 0–10)		4.1 (2.3)		4.5 (2.1)
Disability - NDI (0–50)		12 (6.7)		16 (6.6)
Psychosocial screening - ÖMPQ (0–100)		39 (16)		44 (15)
Psychological distress - HSCL-10 (1–4)		1.6 (0.5)		1.7 (0.5)
General health (VAS 0–100)		71 (19)		69 (21)

SD Standard Deviation, *NP* Neck pain, *NRS* Numeric rating scale, *NDI* Neck Disability Index, *ÖMPQ* Örebro Musculoskeletal Pain Questionnaire, *HSCL-10* Hopkins Symptom Checklist-10

Table 3 Distribution of patients in the defined variation patterns and subgroups

Defined patterns and subgroups	Prevalence $n = 1206$	Number of weeks with pain (0–43)	Number of days with pain per week, in weeks with any pain, (0–7)	Pain intensity in weeks with any pain, (0–10)	Total number of days with pain during 43 weeks, (0–301)	
	n (%)	Median (IQR)	Mean (SD)	Mean (SD)	Mean (SD)	Range
Ongoing						
1 Severe	1 (0.1)	22	7.0 (0)	6.0 (0)	161 (0)	–
2 Moderate	1 (0.1)	40	7.0 (0)	5.0 (0)	280 (0)	–
3 Mild	0 (0)	–	–	–	–	–
4 Minor/ recovered	49 (4.1)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0
Total Ongoing	51 (4.2)	0 (0–0)	7.0 (0)	5.5 (0.7)	4.5 (36)	0–280
Persistent fluctuating						
5 Severe	54 (4.5)	43 (40–44)	6.0 (1.0)	7.2 (0.9)	252 (51)	116–301
6 Moderate	185 (15.4)	43 (39–44)	4.5 (1.5)	5.0 (0.6)	182 (68)	50–301
7 Mild	298 (25.0)	40 (34–43)	3.3 (1.4)	3.4 (0.6)	130 (66)	29–301
8 Minor	45 (3.9)	34 (26–40)	2.6 (1.4)	2.0 (0.5)	87 (68)	20–301
Total Persistent fluctuating	582 (48.3)	41 (35–43)	3.9 (1.7)	4.1 (1.4)	148 (75)	20–301
Episodic						
9 Severe	276 (22.6)	20 (13–27)	2.9 (1.1)	3.9 (1.0)	59 (40)	5–217
10 Moderate	174 (13.9)	14 (8–22)	2.4 (0.9)	2.7 (0.6)	39 (29)	3–153
11 Mild	88 (7.3)	11 (6–18)	2.0 (1.1)	1.9 (0.5)	29 (33)	2–252
12 Minor	9 (0.8)	3 (3–12)	1.5 (0.5)	1.0 (0.0)	13 (13)	1–42
Total Episodic	547 (45.4)	17 (9–25)	2.6 (1.1)	3.2 (1.2)	47 (36)	1–252
Single episode						
13 Severe	5 (0.4)	1 (1–1)	3.4 (1.5)	5.8 (1.1)	4.8 (2.6)	1–8
14 Moderate	11 (0.9)	1 (1–2)	2.5 (1.7)	4.0 (0.5)	4.0 (3.6)	1–14
15 Mild	7 (0.6)	1 (1–1)	2.1 (1.2)	2.4 (0.5)	2.3 (1.1)	1–4
16 Minor	3 (0.3)	1 (1–1)	1.0 (0.0)	1.0 (0.0)	1.0 (0.0)	1–1
Total Single episode	26 (2.2)	1 (1–1)	2.5 (1.5)	3.6 (1.6)	3.7 (2.8)	1–14

IQR Interquartile range, *SD* Standard deviation
No patients were distributed into the Mild Ongoing subgroup. All patients in the Minor Ongoing/Recovered subgroup were recovered and as such had no days with pain per week and a mean NRS = 0

Distribution of NP patients into the defined patterns and subgroups

All but two patients could be classified into one of the defined patterns based on pain intensity and paindays (Table 3). The most common patterns were Persistent fluctuating (48%), and Episodic (45%). The majority of the remaining patients were in the recovered part of the Ongoing/Recovered pattern (4%; all with NRS = 0 each week).

Figure 2 illustrates individual trajectory examples for each of the 16 subgroups. Twenty-five percent of the cohort were classified into the "Mild Persistent fluctuating"

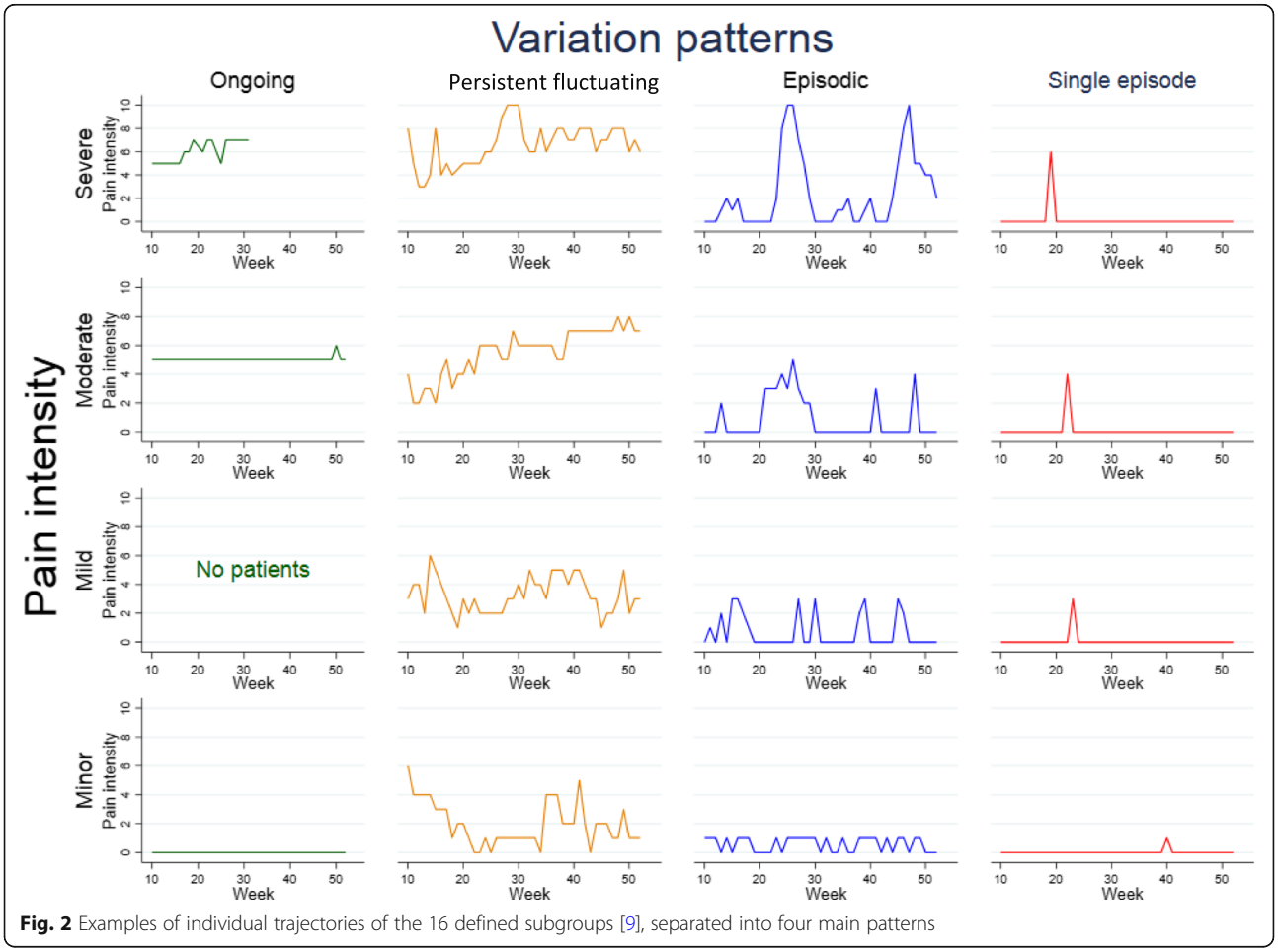

Fig. 2 Examples of individual trajectories of the 16 defined subgroups [9], separated into four main patterns

subgroup, with a mean (SD) pain intensity of 3.4 (0.6) in weeks with pain and a mean (SD) total number of days with pain of 130 (66) (Table 3). The second most common subgroup was "Severe Episodic" (22%), with a mean (SD) pain intensity of 3.9 (1.0), and a mean (SD) total number of days with pain of 58 [30].

Exploring characteristics of the patterns

In weeks when pain was present, patients in the Persistent fluctuating patterns reported a higher total number of days with pain, and higher mean pain intensity than patients in the Episodic patterns (Table 3). Patients with pain every week were almost exclusively in the Persistent fluctuating pattern (99.8%). They had smaller variations in pain intensity, but more frequent than those in the Episodic pattern (mean (SD) 1.9 (0.5) vs 2.4 (0.8) points); frequency 18 (range 12-25) vs 13 (range 6-22), respectively).

The Persistent fluctuating and Episodic patterns included significantly more female patients (76 and 74% respectively, $p \leq 0.001$), patients with pain duration above one month, and less first-time consultation patients. Patients in the Persistent fluctuating pattern scored significantly lower on general health (VAS 66/100), and higher on all other sociodemographic (apart from age and sick leave) and clinical factors than the other three patterns ($p \leq 0.006$) (Table 4).

Patients in the Persistent fluctuating subgroups scored higher on NDI and HSCL-10 across all intensity levels ($p < 0.01$), apart from the Minor subgroups on HSCL-10 ($p = 0.29$). The proportion of patients above the HSCL-10 cut-off ranged from 55.1% (CI 41.2–69.0) in the Severe Persistent fluctuating subgroup to 23.3% (CI 10.1–35.9) in the Minor Persistent fluctuating subgroup (Table 4).

Robustness to inclusion criteria and pattern definitions

When limiting the analyses to patients recruited at their first-time consultation with chiropractor for NP ($n = 186$), a slightly lower percentage of patients were classified into the Persistent fluctuating pattern (41.4%) compared to the whole study cohort (48.3%) (Supplementary Table 1, Additional file 3). When we changed the exclusion criteria from responses to minimum 20 to 10 out of 43 SMS, we could have included 42 (3.5%) more patients. There change in distribution was minimal (see Supplementary Table 1, Additional file 3).

Table 4 Baseline characteristics and clinical findings of patients in the four variation patterns, and eight subgroups of the Persistent fluctuating and Episodic variation patterns

Main patterns and subgroups NP variables	Ongoing/ Recovered *n* = 45 (3.9%)	Persistent fluctuating *n* = 569 (49.5%)	Episodic *n* = 513 (44.6%)	Single episode *n* = 23 (2.0%)
Age, mean (SD)	47 (16)	45 (13)	44 (12)	41 (13)
Female, n (%)	22 (49)	**424 (76)**[a]	**386 (74)**[a]	14 (61)
Currently on sick leave, n (%)	1 (2.2)	34 (6.1)	26 (5.0)	0 (0)
First episode, n (%)	19 (42)	**53 (10)**[a]	**79 (15)**[a]	9 (39)
Duration > 1 month, n (%)	18 (42)	**484 (88)**[a]	**356 (69)**[a]	11 (50)
> 3 previous episodes, n (%)	14 (31)	**449 (81)**[b]	321 (62)	7 (30)
Concomitant LBP, n (%)	13 (30)	**342 (62)**[b]	240 (47)	6 (27)
Headache, n (%)	18 (42)	**447 (81)**[b]	333 (65)	11 (50)
Pain intensity - NRS (0–10), median (IQR)	3 (1–5)	**5 (3–6)**[b]	3 (2–5)	2.5 (1–4)
Psychosocial screening – ÖMPQ Short form (0–100), mean (SD)	26 (19)	**43 (17)**[b]	33 (16)	24 (16)
General health (VAS 0–100), mean (SD)	80 (13)	**66 (20)**[b]	75 (18)	80 (14)
Psychological distress - HSCL-10, mean (SD)	1.4 (0.4)	**1.7 (0.5)**[b]	1.5 (0.5)	1.3 (0.3)
Severe		**2.0 (0.6)**[c]	1.6 (0.5)	
Moderate		**1.8 (0.5)**[c]	1.5 (0.4)	
Mild		**1.7 (0.5)**[c]	1.5 (0.5)	
Minor		1.5 (0.5)	1.4 (0.2)	
Disability – NDI, mean (SD)	5.2 (3.4)	**13.9 (6.6)**[b]	9.4 (5.9)	7.5 (4.8)
Severe		**22.5 (7.9)**[c]	11.2 (5.9)	
Moderate		**15.5 (5.9)**[c]	8.8 (6.1)	
Mild		**12.1 (5.2)**[c]	7.4 (5.0)	
Minor		**10.1 (5.7)**[c]	5.3 (2.9)	
Radiation into arm at baseline, n (%)	24 (56)	**449 (81)**[b]	371 (73)	12 (55)
Severe		41 (84)	194 (75)	
Moderate		**147 (84)**[c]	115 (70)	
Mild		228 (79)	58 (72)	
Minor		33 (75)	4 (56)	

NP, Neck pain; SD, Standard deviation; LBP, Low back pain; EQ-5D; ÖMPQ, Örebro Musculoskeletal Pain Questionnaire Short-form; IQR, Interquartile range; HSCL-10, Hopkins Symptom Checklist-10; CI, Confidence Interval, 95%; NDI, Neck disability index. [a,b,c,d]Calculated with Chi[b] and ANOVA. Results in boldface are statistically significant ($p < 0.05$) differences between: [a]Persistent fluctuating and Episodic patterns and the Ongoing and Single episode patterns respectively, but not between Persistent fluctuating and Episodic patterns, [b]Persistent fluctuating pattern and the three other patterns respectively, [c] between Persistent fluctuating and Episodic subgroups

When changing the criteria for the Episodic pattern from four to two pain-free weeks between episodes, the number of patients in the Episodic pattern increased from < 1 to 14%, and all were originally classified in a Persistent fluctuating pattern (see Supplementary Table 1, Additional file 3). When calculating the mean pain intensity and number of paindays in the first week following a pain-free period for the whole cohort, only small differences were found when altering the duration of the pain-free period from the recommended 4 weeks to any of one to twenty weeks (see Supplementary Table 2, Additional file 4).

Discussion

Using a long follow-up period and frequent measurements on a cohort of 1208 NP patients in chiropractic practice, we found that all but two patients could be classified according to the definitions derived from studies of LBP [9]. Most NP patients experienced pain that was either episodic or persistently fluctuating of mild to severe intensity. Steady, persistent pain was almost non-existing in this study cohort of NP patients. Having pain-free periods during the year of follow-up related to a more benign condition concerning dysfunction and psychological distress compared to patterns with more persistent pain.

Distribution of patterns and subgroups

Using the same pattern definitions as in the Danish LBP cohort [9], 93% of our cohort were classified into Persistent fluctuating and Episodic patterns, compared to 76% in the Danish LBP cohort (see Supplementary

Table 3, Additional file 5). In particular, the proportion of NP patients with a Persistent fluctuating pattern was larger than for LBP patients. In general, patients in both cohorts reported quite low pain intensity throughout the study period. However, severe episodic pain was frequent across both cohorts.

These moderate differences in distributions could have several causes, like differences in the two clinical pain conditions or different study designs. The Danish LBP cohort recruited patients from both chiropractic and GP clinics, while our study included chiropractic patients only. The distribution across subgroups in our cohort with NP more closely mirrored the LBP patients from the Danish GP sample [9], which had similar inclusion criteria concerning previous treatment as in our study. The Danish chiropractic sample, however, excluded patients treated by a chiropractor during the last three months prior to inclusion. When compared with our results, this exclusion seems to have reduced the number of patients with a Persistent fluctuating pattern in the Danish chiropractic sample. Even though small differences in distribution was observed between the two cohorts, we found little to no differences in pain intensity and frequency.

The follow-up period in our study differs from previous long-term studies on NP [6, 10]. We excluded the first 9 weeks after inclusion to describe the course of NP in an expectably steadier phase and thus avoid the period after recruitment that is characterized by improvement regardless of previous pain duration or treatment [31, 32]. This makes further direct comparisons between studies difficult. The two other studies identified trajectories based on rapid or slow change from baseline followed by a phase of recovery, with almost three quarters of patients in a "Recovery from mild pain" subgroup. However, where we had only 2 (0.2%) patients with a persistent high pain, the studies of Ailliet and coworkers [6] and Pico-Espinosa and coworkers [10] had to 7 and 11%, respectively. Further, they had none or very few patients in patterns characterized by episodes or persistent pain with intensity variations. It is unclear whether the different findings in the NP studies are due to population or methodological choices like treatment history, differences in sample size and frequency of missing data, or to the fact that different analytical methods are used.

Robustness of the definitions

To explore the robustness of the definitions, we repeated the classification procedure with altered criteria of the Persistent fluctuating and Episodic patterns. We also applied the definitions to only the group of patients recruited at first-time consultation, as well as to a group where the exclusion criteria was altered from 20 to 10 responses to the 43 weekly SMS. Both approaches resulted in only small differences in distribution into the subgroups.

In contrast to what is expected at the start of a new episode or flare up, there was no increase in pain intensity the first week after a pain-free period ranging from 1 to 20 weeks. In addition, as many as 14% of the patients moved from Persistent fluctuating to Episodic pattern when we changed the definition of an episode from 4 to 2-week pain-free period preceding and following an episode. This indicates that there is a need to further explore and discuss the differences between episodic pain and persistent pain with variations in intensity. The finding can be seen as support to a previously published modified Delphi approach, aiming to standardize LBP recurrence terminology, where concerns were raised about whether timeframes used in definitions of duration of pain and pain-free episodes were arbitrary [33]. The Delphi study defined an episode as follows: with pain intensity of > 2 on an 11-point NRS scale, lasting at least 24 h, and occurring at least 2 times over the past year with at least 30 days pain-free period between episodes [33]. The Episodic pattern used in our study allowed for patients to have only one episode during the follow-up, with pain lasting anything between 3 and 35 weeks. This is in contrast to results from other studies on the course of NP and LBP, where a new episode usually is much shorter and commonly lasts from 2 to 18 weeks [6, 10, 34]. In addition, the definitions used in our study distributed patients with mean pain intensity < 2 into a separate subgroup in each of the four patterns. It could therefore be argued that only 3 intensity levels should be used: Severe (pain intensity ≥6), Moderate (pain intensity 4 ≤ NRS < 6) and Mild (2 ≤ pain intensity < 4), and that patients with pain intensity < 2 should be considered as Recovered.

Our results show that, with the use of the LBP definitions, few NP patients qualified for distribution into the Single episode pattern. The usual curve of improvement from onset of an episode until a more stable pain situation is established, typically lasts 1–2 weeks [34]. For the Single episode pattern definition in our study, the pain could only last 1–2 consecutive weeks followed by completely pain-free weeks. Anything longer, and they were defined as being in the Episodic pattern. The definition criteria, combined with the follow-up period used, could possibly contribute to an increased proportion in the Episodic and decreased the Single episode patterns.

Furthermore, we have not been able to find arguments to support the decision of limiting the number of pain-days per week to at least 4 in the Ongoing pattern. Two patients in our cohort fell outside the Ongoing criteria for this reason. Both reported pain every week with pain variation of no more than ±1 from the mean, but having

few weeks with 2–4 days with pain each week. Therefore, they neither fitted the Ongoing criteria nor the Persistent fluctuating criteria.

When taking into account the results of the robustness analyses of both our study and the Danish LBP study [9], where five of our 16 subgroups contained less than 5 patients each, there seem to be redundancies in the model. The definitions need further refinement, with possibly combining the Minor subgroups as well as the Ongoing and Persistent Fluctuating patterns. There might also be an idea need to further explore the definitions with regard to number and duration of episodes in Episodic and Single Episode patterns.

Patient characteristics of patterns and subgroups

Patients in the Persistent fluctuating pattern were distinctly different from the other 3 patterns on all factors except age and sick leave. We found less differences between patients in the Episodic compared to Ongoing and Single episode patterns, apart from the first which had more females. Due to very few patients in the Ongoing and Single episode patterns, these differences should be interpreted with some caution.

Fewer patients in the Persistent fluctuating and Episodic patterns were recruited at first-time consultation, but this is to be anticipated, as these patterns are characterized as being more chronic in both persistency and flare-ups. The vast majority of the patients in the Ongoing pattern were completely recovered in the whole study period (49 out of 51 patients).

Pain intensity and health characteristics followed a similar decrease in severity gradient throughout both Persistent fluctuating and Episodic subgroups. Patients in the Persistent fluctuating subgroups were significantly more distressed and negatively affected in terms of pain, disability and psychological distress than those in the Episodic subgroups, with the exception of the Minor subgroups.

Minor subgroups contained few patients and interpretation of results with regards to those subgroups should be interpreted with caution. While many of the differences are small, the differences in NDI are all above the clinical significance of 30% [35, 36]. The differences in prevalence of high HSCL-10 scores, though statistically significant, show only a maximum 20% difference between the patterns and subgroups. Furthermore, only Severe Persistent fluctuating subgroup was considered clinically meaningful above the cut-off of 1.85, indicating psychological distress [37]. Still, NP episodes separated by periods without pain appears to have considerably less negative impact on daily life. Similar findings have previously been reported for LBP patients [11, 38, 39]. It can be discussed if trajectories and subgroups are condition and/or population specific. They might simply be characteristics of the course of musculoskeletal pain in general [12, 13, 15, 40], and serve as an initial step for decision-making in patient management, irrespective of pain-site and diagnosis [30, 41]. Regardless, our results highlight the need to customize treatment to previous and expected course of pain for patients with NP.

Whether there are different underlying pain mechanisms for these types of patterns is uncertain [42, 43]. The patients in the Persistent fluctuating pattern might represent a more inflammatory--mediated pain [44, 45], and likely to need more comprehensive, multidisciplinary care, while advice and short-term advice might suffice for patients in certain Episodic patterns. Although subgrouping is needed and called for [2, 46], it is also questioned with regard to clinical relevance and usefulness [47]. However, our study strengthens the evidence that terminology like ‘constant’ and ‘intermittent’ are somewhat misleading, as they do not differentiate on the nuances regarding the importance of variation of pain intensity, or duration and frequency of painful and pain-free episodes [48, 49]. Its immediate usefulness seem to be as basis for future studies and as a tool in communicating realistic outcomes and explain probable future course and subsequent management to patients.

Strengths and limitations

To our knowledge, this is the first study that collected data on treatment-seeking NP patients weekly over 43 weeks, providing evidence on clinical NP development over time. The cohort was large and had a wide geographical distribution. Thus, our data expectably represents NP patients treated by Norwegian chiropractors well. The response rate of SMS was high; between 81 and 84% throughout the study period. Norwegian and Danish populations appear to be rather similar, strengthening the similarities between the two cohorts for comparison purposes.

The chiropractors were asked to invite consecutive patients with NP to limit bias, but we were unable to get usable data for patients who were not invited or declined participation. Selection bias can therefore not be ruled out. We excluded 261 (18%) patients who responded to less than 20 of the 43 SMS to ensure clear-cut subgrouping without imputing data. However, the excluded group did not differ significantly from the analyzed sample suggesting that this did not have substantial influence on the results.

Future indications

Frequent measures over a long period is time consuming, expensive, and impractical for use in clinical practice. The knowledge of self-reported versus data-driven trajectories is emerging for the LBP population [50, 51], and our study has shown that the same approach can be

applied to patients with NP. Although final conclusions cannot be formed from two studies on chiropractic and GP patients, we suggest that reducing the number of subgroups seems logical. It is of clinical interest to explore whether subgroups in general can be used to prioritize patients and identify the need for different types of treatments, and whether this is, in fact, similar across spinal disorders in general.

We excluded data from the first nine weeks as they did in the Danish LBP study, to ensure the comparison of results [9]. It seems, however, relevant to explore if the initial weeks are different to what is considered a more stable period, as the pattern of recovery and relapse in the early phase is often a key factor in treatment planning and prognosis. It is also of interest to explore the stability of the patterns and subgroups over time. Do patients shift between patterns, and do factors like the duration of pain or treatment prior to recruitment influence this? In addition, our study highlights the need to further explore the individual variations in terms of the importance of the duration and frequency of pain-free episodes, as well as further investigation of the difference between duration of a Single Episode/Flare-up versus the Episodic pattern.

Conclusions

Our study was the first to use defined, standardized definitions of subgroups based on LBP patients in a cohort with NP. We found that the definitions were readily applicable to NP patients. Both NP and LBP patients report mostly low pain intensity, and are characterized by persistent pain with variations in intensity or episodic conditions with pain-free periods. Steady, persistent pain was almost non-existing in this cohort. Persistent fluctuating pain indicate a condition that scores higher than the other patterns in terms of reduced function and psychosocial factors irrespective of severity of pain intensity. Thus, neck pain and low back pain appear to share the same trajectories, with similar baseline characteristics being associated with the various trajectories for both conditions. Our results underscore the importance of using both temporal variation and pain intensity when subgrouping patients.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12891-020-03660-0.

Additional file 1. English translation weekly SMS questions.

Additional file 2. English translation baseline questionnaire.

Additional file 3: Supplementary Table 1. Distribution patterns. Distribution of NP patients into pattern and subgroups with 1) original definition criteria, 2) definition of episode duration of two weeks between pain episodes as part of analyses of robustness of pattern and subgroup definitions, 3) patients recruited at first-time consultation for their neck pain only.

Additional file 4: Supplementary Table 2. Intensity of symptoms after pain-free period. NP intensity and weekly days with pain in the first week following a pain-free period of 1 to > 20 weeks for analysis of robustness of pattern and subgroup definitions.

Additional file 5: Supplementary Table 3. Distribution NP and LBP cohort comparison. Distribution of NP cohort in the defined patterns subgroups and Danish LBP cohort from Kongsted et al. [9].

Abbreviations

SMS: Short Message Service; NP: neck pain; LBP: low back pain; NDI: Neck Disability Index; ÖMPQ: Örebro Musculoskeletal Pain Questionnaire Short-form; VAS: visual analogue scale; NPQ: Nordic Pain Questionnaire; HSCL-10: Hopkins Symptom Checklist Short Form; SD: Standard Deviation; IQR: Interquartile range; CI: Confidence Interval; ANOVA: Analysis of Variance; NRS: Numeric rating scale

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Authors' contributions

All authors were involved in developing the design of the study. PI and BLM prepared and cleaned the data. PI did the statistical analysis in consultation with KW and AK. PI, HSR and NKV wrote the first draft. All authors contributed by reviewing previous versions of the manuscript and improving the final version. PI and BLM had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Written permission was from all persons named in the acknowledgment. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to data protection policies, but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by The Norwegian Regional Committees for Medical and Health Research Ethics (2015/89). All procedures followed were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 1983. Participants were asked for and gave a written informed consent, authorizing the use of demographic and clinical data collected as part of this study. Following standard practice in Norway, there was no compensation received for participation by neither patients nor clinicians.

Consent for publication

Written informed consent for publication of their clinical details was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

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Publisher's Note

Additional file 1

SMS questions sent weekly for 52 weeks

SMS 1:

"How many days the last week has your neck been bothersome? Please answer with a number between 0 and 7"

SMS 2:

"How intense has your neck pain typically been the last week? 0= no bother, 10= worst bother imaginable"

SMS 3:

"How many days the last week has your neck limited your daily activities? Please answer with a number between 0 and 7"

Table S1. Distribution patterns.
Distribution of NP patients into pattern and subgroups with 1) original definition criteria, 2) definition of episode duration of two weeks between pain episodes as part of analyses of robustness of pattern and subgroup definitions, 3) patients recruited at first consultation for their neck pain only, 4) exclusion criteria: responses <10 out of 43 weeks.

Patient group	Classified (n=1206)	Classified (n=1206)	Classified patients recruited at first consultation (n=186)	Exclusion criteria: responses >10 out of 43 weeks
Definition criteria	Original	Episode duration 2 weeks	Original	Original
Defined patterns and subgroups	n(%)	n(%)	n(%)	n(%)
1 Severe Ongoing	1 (0.1)	1 (0.1)	0 (0)	0 (0)
2 Moderate Ongoing	1 (0.1)	1 (0.1)	0 (0)	1 (0.1)
3 Minor Ongoing	0 (0)	0 (0)	0 (0)	0 (0)
4 Minor Ongoing/Recovered	49 (4.1)	49 (4.1)	10 (4.8)	58 (4.7)
Total Ongoing	51 (4.0)	51 (4.2)	10 (4.8)	59 84.7)
5 Severe Fluctuating	54 (4.5)	54 (4.5)	6 (3.2)	57 (4.6)
6 Moderate Fluctuating	185 (15.4)	156 (13.1)	23 (12.4)	196 (15.7)
7 Mild Fluctuating	298 (25.0)	192 (15.9)	42 (22.0)	304 (24.4)
8 Minor Fluctuating	45 (3.9)	15 (1.2)	7 (3.8)	50 (4.0)
Total Fluctuating	582 (48.3)	416 (34.7)	78 (41.4)	607 (48.9)
9 Severe Episodic	276 (22.6)	403 (33.5)	45 (24.2)	275 (22.1)
10 Moderate Episodic	174 (13.9)	204 (17.0)	32 (16.9)	177 (14.2)
11 Mild Episodic	88 (7.3)	93 (7.7)	13 (6.9)	91 (7.3)
12 Minor Episodic	9 (0.8)	10 (0.8)	1 (0.6)	7 (0.6)
Total Episodic	547 (45.4)	711 (58.8)	91 (48.6)	550 (44.1)
13 Severe Single episode	5 (0.4)	5 (0.4)	1 (0.5)	7 (0.6)
14 Moderate Single episode	11 (0.9)	11 (0.9)	4 (2.1)	9 (0.6)
15 Mild Single episode	7 (0.6)	7 (0.6)	1 (0.5)	10 (0.8)
16 Minor Single episode	3 (0.3)	3 (0.3)	1 (0.5)	5 (0.4)
Total Single episode	26 (2.2)	25 (2.2)	7 (3.6)	31 (2.5)
Not classified n(% of study cohort, n=1208)	2 (0.2)	2 (0.2)	2 (0.2)	3 (0.2)

Table S2. Intensity of symptoms after pain-free period.
NP intensity and weekly days with pain in the first week following a pain-free period of 1 to >20 weeks for analysis of robustness of pattern and subgroup definitions.

Duration of pain-free periods, weeks	Mean (SD) pain intensity in the first week after a pain-free period, 0-10 NRS	Mean (SD) number of days with NP in the first week after a pain-free period, 0-7 days
1	3.3 (1.7)	2.3 (1.4)
2	3.3 (1.8)	2.2 (1.4)
3	3.2 (1.8)	2.2 (1.4)
4	3.1 (1.8)	2.2 (1.5)
5	3.1 (1.8)	2.1 (1.4)
6	3.1 (1.5)	2.1 (1.2)
7	3.1 (1.6)	2.2 (1.5)
8	3.1 (1.5)	2.2 (1.2)
9	2.9 (1.7)	2.3 (1.5)
10-15	3.2 (1.6)	2.3 (1.4)
15-20	3.6 (2.0)	2.6 (1.5)
>20	3.7 (1.9)	2.6 (2.0)

Table S3. Distribution NP and LBP cohort comparison.
Distribution of NP cohort in the defined patterns subgroups and Danish LBP cohort from Kongsted et al (1).

Defined patterns and subgroups	Prevalence NP n=1206 LBP n=1077 n (%)		Number of days with pain per week, in weeks with any pain		Pain intensity in weeks with any pain		Total number of days with pain during 43 weeks (301 days)	
			Mean (SD)					
Cohort	NP	LBP	NP	LBP	NP	LBP	NP	LBP
1 Severe ongoing	1 (0.1)	3 (0.1)	7.0 (0)	6.9 (1.6)	6.0 (0)	8.1 (1.6)	161 (0)	250 (88)
2 Moderate ongoing	1 (0.1)	1 (0.1)	7.0 (0)	7 (0)	5.0 (0)	4.2 (0)	280 (0)	301 (0)
3 Mild ongoing	0 (0)	2 (0.1)	-	6.1 (3.1)	-	3.0 (1.1)	-	200 (76)
4 Minor ongoing/ recovered	49 (4.1)	155 (14.4)	0 (0)	2.2 (2.1)	0.0	1.3 (0.4)	0 (0)	2.0 (22)
Total Ongoing pattern	51 (4.0)	161 (14.9)	7.0 (0)	N/A	5.5 (0.7)	N/A	4.5 (36)	N/A
5 Severe fluctuating	54 (4.5)	43 (4.0)	6.0 (1.0)	6.1 (1.3)	7.2 (0.9)	7.3 (0.9)	252 (51)	239 (61)
6 Moderate fluctuating	185 (15.4)	87 (8.1)	4.5 (1.5)	5.2 (1.5)	5.0 (0.6)	5.1 (0.6)	182 (68)	206 (69)
7 Mild fluctuating	298 (25.0)	113 (10.5)	3.3 (1.4)	4.0 (1.7)	3.4 (0.6)	3.2 (0.7)	130 (66)	155 (81)
8 Minor fluctuating	45 (3.9)	22 (2.0)	2.6 (1.4)	3.9 (2.1)	2.0 (0.5)	1.8 (0.5)	87 (68)	143 (90)
Total Fluctuating pattern	582 (48.3)	265 (24.6)	3.9 (1.7)	N/A	4.1 (1.4)	N/A	148 (75)	N/A
9 Severe episodic	276 (22.6)	270 (25.1)	2.9 (1.1)	3.3 (1.3)	3.9 (1.0)	4.2 (1.2)	59 (40)	51 (44)
10 Moderate episodic	174 (13.9)	163 (15.1)	2.4 (0.9)	2.6 (1.2)	2.7 (0.6)	3.0 (0.7)	39 (29)	29 (28)
11 Mild episodic	88 (7.3)	111 (10.3)	2.0 (1.1)	1.9 (1.1)	1.9 (0.5)	1.9 (0.5)	29 (33)	19 (26)
12 Minor episodic	9 (0.8)	8 (0.7)	1.5 (0.5)	1.2 (0.4)	1.0 (0.0)	1.0 (0.0)	13 (13)	6.0 (7.0)
Total Episodic pattern	547 (45.4)	552 (51.3)	2.6 (1.1)	N/A	3.2 (1.2)	N/A	47 (36)	N/A
13 Severe single episode	5 (0.4)	18 (1.7)	3.4 (1.5)	4.3 (1.9)	5.8 (1.1)	6.4 (1.0)	4.8 (2.6)	6.0 (4.0)
14 Moderate single episode	11 (0.9)	23 (2.1)	2.5 (1.7)	2.4 (1.2)	4.0 (0.5)	4.4 (0.6)	4.0 (3.6)	3.0 (2.0)
15 Mild single episode	7 (0.6)	49 (5.0)	2.1 (1.2)	1.8 (1.0)	2.4 (0.5)	2.5 0(.5)	2.3 (1.1)	2.0 (2.0)
16 Minor single episode	3 (0.3)	9 (0.7)	1.0 (0.0)	1.1 (0.2)	1.0 (0.0)	1.0 (0.0)	1.0 (0)	1.0 (1.0)
Total Single episode pattern	26 (2.2)	99 (9.2)	2.5 (1.5)	N/A	3.6 (1.6)	N/A	3.7 (2.8)	N/A

NP, Neck Pain; LBP, Low Back Pain; SD, Standard Deviation; N/A, Not Applicable

References

1. Kongsted A, Hestbaek L, Kent P. How can latent trajectories of back pain be translated into defined subgroups? BMC musculoskeletal disorders. 2017;18(1):285.

English translation of baseline questionnaire:

Date (ddmmyy):_____

1. Gender:

- ❑ Female
- ❑ Male

2.How old are you?:__ __ years

3. Weight:_____kg
4. Height:_____cm

5. Are you a smoker? (check one box)

- ❑ Yes
- ❑ No, but I did smoke earlier
- ❑ No

6. Marital status: (check only one box)

- ❑ Married/partnership
- ❑ Divorced
- ❑ Widowed/widower
- ❑ Single

7. Are you caring for children under the age of 18 on a daily basis? (check only one box)

- ❑ No
- ❑ Yes: number of children_____

Education and employment

8. What is your highest completed education?
(check only one box)

- ❑ Elementary school 7-10 years
- ❑ Vocational high school, vocational school, secondary school
- ❑ High school with general studies
- ❑ College or university (less than 4 years)
- ❑ College or university (4 years or more)

9. Your current employment status: (check all that apply)

- ❑ Employed
  - ❑ Full time
  - ❑ Part time
- ❑ Unemployed
- ❑ Pupil/student?
- ❑ Retired
- ❑ Disabled: _____%
- ❑ Sick-listed : _____%
  - ❑ By general practitioner
  - ❑ By chiropractor
  - ❑ By manual therapist
- ❑ Work assessment allowance
- ❑ Stay-at-home/not in paid work
- ❑ Other_____

10. How will you describe your current employment? (check all that apply)

- ❑ Mostly sedentary work (e.g. desk work, assembly work)
- ❑ Work which require a lot of walking (e.g. clerk work, light industrial work, teaching)
- ❑ Work which require a lot of walking as well as lifting (e.g. postman, nurse, kindergarten, construction work)
- ❑ Heavy body work (e.g. forestry work, heavy agricultural work, heavy construction work)
- ❑ Repetitive work with time pressure
- ❑ Self-employed/freelance
- ❑ Not in paid work

11. Describe your current work ability compared to when it was at its best in your life:
Your best work ability ever is set to 10 points. What number would you put on your present work ability? (Put a circle around the number that best describes your present work ability. 0 points means that you are unable to work at all, whereas 10 points mean that your work ability is currently at its best – please put a circle even if you are not in a paid work situation).

0	1	2	3	4	5	6	7	8	9	10
Unable to work										work ability is at its best

12. Do you enjoy your job, how is your job satisfaction? (Put a ring around the value that suits you best)

0	1	2	3	4	5	6	7	8	9	10
Strongly dissatisfied										Thrive very well

General health and physical activity

13. Other health problems/issues: (check all that apply)

- ❑ no serious or cronic diseases
- ❑ cardio vascular diseases
- ❑ lung diseases
- ❑ gastrointestinal problems
- ❑ depression
- ❑ urinary tract problems
- ❑ diabetes
- ❑ cancer
- ❑ asthma/allergies
- ❑ neurological disorders
- ❑ rheumatic disorders
- ❑ other musculoskeletal disorders

14. How often do you exercise? (take an average)

By exercise/training we mean e.g. walking, cycling, skiing, swimming or other forms of training/sports.

- ❑ Never
- ❑ Less often than once a week
- ❑ Once a week
- ❑ 2-3 times a week
- ❑ More than 3 times a week

15. Are you using your bicycle on a daily basis, e.g. as exercise, for leisure activities or as transportation? (check only one box)

- ❑ Yes
- ❑ No

Your neck complaint

16. How did your neck complaint occur? (Check only one box)

- ❑ Acute
- ❑ Gradually
- ❑ I do not know

17. Did the neck complaint occur as a consequence of: (check all that apply)

- ❑ Physical trauma or injury
- ❑ Prolonged load
- ❑ Stress-related causes
- ❑ Without known triggering cause/Do not know
- ❑ Other:_____

18. How would you rate your pain <u>right now:</u> (circle one of the numbers below)

0	1	2	3	4	5	6	7	8	9	10
No pain										Worst imaginable pain

19. How many whole days during the last 4 weeks have you been away from your work due to your neck problems?
This applies to all absences; <u>self-reported absence as well as sick leave from the doctor</u> (circle only one number).

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

Kinesiophobia [6]

20. How much fear do you have that these complaints would be increased by physical activity? (circle only one number)

0	1	2	3	4	5	6	7	8	9	10
No fear										Very much fear

21. How do you evaluate the risk for your present complaint developing into persistent problems? (circle only one number)

0	1	2	3	4	5	6	7	8	9	10
No risk										Very high risk

22. Have you had neck complaints previously? (check only one box)

- ❑ No, this is the first time
- ❑ Yes, 1-3 times previously
  Last time:_____months ago
- ❑ Yes, more than 3 times previously
  Last time:_____months ago
- ❑ Yes, I do suffer from more or less chronic neck complaints

23. If the answer is yes, for how many years have you suffered from neck complaints? (check only one box)

- ❑ Less than one year
- ❑ 1-5 years
- ❑ 6-10 years
- ❑ More than 10 years
- ❑ As long as I can remember
- ❑ I do not know

Pain medication

24. Are you taking pain medication in order to reduce your neck complaint? (check only one box)

- ❑ Never
- ❑ No
- ❑ Yes:

Over-the counter painkillers (check only one box)
- ❑ Never
- ❑ Less often than every month
- ❑ Every month
- ❑ Every week
- ❑ Daily
- ❑ More times daily

Prescription painkillers (check only one box)
- ❑ Never
- ❑ Less often than every month
- ❑ Every month
- ❑ Every week
- ❑ Daily
- ❑ More times daily

Treatment for my neck complaint

25. What is your goal for the actual treatment of your neck complaint? (check all that apply)

Pain improvement :
- ❑ Become pain free
- ❑ Pain reduction
- ❑ Excercise without pain
- ❑ Prevent pain aggrevation

Improvement of function:
- ❑ Improved function in activities of daily living
- ❑ Return to earlier activities
- ❑ Prevent reduced function

Other goals: _____

❑ I do not know/I have no treatment goals

26. Have you seen any other therapists concerning your current neck complaint (check only one box)

❑ No
❑ Yes

If the answer is yes, what effect did the treatment have on your current neck complaint? (check all that apply)

	Better	Unchanged	Worse
Physiotherapy with active excercises	❑	❑	❑
Physiotherapy with passive treatment modalities (massage, hot packs, electrotherapy an so on)	❑	❑	❑
Manual therapy	❑	❑	❑
General practitioner	❑	❑	❑
Chiropractor	❑	❑	❑
Specialist	❑	❑	❑
Other treatments	❑	❑	❑

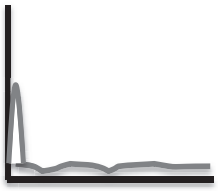
please specify _____

27. Are you, or have you ever been, involved in an insurance claim due to your current or previous neck complaints. (check only one box)

- ❑ No
- ❑ Yes, for the current neck complaint
- ❑ Yes, for previous neck complaint(s)

Previous course of pain

28. Below are descriptions of how some people describe their neck pain. Please check the description that you think best represents how your neck pain has been **the previous 12 months.**

a) 

No neck pain or just a single episode of neck pain ☐

b) 

Few episodes of neck pain separated by pain free periods ☐

c) 

Mild neck pain most of the time ☐

d) 

Neck pain of varying intensity but never completely pain free ☐

e) 

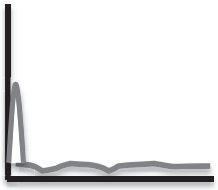
Severe neck pain most of the time ☐

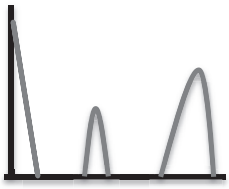
f) **None of the above illustrated** ☐

g) **Do not know** ☐

Future course of pain

29. Below are descriptions of how some people describe their neck pain. Please check the description that you think best represents how your neck pain has been **the next 12 months.**

a)  No neck pain or just a single episode of neck pain ☐

b)  Few episodes of neck pain separated by pain free periods ☐

c)  Mild neck pain most of the time ☐

d)  Neck pain of varying intensity but never completely pain free ☐

e)  Severe neck pain most of the time ☐

f) **None of the above illustrated** ☐

g) **Do not know** ☐

In addition to the above questions, patients also completed the following standardized questionnaires:

Örebro Musculoskeletal Pain Screening Questionnaire [4]

Neck Disability Index (NDI) [5]

Hopkins symptom Checklist (HSCL-10) [1]

Health-related Quality of Life (EuroQol) [2]

Nordic Pain Questionnaire (NPQ) [3]

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ORIGINAL ARTICLE

The clinical course of neck pain: Are trajectory patterns stable over a 1-year period?

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Abstract

Background: Recent studies with data-driven approaches have established common pain trajectories. It is uncertain whether these trajectory patterns are consistent over time, and if a shorter measurement period will provide accurate trajectories.

Methods: We included 1,124 patients with non-specific neck pain in chiropractic practice. We classified patients into pre-defined trajectory patterns in each of four quarters of the follow-up year (persistent, episodic, and recovery) based on measures of pain intensity and frequency from weekly SMS. We explored the shifts between patterns and compared patients with stable and shifting patterns on baseline characteristics and clinical findings.

Results: 785 (70%) patients were in the same pattern in 1st and 4th quarters. Patients with episodic pattern in the 1st quarter shifted to other patterns more frequently than patients in the other patterns. A stable persistent pattern was associated with reduced function and higher scores on psychosocial factors. There was a decreased frequency of patients classified as persistent pattern (75% to 63%) and an increase of patients in recovery pattern (4% to 15%) throughout the four quarters. The frequency of patients classified as episodic remained relatively stable (21% to 24%).

Conclusions: We found an overall stability of the persistent pattern, and that episodic patterns have more potential for shifts. Shifts mostly occurred between patterns closest in pain variation. The deviation in pattern distribution compared with previous studies suggests that the duration of measurement periods has an impact on the results of the classification.

Significance: Having persistent pain and having very minor pain is relatively stable over one year, while episodic pain has more potential for shifts. The duration of measurement periods appears to have an impact on the results of the classification. The given criteria resulted in a reduced frequency of episodic pattern due to shorter measurement periods. Our findings contribute to improved understanding and predicting NP using a combination of patient characteristics and trajectory patterns.

1 | INTRODUCTION

Neck pain (NP) is the second most common musculoskeletal complaint, causing a considerable impact on quality of life and large economic consequences for patients and society (Hoy et al., 2014; Hurwitz et al., 2018). The majority of patients have no clinically identifiable pathoanatomic cause (non-specific neck pain) and are treated in primary care settings (Kinge et al., 2015; Kovacs et al., 2019). Several studies show that most patients display an initial attenuation in symptoms and disability subsequent to the onset of an acute episode of spinal pain (Burns et al., 2020; Carroll et al., 2008; Vasseljen et al., 2013; Vos et al., 2008). Although this initial improvement is also found in patients already in a long-lasting course of pain, it seems to be larger and more rapid in patients presenting at the onset of an acute episode (Bot et al., 2005; Knecht et al., 2020; Langenfeld et al., 2015; Leaver et al., 2013; Peterson et al., 2012; Rubinstein et al., 2008). Previous research is mainly based on outcomes measured as mean values at single time points. These methods miss the variations found in individual trajectories of pain and provide only general trends of recovery. However, trajectories based on frequent pain measures to capture temporal variation also show that a large majority of patients with spinal pain display patterns of initial improvement (Ailliet et al., 2018; Axén et al., 2012; Chen et al., 2018; Dunn et al., 2006, 2013; Kongsted et al., 2015; Pico-Espinosa et al., 2019). Also, patients with long-lasting pain have a dynamic course of pain (Ailliet et al., 2018; Irgens et al., 2020; Kongsted et al., 2016; Pico-Espinosa et al., 2019). A better understanding of various clinical courses may be helpful in communicating the likely pain prognosis with the patient and in decisions regarding treatment.

Previous studies on low back pain (LBP) patients have suggested criteria for classifying trajectories of LBP based on pain variation patterns (ongoing, fluctuating, episodic and recovery) and pain severity (severe, moderate, mild and minor) (Kongsted et al., 2016). Sixteen subgroups based on these criteria matched well with trajectories of LBP, and identified subgroups that also differed in severity on other parameters (Irgens et al., 2020; Kongsted et al., 2017). We have previously found that the same definitions fit readily to NP patients in a chiropractic setting, but also that they needed refinement (Irgens et al., 2020).

Based on the previous findings that most patients report an improvement in symptoms and disability in a follow-up period, one may hypothesize that they will shift from more severe trajectory patterns (e.g. persistent pain) to milder patterns (e.g. episodic pain or recovered). However, it is also demonstrated that spinal pain tends to affect people in similar ways over many years (Dunn et al., 2013; Lemeunier et al., 2012). Still, it is unknown to what extent trajectory patterns based on frequent pain measures are stable over time. Hence, the aims of the present study were to (1) describe the NP trajectories in four consecutive quarters and examine to what extent patients shift from one trajectory pattern to another, and (2) describe and compare patient characteristics within stable and shifting trajectories during 1-year follow-up. We investigated this in patients with non-specific NP in a chiropractic setting.

2 | METHODS

2.1 | Study design, population and setting

In this study, we used data from a one-year observational, multi-center practice-based cohort consisting of patients with non-specific NP in a chiropractic care setting in Norway. Seventy-one chiropractors located across Norway invited eligible patients with NP to participate in the study between September 2015 and June 2016. Decisions regarding treatment and follow-up were at the chiropractors' discretion. Descriptions of cohort recruitment and study procedures, including the comparison of our cohort with a cohort of LBP patients from Kongsted et al., are published previously (Irgens et al., 2020; Myhrvold et al., 2019, 2020). The Regional Committee for Medical and Health Research Ethics (2015/89) approved the study protocol.

We included patients aged 18 years or more, that presented with NP as their primary or secondary complaint and visited the chiropractor for the first time or were already in a treatment course. Patients had to have basic Norwegian reading and writing skills, as well as own and be able to operate a mobile phone. We excluded patients with suspected inflammatory diseases, fractures, systemic pathology, or nerve root involvement requiring referral to surgery. Participants received oral and written information about the study from the chiropractor and signed a written consent if they agreed to participate.

2.2 | Data collection

Once a week over a 1-year period, the participants received an automated short message service (SMS) with the following questions: "How many days the last week has your neck been bothersome? Please answer with a number between 0 and 7" (hereafter 'paindays'). If the answer to the first SMS was 0, question 2 was not sent. If the answer was between 1 and 7, the patient received a second SMS "How intense has your NP typically been the last week? 0= no bother, 10= worst possible bother" (hereafter 'pain intensity'). All participants received a third SMS "How many days the last week has your neck limited your daily activities? Please answer with a number between 0

and 7" (hereafter 'limitation days'). The SMS collection through SMS-Track has been used in several data collections (Ailliet et al., 2018; Axen et al., 2012; Kongsted et al., 2015), with acceptable reliability (Johansen & Wedderkopp, 2010).

2.2.1 | Baseline data

Characteristics of symptoms included duration of NP history (<5 years, ≥5 years), duration of current episode (<1 month, 1–3 months, >3 months), and functional status measured by the Neck Disability Index (NDI). NDI consists of 10 items regarding pain and function scoring from 0 to 5. The sum score ranges from 0 to 50 points, with higher scores indicating more disability (Johansen et al., 2014; Vernon & Mior, 1991). For this study, we used the pain intensity from SMS question 2. Number of musculoskeletal pain sites (0–10) was measured by the Nordic pain questionnaire (NPQ) (0–10) (Kuorinka et al., 1987). Patients who responded "Yes" to pain in shoulder, elbow and/or hand in the NPQ were defined as having radiating pain. Emotional stress was measured by the Hopkins Symptom Checklist (HSCL-10), scores ranging from 1 to 4 (Derogatis et al., 1974; Strand et al., 2003). Higher scores indicate higher emotional distress. Psychosocial risk factors were measured by the Örebro-screening questionnaire. The sum score ranges from 0 to 100 points, where higher scores indicate higher risk of persistent pain and disability (Grotle et al., 2006; Linton & Boersma, 2003). We measured recovery expectations from Item 7 of the Örebro Musculoskeletal Pain Questionnaire (Linton et al., 2011), "In your view, how large is the risk that your current pain may become persistent?" (0–10, 0 = no risk, 10 = very large risk).

We defined consultation type as follows; "first-time consultation" as patients recruited at the first visit for a new episode of NP, "follow-up consultation" as patients recruited arbitrarily during the treatment course, and "maintenance consultation" as patients recruited at a regular visit according to a pre-planned schedule (check-up irrespective of symptoms) to maintain improvement and/or prevent flare-ups (Axen et al., 2020; Bringsli et al., 2012; Myburgh et al., 2013).

All of these were from questionnaires completed by participants at baseline.

2.3 | Data analyses

We present descriptive variables as frequencies and percentages or means with standard deviations (SD). We imputated missing values on the weekly pain intensity measures in three stages as follows: (1) replaced missing responses in week 1 and 52 by the values in week 2 and 51 respectively, (2) replaced one-week or two-week gaps between weeks with the same pain intensity with that same value. A total of 333 (23%) of patients had one or more weeks where the data were imputed. However, the majority needed only one imputation. The most commonly imputed value was zero (51%). We omitted from analyses participants who after steps 1 And 2 had less than 6 SMS responses in each 13-week quarter.

2.3.1 | Categorization into variation patterns, trajectory pattern shifts, and subgroups

To be able to explore the research question regarding the stability of trajectories over one year, we needed to reduce the previously identified sixteen subgroups into fewer subgroups. We did that according to the suggestions from two previous studies (Irgens et al., 2020; Kongsted et al., 2017). These found that very few patients fit into the Ongoing and single episode variation patterns. Also, Ongoing and Persistent fluctuating patterns were found to be very similar with persistent pain rarely being absolutely steady in pain intensity. We, therefore, decided to combine the Ongoing and persistent fluctuating variation patterns into one pattern called persistent pattern. In our previous study (Irgens et al., 2020), we found that patients in the minor subgroups of Ongoing episodic and single episode shared similar demographic, functional and psychosocial characteristics, and patients were only negligibly affected by their pain. Also, pain intensity was below what is considered clinically significant (<2 on NRS) (Kovacs et al., 2008; Pool et al., 2007). We therefore included all patients with maximum pain intensity <2 in a new pattern called recovery. Patients in the Minor Persistent fluctuating subgroup were significantly more affected by their pain than the other three minor subgroups and were not included in the recovery pattern. Initial analyses showed that the single episode pattern included too few patients for comparison with the other patterns. We also considered that having one short episode of pain per quarter to be different from having no pain. We, therefore, combined the single episode pattern with the episodic pattern. This led to three variation patterns for analysing the stability persistent, episodic and recovery, defined as follows: In the persistent pattern, patients could have no pain-free period lasting four weeks or longer. Patients in the episodic pattern must have at least one pain-free period of minimum four weeks in a row between weeks with pain. The duration of the pain-free period was based on consensus-formed definitions (Stanton et al., 2011; de Vet et al., 2002), and has been tested in an LBP cohort (Eklund et al., 2016).

In order to assess the stability of the patterns over one year, we divided the year into four quarters (hereafter '1st quarter', '2nd quarter', etc.). We classified patients to one of the three patterns (persistent, Episodic or Recovery) within each of the quarters based on their SMS responses.

It was the main aim to study the shift in patterns between quarters during one year. To explore the development over time further, we also studied the shift of intensity levels within and/or between each pattern. For that purpose, we split the persistent pattern into four subgroups based on mean pain intensity as follows: severe (pain intensity ≥6), moderate (4≤pain intensity<6), mild (2≤pain intensity<4), and minor (pain intensity <2), in line with previously suggested cut-off values for pain (Boonstra et al., 2014, 2016; Fejer et al., 2005; Serlin et al., 1995). We split the episodic and single Episode patterns into three subgroups each, based on the maximum pain intensity reported throughout the quarter: Severe (pain intensity ≥6), Moderate (4≤pain intensity<6) and Mild (2≤pain intensity<4). Altogether this resulted in 11 subgroups, hereafter called 'subgroups' (see Table S1).

2.4 | Statistical analyses

To describe the course of NP in the four quarters, we report proportion of patients in each subgroup per quarter. For this part, we kept the single episode as a separate pattern.

We used Sankey diagrams to illustrate the proportions of patients shifting pattern from one quarter to the next, based on the patients' pattern in the 1st quarter. The columns represent the proportion of patients in the respective patterns in each quarter (Figure 1). The flow between columns represents the proportion of the patients shifting from one into another pattern.

The Sankey diagrams showed similar shifts between the quarters two through four. We therefore decided to define patients who were classified with the same pattern in the 1st and 4th quarter to have a stable trajectory pattern. We defined patients classified with different patterns in the 1st and 4th quarter to have a shifting trajectory pattern. This left us with three possibilities for patients in each of the patterns in the 1st quarter (staying in the same pattern or shifting to either of the other two).

All data were assessed for normality prior to analyses, and were found to have distributions close to normal. To compare the differences between patients in stable and shifting trajectory patterns, we used one-way analysis of variance (ANOVA) between the three possible shifts on the following baseline data: NDI, HSCL-10, Örebro, and pain intensity. We used Chi-square and Fisher exact tests (when appropriate) to examine differences in pain duration and total history of NP and to investigate the association between how patients shift trajectories within each consultation type. For all analyses of shifts, we performed pairwise comparisons with Bonferroni corrections. As a sensitivity analysis of the definition of a stable trajectory pattern, we performed the same analyses looking at the shifts occurring from the 3rd to 4th quarter instead of from the 1st to the 4th. All analyses were carried out using STATA 16.1 (StataCorp, Texas, USA).

3 | RESULTS

A total of 1,469 patients received SMS weekly of whom 1,124 (77%) responded to a sufficient number of SMSs to be classified as a pattern in all four quarters and formed the study sample. Seventeen percent of the sample were recruited at first consultation. There were few and mostly small differences between the included and excluded patients (Table 1).

3.1 | Distribution of patients into patterns in the four quarters

Seventy-five percent of the patients had a persistent pattern in first quarter. In the three consecutive quarters the frequency was reduced to about 65%. This reduction occurred mainly in the Moderate and Mild subgroups. The frequency of patients with episodic or single episode patterns remained stable at around 20% and less than 5%, respectively. The recovery group increased initially from 4% in the first quarter to 11–15% thereafter. The episodic pattern in the first quarter and the recovery pattern in all four quarters had the largest proportion of patients with imputed data, indicating that patients were most commonly pain-free when not responding to SMS for one or two weeks (Table 2).

3.2 | Shifts of trajectory patterns between quarters

In total, 785 (70%) patients were in the same trajectory pattern in the 1st and the 4th quarter, of whom 648 (82%) were in a stable persistent trajectory pattern, and 104 (13%) and 33 (4%) were in the episodic and recovery trajectory patterns, respectively.

Figure 1 shows the proportion of patients shifting between patterns from one quarter to the next, based on their pattern classification in the 1st quarter. Very few patients shifted directly between the Persistent and Recovery patterns after the 1st quarter. Patients classified as Persistent and Recovery in the 1st quarter showed similar trends for shifts. The majority of these

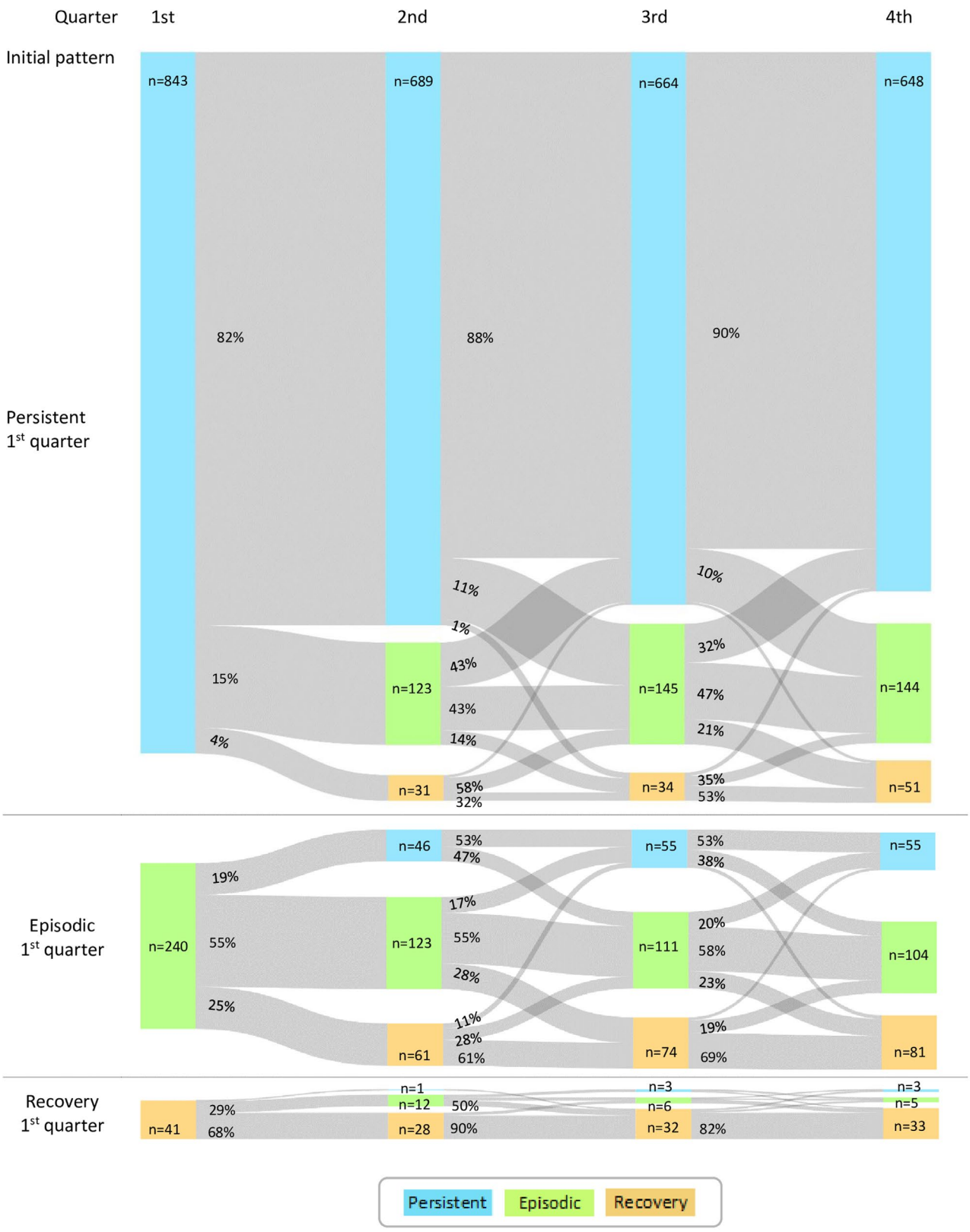

FIGURE 1 Sankey diagram showing the proportion[1] shifting from 1st Quarter through to 4th Quarter, in persistent, episodic (episodic and single Episode patterns) and recovery patterns. Explanatory legend: [1]The height of the columns reflect the number of patients in each quarter. The percentage reflects the proportion of patients responding to sufficient SMS for distribution from one quarter to the next. Shifts with $n \leq 10$ are not presented with percentage for flow. For instance, 15% of patients who were in the persistent pattern during the 1st quarter shifted to episodic during the 2nd quarter, and among these, 43%, 43%, and 14%, respectively, returned to persistent, stayed in episodic, and further shifted to recovery in the 3rd quarter

TABLE 1 Characteristics and clinical findings of patients at baseline

Characteristics	Study cohort *n* = 1,124 %	Study cohort *n* = 1,124 Mean (SD)	Excluded cohort *n* = 235[a] %	Excluded cohort *n* = 235[a] Mean (SD)
Age Mean (SD) [range 18–85]		45 (14)		41 (12)
Females	74		75	
Radiating pain	76		78	
Headache	87		87	
Concomitant low back pain	77		80	
Consultation type at recruitment				
First episode	23		24	
Follow-up	15		14	
Maintenance treatment plan	62		62	
Duration of NP				
<1 month	23		21	
1–3 months	14		19	
>3 months	63		60	
>5 year history of NP	32		32	
Traumatic cause	18		15	
Recovery expectations[b](0–10)		5.8 (3.1)		5.8 (3.1)
Baseline intensity of NP (NRS 0–10)		4.0 (2.2)		3.9 (2.2)
Disability - NDI (0–50)		12 (6.8)		12 (6.5)
Psychosocial screening - ÖMPQ (0–100)		38 (17)		31 (23)
Psychological distress - HSCL−10 (1–4)		1.7 (0.5)		1.6 (0.5)
General health (VAS 0–100)		71 (19)		69 (21)

HSCL-10, Hopkins Symptom Checklist-10; NDI, Neck Disability Index; NP, Neck pain; NRS, Numeric rating scale; ÖMPQ, Örebro Musculoskeletal Pain Questionnaire; SD, Standard Deviation.

[a]Patients responding to baseline questionnaire.

[b]Recovery expectations from Item 7 of the Örebro Musculoskeletal Pain Questionnaire.

patients (82–90% for persistent and 68–90% for recovery) remained in their initial pattern from one quarter to the next. Of the patients in a shifting persistent trajectory pattern, most shifted between Episodic and Persistent patterns.

Patients in an episodic pattern in the 1st quarter were more likely to shift but had no specific trend of shifts. About half of the patients remained in the episodic pattern from one quarter to the next, and about equal parts of the other half shifted to persistent or single episode.

On a subgroup level, there was a trend showing that patients remaining in one pattern from one quarter to the next still shifted between severity subgroups within their respective pattern (see Table S2). Of the patients starting in and then shifting away from a persistent pattern from one quarter to the next, the shift primarily occurred from the Minor Persistent subgroup to the Severe or Moderate episodic subgroups. No patients shifted from Severe or Moderate persistent subgroups into the recovery pattern from one quarter to the next. Patients in the Severe and Moderate episodic subgroups tended to shift to the lower intensity persistent subgroups or the recovery pattern.

3.3 | Characteristics of patients in stable and shifting patterns

Patients in the persistent pattern in the 1st quarter staying in the same pattern had worse baseline scores and a longer history of NP than those shifting away from that pattern (Table 3). For patients starting in an episodic pattern, there was a tendency for worse scores in those moving to a persistent pattern, but most differences were small. For those in a recovery pattern in the 1st quarter, a shift in pattern was only observed in very few patients and baseline profiles should be interpreted with great caution. It appears that those staying in the recovery pattern are relatively mildly affected and more often reported short episode duration.

TABLE 2 Distribution of patients into patterns and subgroups by the four quarters (n = 1,124)

Period	First Quarter (Week 1–13)	Second Quarter (Week 14–26)	Third Quarter (Week 27–39)	Fourth Quarter (Week 40–52)
Pattern	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**
Persistent				
Severe	65 (6)	53 (5)	64 (6)	73 (6)
Moderate	245 (22)	192 (17)	188 (17)	185 (16)
Mild	413 (37)	360 (32)	341 (30)	318 (28)
Minor	120 (11)	131 (12)	129 (11)	130 (12)
Total	843 (75)	736 (66)	722 (64)	706 (63)
Episodic				
Severe	81 (7)	63 (6)	53 (5)	49 (4)
Moderate	82 (7)	74 (7)	72 (6)	81 (7)
Mild	66 (6)	85 (8)	77 (7)	63 (6)
Total	229 (20)	222 (20)	202 (18)	193 (17)
Single Episode				
Severe	2 (<1)	7 (<1)	6 (<1)	14 (1)
Moderate	4 (<1)	13 (1)	18 (2)	15 (1)
Mild	5 (<1)	26 (2)	36 (3)	31 (3)
Total	11 (1)	46 (4)	60 (5)	60 (5)
Recovery	41 (4)	120 (11)	140 (12)	165 (15)

TABLE 3 Baseline characteristics of patients with stable or shifting trajectories between the first and fourth quarter

Variable		Pain intensity	HSCL−10	NDI	Örebro	Duration >4weeks	NP history >5 years
Shifts	***n* (%)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	**Mean(SD)**	***n*(%)**	***n*(%)**
From persistent							
Stable persistent	652 (77)	4.6 (2.0)*	1.7 (0.5)*	13.6 (6.6)*	42.5 (16.4)*	533 (86)***	419 (73)**
to episodic	145 (17)	3.8 (2.0)	1.6 (0.5)	10.2 (5.7)	35.8 (16.1)	108 (79)	76 (67)
to recovery	53 (6)	3.4 (2.1)	1.5 (0.4)	10.0 (9.0)	31.5 (18.3)	34 (74)	14 (42)
From episodic							
to persistent	55 (23)	3.3 (2.3)	1.6 (0.4)	9.1 (5.4)	33.7(16.3)**	34 (65)	28 (64)
Stable episodic	104 (43)	2.8 (2.1)	1.5 (0.4)	7.9 (4.5)	29.6 (15.3)	55 (57)	55 (61)
to recovery	81 (34)	3.2 (2.1)	1.4 (0.4)	8.0 (4.9)	26.7 (15.1)	38 (52)	30 (53)
From recovery							
to persistent	3 (7)	0.3 (0.6)	1.2 (0.2)	1.3 (2.3)	20.0 (10.1)	2 (67)	1 (50)
to episodic	5 (12)	0.2 (0.4)	1.4 (0.4)	6.8 (5.3)	26.4 (16.5)	2 (40)	3 (100)
Stable recovery	34 (81)	0.1 (0.3)	1.3 (0.3)	3.7 (3.1)	19.5 (12.9)	12 (41)	6 (38)

Note: Differences: ANOVA or Pearson Chi2/Fisher's exact, Bonferroni corrected, *$p < 0.005$ between stable Persistent and Persistent to Episodic and Persistent to Recovery; **$p < 0.005$ between stable Persistent and Persistent to Recovery and between Episodic to Persistent and Episodic to Recovery; ***$p < 0.05$ between stable Persistent and Persistent to Recovery.

HSCL-10 short form, The Hopkins Symptom Checklist; NDI, Neck Disability Index; NP, Neck pain; SD, Standard deviation.

For the sensitivity analysis of the definition of a stable trajectory pattern, we found almost identical results in patient characteristics when we assessed the shift from third to fourth quarter, compared to first to fourth quarter (see Table S3).

4 | DISCUSSION

This study explored the stability of trajectories for patients with non-specific NP over one year. We classified patients from chiropractic practice into pre-defined trajectory

patterns of NP in each of four consecutive quarters of the follow-up year. The majority of patients stayed in the same trajectory pattern from one quarter to the next. The lowest frequency of shifts was found for patients classified as persistent. Patients showing a stable persistent trajectory had reduced function and higher scores on psychosocial factors compared with those reporting pain-free periods (classified as Episodic or Recovery) in one or more quarters.

4.1 | Patient distribution and shifts between subgroups and patterns

With 70% of patients in a stable pattern across four quarters, our findings indicate that the patterns remain relatively stable. A similar stability is found in other studies on LBP in GP practice (Dunn et al., 2013) and the general population (Lemeunier et al., 2013). In these studies, the majority of subjects were classified in the same pain pattern 7 and 8 years after the first measurement period.

Patients with a shifting pattern were most often classified as episodic in the first quarter. They shifted mainly to the nearby pattern, and rarely had a large change in pain- or pain-free duration (e.g. Shift from Persistent to Recovery). Overall there was a small trend of improvement across the 4 quarters, with decreased frequency of patients showing persistent pattern. This is in agreement with results from other studies with weekly measurements (Ailliet et al., 2018; Pico-Espinosa et al., 2019).

Apart from a small decrease in the frequency of persistent pattern and an increase in recovery pattern from first to second quarter, we found only minor differences in the distribution of patients into pre-defined patterns in each of the four quarters. However, the shorter measurement period of one quarter used led to a marked decrease in the number of patients classified as episodic (21–24% in the 4 quarters) when compared to our previous study of with a measurement period of 43 weeks (45%) (Irgens et al., 2020). While the shorter measurement period does not make a large impact on the stability of the patterns, it does appear to have an impact on the distribution of the patients. The definitions of an episode require a pain-free period of 4 weeks or longer (Kongsted et al., 2016, 2017; de Vet et al., 2002). It is more probable for such a period to occur during a full year compared to the quarter used in this study. Also, it is likely that some patients, by chance, have a painful episode that extends past the one quarter, thus classifying the patient as persistent. Previous trajectory studies on NP found that pain episodes could last from 3 to 20 weeks (Ailliet et al., 2018; Pico-Espinosa et al., 2019). Thus, the likely explanation for why more patients are classified as persistent during one quarter than during 43 weeks is a combination of a shorter measurement period and the criteria for the subgroup definitions.

4.2 | Characteristics of patients with stable and shifting trajectory patterns

Patients in a stable persistent trajectory pattern had more psychological stress and pronounced symptom histories compared to patients in the shifting trajectory patterns regardless of their initial pattern. This was similar to results from two other NP studies with frequent measures (Ailliet et al., 2018; Pico-Espinosa et al., 2019). Our findings can support the phenotypes recently described by Meisingset et al (2020), where the majority of the patients with continuous pain were in phenotypes characterized by poorer scores on all measured health-related factors. This opens up the possibility that an optimal prediction of the long-term course of pain needs a combination of early trajectory patterns and clinical phenotypes.

4.3 | Strengths and limitations

The main strengths in the present study were weekly SMS responses through one year, in a large cohort of NP patients. The high response rate on the SMS, ranging from 81% to 95%, throughout the study period ensured a solid basis for the analyses and the conclusions. Close to 75% of the recruited patients responded with sufficient SMS data to be classified into a pattern in each of the four quarters. In addition, there were only minor differences between the included participants and those excluded. Yet, we cannot completely rule out that missing data have influenced the distribution and the shifting of patterns. Moreover, we followed the recommendations for trajectory research proposed in a recent review (Kongsted et al., 2016) and used recognizable definitions as well as common, descriptive terminology (Stanton et al., 2011). Hence, the study can be replicated in different cohorts, settings and countries.

The small number of patients in the single episode pattern in all quarters can be a limitation and might indicate that patients with acute episodes were not recruited. Although instructed to document the number of patients not invited, or unwilling, to participate, very few chiropractors actually did so. However, reported baseline characteristics and outcomes of the participants are similar to other cohort studies from both primary care and the general population (Bruls et al., 2018; Hill et al., 2007; Vos et al., 2008), as well as other trajectory studies on NP (Ailliet et al., 2018; Pico-Espinosa et al., 2019). Also, it could be the result of it being quite unlikely to have only

one, very specific type of episode and thus, not surprisingly, it is seldom found. Furthermore, although patients received treatment at the chiropractors' discretion during the study period, this study does not include the assessment of the possible influence of this treatment on their course of pain.

This study was performed on patients in chiropractic practice. We have previously shown that our cohort distribution resembles that of LBP patients in GP practice (Irgens et al., 2020), and in Norway chiropractic patients represent 16% of patients who seek conservative treatment for musculoskeletal pain conditions (Kinge et al., 2015). Even with differences in distributions across patterns, the shifts over time are likely to be the same across settings, and we therefore consider it likely that our results are generalizable to other populations.

4.4 | Implications for clinical practice and future studies

Our study provides new information about the individual variations within trajectory patterns and the clinical course of pain. In particular, what is meant by chronic pain is challenged. It is well established that defining pain as chronic purely based on persistent pain lasting three months or longer is too simple. Persistent pain fluctuates (Irgens et al., 2020; Kongsted et al., 2017), and we have shown that an episode of pain can last for more than three months, yet still be followed by pain-free weeks and that these patients have a possibility of recovering. Moreover, patients with pain-free periods are less bothered by their pain and appear to have a potential for improvement compared to patients with little to no pain-free periods. However, patients classified as episodic also have a risk for shifting into persistent pain. Thus, including questions during the clinical consultation regarding the variations of the course of pain, may help identify which patients to target for (new) follow-up strategies, and which patients need only short-term advice. It is still to be investigated if persistent NP can be altered by effective treatment strategies, or how these patients are best supported in their ongoing self-management of NP. Investigating shifts in patterns may also be helpful for identifying prognostic factors that have not been revealed in 'traditional' prognostic research.

Our results can also be combined with phenotypes from prognostic studies (Meisingset et al., 2020; Myhrvold et al., 2019), and possibly be used in developing clinical tools for more targeted patient care. What remains to be learnt from these trajectory patterns in their current form with regard to clinical importance needs to be studied further. In particular, the relationship between treatment (intensity, content and timing) and clinical course is of great interest. However, frequent measures over a long period are time consuming, expensive, and impractical for use both in clinical practice and research. A next step should therefore examine if the trajectories can be found in drawings of corresponding visual patterns. The knowledge of such self-reported versus data-driven trajectories is emerging (Dunn et al., 2017; Hestbaek et al., 2019; Myhrvold et al., 2019, 2020), and visual trajectories have the potential to substitute long-term follow-ups in research. Our study can form a basis for applying the same approach to NP.

5 | CONCLUSION

This is the first study to assess the stability of non-specific NP trajectory patterns over consecutive periods. Having persistent pain and having very minor pain is relatively stable over one year, while episodic pain has more potential for shifts. The duration of measurement periods appears to have an impact on the results of the classification. The given criteria resulted in a reduced frequency of episodic pattern due to shorter measurement periods. Our findings contribute to improved understanding and predicting NP using a combination of patient characteristics and trajectory patterns.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

All authors were involved in developing the design of the study. PI and BLM prepared and cleaned the data. PI did the statistical analysis in consultation with KW. PI, HSR and NKV wrote the first draft. All authors contributed by discussing the results, reviewing previous versions of the manuscript and approving the final version. PI and BLM had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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Supplementary Table S1 Definitions of the patterns

	Pattern label	Variation pattern	Intensity
Persistent	1. Severe persistent	No pain-free 4-weeks periods	**Mean** intensity ≥6 No restrictions on maximum intensity
	2. Moderate persistent	No pain-free 4-weeks periods	**Mean** intensity ≥4 and <6 No restrictions on maximum intensity
	3. Mild persistent	No pain-free 4-weeks periods	**Mean** intensity ≥2 and <4 No restrictions on maximum intensity
	4. Minor persistent	No pain-free 4-weeks periods	**Mean** intensity <2 No restrictions on maximum intensity
Episodic	5. Severe episodic pain	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.	**Maximum** intensity ≥6 No restriction on mean intensity
	6. Moderate episodic pain	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.	**Maximum** intensity ≥4 and <6 No restriction on mean intensity
	7. Mild episodic pain	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.	**Maximum** intensity ≥2 and <4 No restriction on mean intensity
Single Episode	8. Severe single episode	One episode lasting 1 - 2 weeks (which are not the first or the last week of measurement)	**Maximum** intensity ≥6 No restriction on mean intensity
	9. Moderate single episode	One episode lasting 1 - 2 weeks (which are not the first or the last week of measurement)	**Maximum** intensity ≥4 and <6 No restriction on mean intensity
	10. Mild single episode	One episode lasting 1 - 2 weeks (which are not the first or the last week of measurement)	**Maximum** intensity ≥2 and <4 No restriction on mean intensity
Recovery	11. Recovery	Pain that is either Episodic or Single episode, or where mean intensity equals zero	**Maximum** intensity <2

Supplementary Table S2 Distribution into subgroups from one quarter to the next during the 1-year follow-up- n(%)

Subgroup 2nd quarter		Persistent				Episodic			Single episode			Recovery	Total (100)
Subgroup 1st quarter		Severe	Moderate	Mild	Minor	Severe	Moderate	Mild	Severe	Moderate	Mild		
Persistent	Severe	38 (59)	22 (34)	3 (5)	1 (2)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	65
	Moderate	14 (6)	125 (51)	86 (35)	4 (2)	5 (2)	4 (2)	2 (1)	0 (0)	0 (0)	0 (0)	5 (2)	245
	Mild	1 (<1)	40 (10)	222 (54)	71 (17)	23 (6)	23 (6)	17 (4)	1 (<1)	1 (<1)	4 (1)	10 (2)	413
	Minor	0 (1)	1 (1)	30 (25)	31 (26)	7 (6)	9 (8)	22 (18)	0 (0)	2 (2)	2 (2)	16 (13)	120
Episodic	Severe	0 (0)	3 (4)	10 (12)	8 (10)	12 (15)	10 (12)	10 (12)	2 (3)	3 (4)	2 (3)	21 (26)	81
	Moderate	0 (0)	1 (1)	6 (7)	12 (15)	11 (13)	15 (18)	12 (15)	1 (1)	4 (5)	7 (9)	13 (16)	82
	Mild	0 (0)	0 (0)	2 (3)	3 (5)	4)6)	9 (14)	17 (26)	2 (3)	1 (2)	6 (9)	22 (33)	66
Single Episode	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	2
	Moderate	0 (0)	0 (0)	1 (25)	0	1 (25)	1 (25)	0 (0)	1 (25)	0	0	0	4
	Mild	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	4 (80)	5
Recovery		0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	2 (5)	4 (10)	0 (0)	2 (5)	4 (10)	28 (68)	41
	Total	53 (5)	192 (17)	360 (32)	131 (12)	63 (6)	74 (7)	85 (8)	7 (1)	13 (1)	26 (2)	120 (11)	1,124

Subgroup 3rd quarter		Persistent				Episodic			Single episode			Recovery	Total (100)
Subgroup 2nd quarter		Severe	Moderate	Mild	Minor	Severe	Moderate	Mild	Severe	Moderate	Mild		
Persistent	Severe	41 (78)	12 (23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	53
	Moderate	20 (10)	113 (59)	52 (27)	3 (2)	3 (2)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	192
	Mild	3 (1)	55 (15)	212 (59)	35 (10)	21 (6)	19 (5)	12 (3)	0 (0)	2 (1)	0	1 (<1)	360
	Minor	0 (0)	2 (2)	32 (24)	53 (40)	4 (3)	11 (8)	13 (19)	0 (0)	3 (2)	6 (5)	7 (5)	131
Episodic	Severe	0 (0)	4 (6)	20 (32)	7 (11)	12 (19)	5 (8)	8 (13)	0 (0)	0 (0)	4 (6)	3 (5)	63
	Moderate	0 (0)	2 (3)	13 (18)	7 (9)	5 (7)	14 (19)	11 (15)	1 (1)	3 (4)	6 (8)	12 (16)	74
	Mild	0 (0)	0 (0)	9 (11)	16 (19)	2 (2)	11 (13)	18 (21)	1 (1)	3 (4)	4 (5)	21 (25)	85
Single Episode	Severe	0 (0)	0 (0)	0 (0)	0 (0)	2 (29)	0 (0)	0 (0)	1 (14)	0 (0)	0 (0)	4 (57)	7
	Moderate	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	1 (8)	2 (15)	0 (0)	0 (0)	1 (8)	8 (62)	13
	Mild	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	3 (12)	3 (12)	0 (0)	0 (0)	6 (23)	12 (46)	26
Recovery		0 (0)	0 (0)	3 (3)	7 (6)	2 (2)	7 (6)	10 (8)	3 (3)	7 (6)	9 (8)	72 (60)	120
	Total	64 (6)	188 (17)	341 (30)	129 (11)	53 (5)	72 (6)	77 (7)	6 (1)	18 (2)	36 (3)	140 (12)	1,124

Subgroup 4th quarter		Persistent				Episodic			Single episode			Recovery	Total (100)
Subgroup 3rd quarter		Severe	Moderate	Mild	Minor	Severe	Moderate	Mild	Severe	Moderate	Mild		
Persistent	Severe	50 (78)	14 (22)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	64
	Moderate	20 (11)	111 (59)	50 (27)	2 (1)	3 (2)	1 (1)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	188
	Mild	2 (1)	50 (15)	206 (60)	41 (12)	12 (4)	17 (5)	8 (2)	0 (0)	0 (0)	2 (1)	3 (1)	341
	Minor	0 (0)	2 (2)	32 (25)	46 (36)	8 (6)	14 (11)	14 (11)	1 (1)	1 (1)	5 (4)	6 (5)	129
Episodic	Severe	1 (2)	6 (11)	6 (11)	6 (11)	6 (11)	9 (17)	0	7 (13)	1 (2)	3 (6)	8 (15)	53
	Moderate	0 (0)	1 (1)	15 (21)	9 (13)	7 (10)	12 (17)	11 (15)	2 (3)	3 (4)	5 (7)	7 (10)	72
	Mild	0 (0)	0 (0)	5 (6)	15 (19)	7 (9)	14 (18)	16 (21)	0 (0)	1 (1)	5 (6)	14 (18)	77
Single Episode	Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (17)	0	0	5 (83)	6
	Moderate	0 (0)	0 (0)	2 (11)	0 (0)	2 (11)	1 (6)	1 (6)	1 (6)	1 (6)	1 (6)	9 (50)	18
	Mild	0 (0)	0 (0)	1 (3)	3 (8)	1 (3)	3 (8)	4 (11)	0	4 (11)	4 (11)	16 (44)	36
Recovery		0 (0)	1 (1)	1 (1)	8 (6)	3 (2)	10 (7)	9 (6)	2 (1)	3 (2)	6 (4)	97 (69)	140
	Total	73 (6)	185 (16)	318 (28)	130 (12)	49 (4)	81 (7)	63 (6)	14 (1)	15 (1)	31 (3)	165 (15)	1,124

Patients in the same subgroup in two consecutive quarters are marked in grey

Supplementary Table S3 Baseline characteristics of patients with stable or shifting trajectories between the third and fourth quarter

Variable Shifts	Pain intensity Mean(SD)	HSCL-10 Mean(SD)	NDI Mean(SD)	Örebro Mean(SD)	Duration >4weeks n(%)	NP history >5 years n(%)
From Persistent						
Stable Persistent	4.6 (2.0)[ac]	1.7 (0.5)[a]	13.7 (6.6)[a]	42.7 (16.4)[a]	514 (86)[c]	403 (74)[b]
to Episodic	3.5 (2.1)	1.5 (0.5)	9.9 (5.3)	35.0 (16.1)	65 (76)	49 (65)
to Recovery	2.1 (1.9)	1.4 (0.4)	5.9 (5.0)	35.5 (16.6)	7 (78)	2 (40)
From Episodic						
to Persistent	3.7 (2.2)	1.6 (0.4)	10.3 (5.4)	35.4(14.5)	52 (78)	40 (63)
Stable Episodic	3.5 (2.2)	1.5 (0.5)	9.0 (5.6)	33.3 (17.0)	85 (68)	70 (65)
to Recovery	3.2 (2.0)	1.5 (0.4)	9.3 (7.5)	28.0 (17.3)[d]	29 (57)	21 (53)
From Recovery						
to Persistent	1.8 (1.6)	1.2 (0.2)	5.5 (4.1)	23.2 (15.4)	23 (33)	5 (71)
to Episodic	2.5 (2.1)	1.4 (0.4)	7.2 (4.7)	26.9 (13.6)	15 (50)	15 (63)
Stable Recovery	2.4 (2.1)	1.4 (0.4)	7.0 (6.0)	26.1 (16.3)	48 (54)	27 (44)

Differences: ANOVA or Pearson Chi2/Fisher's exact, Bonferroni corrected, [a]p<0.005 between stable Persistent and Persistent to Episodic and Persistent to Recovery; [b]p<0.005 between stable Persistent and Persistent to Recovery and between Episodic to Persistent and Episodic to Recovery; [c]p<0.05 between stable Persistent and Persistent to Recovery; [d]p<0.05 between Episodic to Recovery and stable Episodic and Episodic to Persistent

HSCL-10 short form, The Hopkins Symptom Checklist; NDI, Neck Disability Index; NP, NP; SD, Standard deviation

III

Exploring visual pain trajectories in neck pain patients, using clinical course, SMS-based patterns, and patient characteristics: a cohort study

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Abstract

Background: The dynamic nature of neck pain has so far been identified through longitudinal studies with frequent measures, a method which is time-consuming and impractical. Pictures illustrating different courses of pain may be an alternative solution, usable in both clinical work and research, but it is unknown how well they capture the clinical course. The aim of this study was to explore and describe self-reported visual trajectories in terms of patients' prospectively reported clinical course and SMS-based pattern classification of neck pain.

Methods: Prospective cohort study including 888 neck pain patients from chiropractic practice, responding to weekly SMS-questions about pain intensity for 1 year from 2015-2017. Patients were classified into one of three clinical course patterns using definitions based on previously published descriptors. At 1-year follow-up, patients selected a visual trajectory that best represented their retrospective 1-year course of pain: Single episode, Episodic, Mild ongoing, Fluctuating and Severe ongoing.

Results: The visual trajectories generally resembled the 1-year clinical course characteristics on group level, but there were large individual variations. Patients selecting Episodic and Mild ongoing visual trajectories were similar on most parameters. The visual trajectories generally resembled more the clinical course of the last quarter.

Discussion: The visual trajectories reflected the descriptors of the clinical course of pain captured by weekly SMS measures on a group level and formed groups of patients that differed on symptoms and characteristics. However, there were large variations in symptoms and characteristics within, as well as overlap between, each visual trajectory. In particular, patients with mild pain seemed predisposed to recall bias. Although the visual trajectories and SMS-based classifications appear related, visual trajectories likely capture more elements of the pain experience than just the course of pain. Therefore, they cannot be seen as a proxy for SMS-tracking of pain over 1 year.

Key words:

Visual trajectories; Longitudinal; Subgrouping; Recall bias; Chiropractic; SMS; Questionnaire

1. Background

Non-specific neck pain is costly and common (1-3). Close to one third of all adults is likely to experience neck pain during one year (4). During the last years, considerable research on spinal pain has focused on subgrouping patients based on prognostic factors and individual clinical course of pain. Categorizing pain, based on the temporal variation, as either persistently fluctuating or episodic seems to have replaced the more traditional categories of chronic and acute pain (5-8). Furthermore, common pain trajectories have been established for low back pain (5), and are also found in neck pain (9-12). Definitions and terminology of trajectories for low back pain have been translated into subgroup criteria (9), which fit readily to neck pain patients (10).

Trajectories appear to be stable over time (13, 14), as well as represent different patient profiles across various health domains (5, 10, 12). Hence, it is likely they are better measures in clinical studies than single pain measures at single time-points. They may also be useful as a stratification tool, or as a tool in clinical management and communication. However, identifying accurate pain trajectories is time-consuming, expensive, and not feasible in clinic or most research, and methodological quality is still unknown.

A recent study on low back pain has introduced a novel and simple alternative to long-term follow-ups with frequent measurements to identify clinical course, namely, to use pictures illustrating the different pain trajectories (visual trajectories) (15). Patients were asked to choose the picture that best represented their clinical course of pain (trajectory) among eight illustrations. Patients and clinicians easily identified with the visual trajectories, indicating good face validity. This method is straightforward, quick and cheap to administer, and therefore probably more easily applicable in clinical practice. Similar visual trajectories were recently found to improve a clinical prediction rule for neck pain (16). We have recently shown that classification of patients based on visual trajectories reflected group differences in severity regarding symptoms and distress (17).

To our knowledge, no study has explored the association between SMS-based and visual trajectories in neck pain patients. While SMS-based trajectories describe the prospectively reported course of pain, visual trajectories provide the patients' retrospective perception of the course. Visual trajectories may represent anything from a recall that is largely disconnected from the experienced course, to a recall that closely resembles the patient's SMS-based trajectory. For visual trajectories to be useful in research and clinic, it is essential to understand what they capture regarding the clinical course from prospective frequent measures. Thus, the aim of this study was to explore and describe self-reported visual trajectories in terms of patients' prospectively reported clinical course and SMS-based pattern classification of neck pain.

2. Method

2.1 Study design, population and setting

We used data from a 1-year observational, multi-center, practice-based cohort consisting of patients with neck pain in a chiropractic care setting in Norway. Seventy-one chiropractors located across Norway invited eligible patients with neck pain to participate in the study between September 2015 and June 2016. Decisions regarding treatment and follow-up were at the chiropractors' discretion. Descriptions of cohort recruitment and study procedures are published previously (10, 14, 16, 17). The Regional Committee for Medical and Health Research Ethics (2015/89) approved the study protocol. The study was reported according to the STROBE statement (18).

Population

We included patients aged 18 years or more, presenting with neck pain as their primary or secondary complaint, independent of being acute or long-term or in a treatment plan. Patients had to have basic Norwegian reading and writing skills and be able to operate a mobile phone. We excluded patients with suspected inflammatory diseases, fractures, systemic pathology, or nerve root involvement requiring referral to surgery. The chiropractors recruited 1,478 patients with neck pain. Of these, 888 (60%) had completed both 1-year and baseline questionnaires and provided enough SMS to be classified to a SMS-based pattern, and thus, constituted the study sample (Figure 1).

Figure 1 Flow-chart of study population

2.2 Data collection

Patients received questionnaires electronically or on paper. Paper questionnaire was given by the chiropractor at recruitment. For patients selecting electronic questionnaire, the chiropractor gave the patient's e-mail address to the research group, who sent an e-mail to the patient with a link to the questionnaire within two days after recruitment. We collected questionnaire data at baseline and 1-year follow-up. Patients not responding within 7 days received one written reminder, followed by a phone call two weeks later. Patients also received 2-3 mobile text messages (SMS) at the same day and time every week over a 1-year period, with a reminder 2 days later should they fail to respond to the initial SMS. We collected the following patient demographics at baseline: age, sex, history of neck pain and consultation type, as well as pain intensity at recruitment. History of neck pain was categorized into those with a history of neck pain less than 5 years, and those with equal to, or more than, 5 years history. We defined patients recruited at their first visit for a new episode of neck pain as "first consultation".

2.2.1 1-year questionnaire data

We measured current neck pain intensity on a Numeric Rating Scale (NRS) by a 0–10 numeric rating scale (0 = no pain; 10 = worst pain imagined) (19). Functional status was measured by the Neck Disability Index (NDI). NDI consists of 10 items regarding pain and function with scoring from 0 to 5. The sum score ranges from 0-50 points, with higher scores indicating more disability (20, 21). We measured emotional stress by the Hopkins Symptom Checklist (HSCL-10), with scoring from 1 (low) to 4 (high) (22, 23), and psychosocial risk factors by the Örebro Musculoskeletal Pain Questionnaire (24, 25). The Örebro sum score ranges from 0-100 points, where higher scores indicate higher risk of persistent pain and disability. Studies have shown that expectations are partly, but not completely, formed by pain history (26, 27). We therefore measured recovery expectations from Item 7 of the Örebro screening questionnaire (28), "In your view, how large is the risk that your current pain may become persistent?" (0-10, 0=no risk, 10=very large risk). We also recorded characteristics of symptoms regarding duration of the current episode (<1 month, 1-3 months, >3 months) and pain radiating into the shoulder and/or the elbow (yes/no). Number of pain sites was measured by the Nordic pain questionnaire (NPQ (0-10)) (29). We used functional status (NDI), emotional stress (HSLC-10), psychological risk factors (Örebro screening questionnaire), and recovery expectations (28) to calculate change in the relevant scores between baseline and 1-year follow-up. As there is uncertainty about the concept and measurement of minimal important change (MIC) (30), we decided to calculate the patients' change in scores as follows: We subtracted the baseline score from the 1-year score. Patients with a change score equal to or higher than the 80^{th} percentile score for the whole cohort, were defined as having a positive change.

2.2.2 Visual trajectories

In the 1-year questionnaire, we asked patients to identify their neck pain course the previous year, using a self-reported visual trajectory pattern questionnaire (5) (hereafter 'visual trajectory'). The questionnaire has previously been used in two studies from our cohort (16, 17). It includes drawings and descriptions of five different neck pain trajectories; No neck pain or Single episode (hereafter 'Single episode'), Episodic, Mild ongoing, Fluctuating, and Severe ongoing, with the corresponding question: "Please tick off the description below that you think best represents how your neck pain has been **the previous 12 months**" (Figure 2). The questionnaire also included the answer alternatives "None of the above" and "Do not know".

2.2.3 Clinical course from SMS data

Patients received the following questions weekly on SMS "How many days the last week has your neck been bothersome? Please answer with a number between 0 and 7" (hereafter 'paindays'). If the answer was between 1 and 7, the patient received a second SMS "How intense has your neck pain typically been the last week? 0= no bother, 10= worst possible bother" (hereafter 'pain intensity'). A third SMS (not used in the present study) "How many days this last week has your neck limited your daily activities? Please answer with a number between 0 and 7".

For the descriptors of the course of pain, we calculated the total number of painful days, the mean pain intensity across the 52 weeks, the duration and frequency of pain-free and painful weeks, as well as the proportion of the weeks that were pain-free, in the minor, mild, moderate, and severe pain range (defined below) for each patient. As a measure of variation in pain intensity within individuals, we calculated the standard deviation (SD) of the mean of the individual's weekly pain intensity (1-year and the last quarter) (hereafter 'intensity variation').

Classification into SMS-based patterns

We described the patients' clinical course, using the same criteria as in recently published articles (9, 10, 14). Patients were classified into patterns based on pain intensity from the weekly SMS data collected over 1 year (hereafter 'SMS-based pattern'). The predefined SMS-based patterns included four variation patterns, Persistent fluctuating, Episodic, Single episode and Recovery: In the Persistent fluctuating pattern, no pain-free period could last four weeks or longer. Patients in the Episodic pattern must have at least one pain-free period of minimum four consecutive weeks between weeks with pain. The pain-free duration was based on consensus-formed definitions (31, 32), and has been tested in a low back pain cohort (33). The Single episode was defined as a short flare-up lasting 1-2 weeks anywhere during the study period. The Recovery pattern included all patients with <u>maximum</u> pain intensity < 2. We subsequently split the

Persistent fluctuating pattern into four subgroups based on mean pain intensity as follows: Severe (pain intensity ≥ 6), Moderate (4 ≤ pain intensity < 6), Mild (2 ≤ pain intensity < 4), and Minor (pain intensity < 2). This is in line with previously suggested cut-off values for pain (34-37). We split the Episodic and Single Episode patterns into three subgroups each, based on the maximum pain intensity reported throughout the period: Severe (pain intensity ≥ 6), Moderate (4 ≤ pain intensity < 6) and Mild (2 ≤ pain intensity < 4). We combined the Recovery pattern and the Single episode pattern into one pattern called "Single episode/Recovery". This left us with 3 patterns and 11 subgroups for analyses. The process of reducing the number of subgroups from the original 16 (9) to the 11 used in this study is described in Supplementary Files S1 and S2.

We have previously found that patients in an episodic pain course have large individual and group variations in painful- and pain-free periods (14). We therefore wanted to explore the relationship between the stability of the patients' SMS-based pattern over 1 year and their selected visual trajectory. We therefore used the above-mentioned classification procedure on data from two shorter periods: the first and the last quarter (weeks 1 to 13 and weeks 40 to 52, respectively) of the follow-up year. We defined patients allocated to the same pattern in the first and last quarter as having a stable trajectory, and those with different patterns as having a shifting trajectory, as done previously (14). We calculated the proportion of patients that had a stable pattern.

2.4. Data Analyses

Few of our variables were normally distributed and accordingly we present descriptive variables as frequencies and percentages or median with interquartile range (IQR) when appropriate. We combined the visual trajectory alternatives "None of the above" and "Do not know" into one group, called "Neither" for analytical purposes. The methods used for imputing the missing values on the weekly pain intensity measures for the SMS-based pattern is described in detail in Supplementary files S1.

We cross-tabulated visual trajectories with the eleven SMS-based patterns to explore and describe the distribution of SMS-based pattern classifications for each of the visual trajectories. We present the distribution of SMS-based patterns as a stacked bar graph for each of the visual trajectories at 1-year follow-up. To explore pain recall in relation to the selection of visual trajectory, we did the same cross-tabulation and stacked bar graph presentation between the visual trajectories and the last quarter SMS-based patterns.

This study was part of a larger project that also aimed to assess 11 possible variables for prognostic factors. Using the prognostic model "rule of thumb" where 10 events per candidate variable is required (=1100 patients) (38) and possible 20% drop-out, a sample size of 1320 patients was considered sufficient.

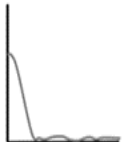
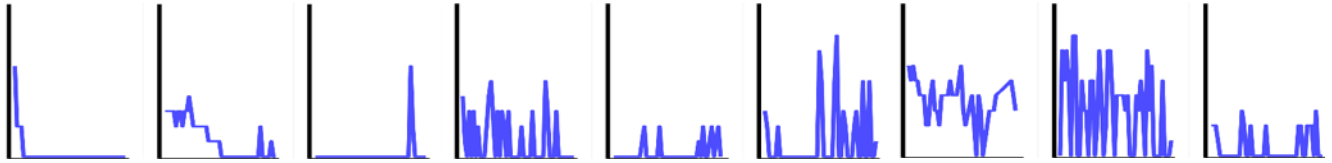
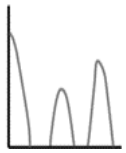
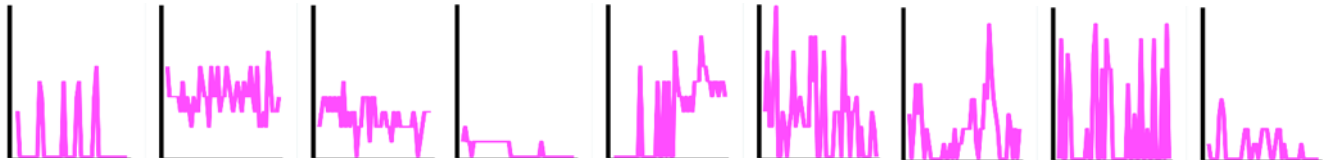
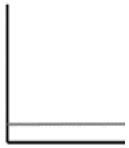
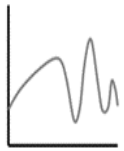
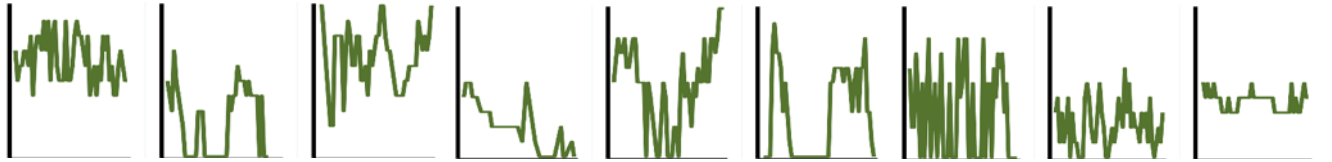
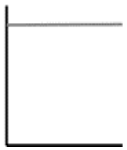
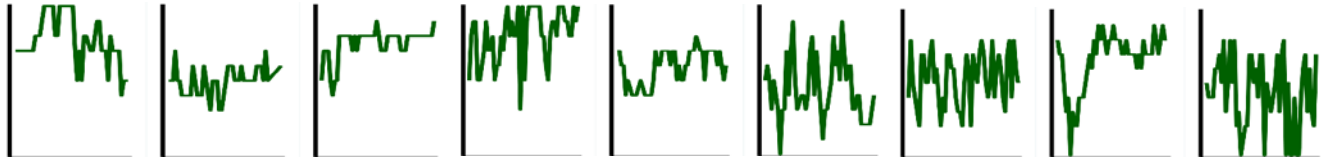
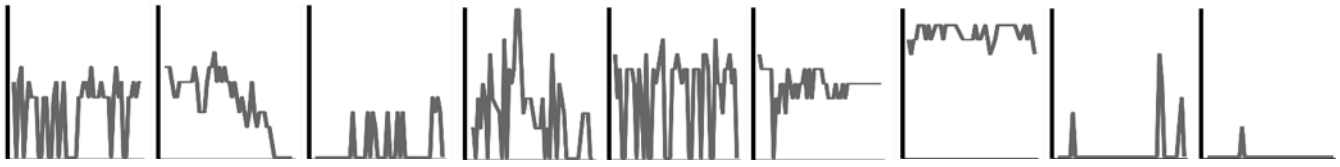
We carried out all analyses using STATA 16 (StataCorp, Texas, USA).

3. Results

The 888 participants had a mean age of 45 (SD 13) years and 663 (75%) were women. The mean pain intensity (SD) at baseline and 1-year follow-up was 4.1 (2.3) and 2.5 (2.4) respectively. Close to 50% reported previous neck pain duration of 1 year or longer at baseline. There were no substantial differences between the study sample and those lost to follow-up. The cohort has been described in detail previously (17).

In total, 37% (n=331) of patients selected the Episodic visual trajectory, 36% (n=323) the Fluctuating trajectory, and 14% (n=121) the Single episode trajectory on the visual trajectory questionnaire. Furthermore, 9% (n=83) selected Mild Ongoing and 2% (n=14) selected the Severe Ongoing trajectory. Two percent of patients (n=22) did not recognize any of the five visual trajectories. Using the SMS-based classification, 48% of the study sample were classified as Persistent fluctuating and 49% as Episodic. Examples of individual SMS-based trajectories for each of the visual trajectories are displayed in Figure 2. These examples are selected to illustrate the variability of the individual clinical courses of pain.

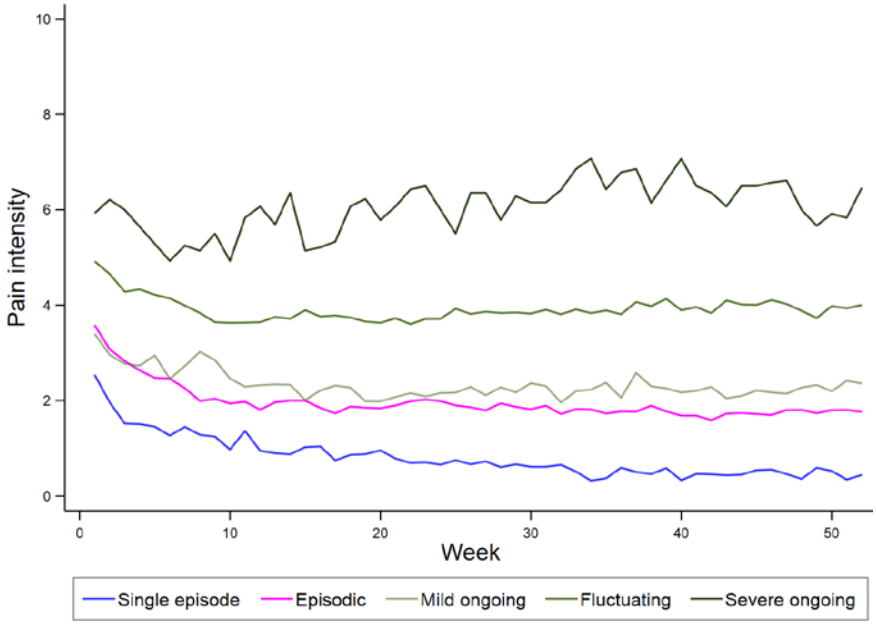
Figure 2 Description of the visual trajectories and examples of 1-year individual SMS-based clinical course

1) Single episode	121 (14)		No neck pain or just a single episode of neck pain	
2) Episodic	331 (37)		Few episodes of neck pain separated by pain free periods	
3) Mild ongoing	81 (9)		Mild neck pain most of the time	
4) Fluctuating	315 (36)		Neck pain of varying intensity but never completely pain free	
5) Severe ongoing	14 (2)		Severe neck pain most of the time	
6)	22 (2)	Neither	None of the above Don't know	

3.1 Clinical course characteristics

The variability in the details of the clinical course was large among participants selecting the same visual trajectory. However, there were clear differences between the visual trajectories concerning the mean course of pain for all but between the episodic and mild ongoing visual trajectories (Figure 3), as well as the descriptors of the clinical course (Table 1).

Figure 3 Weekly mean pain intensity over 1 year in the five visual trajectories



In general, the visual trajectory resembled well the predefined clinical course descriptors on a group level. For instance, patients selecting the Single episode visual trajectory were likely to have the highest proportion of pain-free weeks (median 79%, Inter-Quartile Range (IQR) 58-92%) with only short periods with pain, and they rarely or never report painful periods with moderate or severe pain. However, they reported large variations concerning the number of painful periods during the 1-year follow-up (median 4, IQR 1-8). Patients selecting a Fluctuating visual trajectory were likely to have minimal numbers of pain-free weeks, report moderate to high pain intensity most weeks, but the weekly variation in pain were similar to the patients selecting the Episodic visual trajectory. Similarly, patients selecting the Severe ongoing visual trajectory have variations in weekly pain, but they report the highest pain intensity, most days with pain, and no pain-free weeks. Patients selecting Episodic or Mild ongoing visual trajectories have a clinical course in between those selecting the Single episode and Fluctuating trajectories, namely frequent pain episodes with mostly minor or mild pain. The mean course of pain differed for each of the visual trajectories apart from Episodic and Mild ongoing, which again were very similar (Figure 3). Although the visual trajectories are generally different, there was a large overlap in the detailed course for the patients selecting them, as seen from IQRs in Table 1, especially between those selecting the Episodic and Mild ongoing visual trajectories.

Table 1 Clinical course details and characteristics of patients presented for each of the visual trajectories

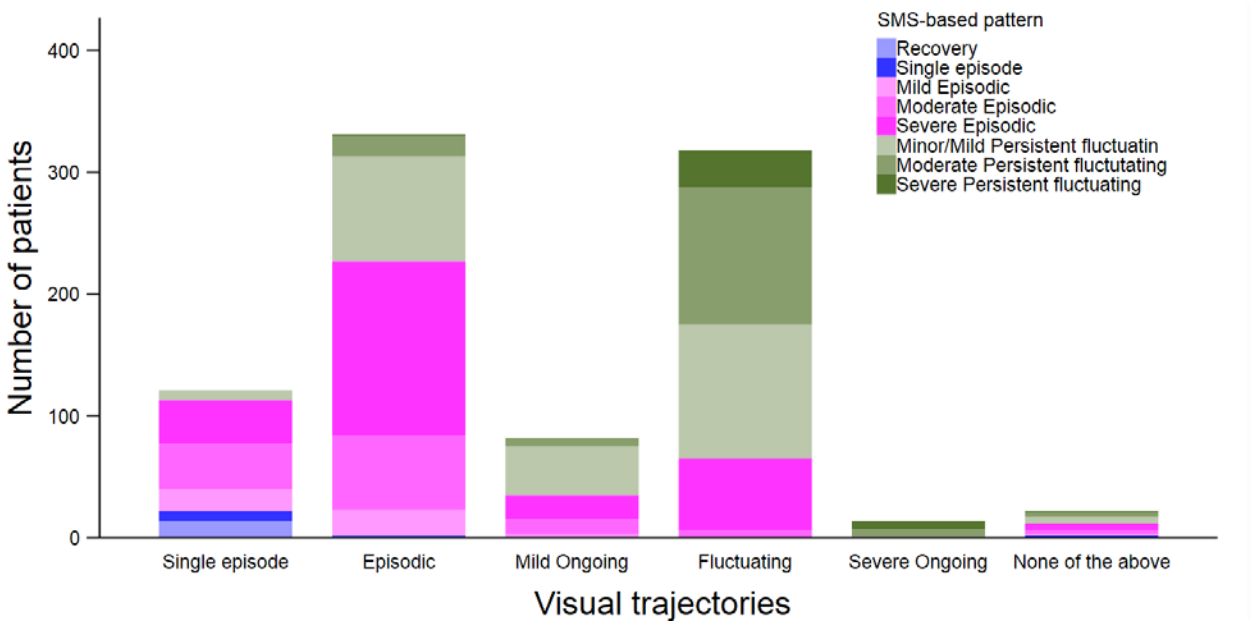
	Single episode	Episodic	Mild Ongoing	Fluctuating	Severe Ongoing	Neither
Number, n (%)	121 (14)	331 (37)	81 (9)	315 (36)	14 (2)	22 (2)
Weekly SMS-based details						
Total number of days with pain, median (IQR)	93 (75-118)	138 (112-177)	182 (138-228)	249 (198-332)	384 (332-401)	139 (90-208)
Proportion (%) of weeks, median (IQR)						
No or minor pain (<2)	83 (67-94)	49 (26-71)	26 (3-60)	4 (0-24)	0 (0-2)	31 (4-79)
Mild pain (≥2<4)	10 (2-24)	25 (16-40)	38 (20-59)	26 (12-41)	7 (0-20)	19 (2-35)
Moderate pain (≥4<6)	4 (0-8)	12 (6-25)	17 (4-28)	29 (19-44)	25 (12-35)	20 (4-37)
Severe pain intensity (≥6)	0 (0-2)	4 (0-10)	2 (0-8)	17 (4-37)	62 (27-86)	6 (0-17)
Mean pain intensity, median (IQR)[1]	0.5 (0.2-1.1)	1.8 (1.1-2.6)	2.3 (1.4-3.2)	3.8 (2.8-4.9)	6.1 (4.5-7.5)	2.5 (0.7-3.6)
Mean duration of pain-free periods (weeks), median (IQR)	9 (5-23)	3 (2-4)	2 (1-3)	2 (1-3)	0 (0-0)	2 (2-11)
Longest pain-free period (weeks), median (IQR)	22 (10-38)	6 (3-11)	3 (1-7)	1 (0-1)	0 (0-0)	5 (1-15)
No pain last four weeks, %	64	23	9	3	0	23
Number of painful periods, median (IQR)	3 (1-8)	7 (5-9)	5 (4-8)	1 (1-5)	1 (1-1)	4 (1-9)
Longest painful period (weeks), median (IQR)	4 (2-9)	9 (5-15)	12 (7-21)	20 (10-52)	39 (10-52)	9.5 (4-16)
Pain intensity variation 1 year[2], median (IQR)	1.1 (0.7-1.5)	1.7 (1.3-2.1)	1.3 (1.0-1.8)	1.6 (1.2-2.0)	1.7 (1.0-2.0)	1.7 (1.1-2.0)
Pain intensity variation last quarter[2], median (IQR)	0.3 (0.0-1.1)	1.5 (0.9-2.0)	0.9 (0.6-1.4)	1.3 (0.9-1.8)	1.0 (0.8-1.7)	1.3 (0.6-1.7)
Stable SMS-based pattern, yes %	38	62	77	91	100	68
1-year questionnaire data						
Pain intensity, median (IQR)	0 (0-0)	1 (0-3)	2 (1-4)	4 (3-5)	6 (5-8)	0.5 (0-3)
Duration of episode <1 month, %	46	17	10	3	0	19
Radiating pain to shoulder/elbow, %	34	50	76	86	92	36
Recovery expectations, median (IQR)	0 (0-2)	5 (2-8)	6 (4-9)	9 (7-10)	10 (8-10)	4 (1-7)
Örebro screening questionnaire, median (IQR)	17 (11-23)	30 (22-38)	32 (23-40)	46 (37-54)	60 (49-65)	26 (14-44)
HSCL-10, median (IQR)	1.1 (1.0-1.4)	1.4 (1.2-1.7)	1.4 (1.2-1.7)	1.6 (1.3-2.0)	2.0 (1.5-2.2)	1.2 (1.0-1.5)
NDI, median (IQR)	2 (1-4)	7 (4-10)	7 (5-11)	14 (10-18)	23 (18-30)	5 (2-11)
Number of MSK pain sites, median (IQR)	2 (0-3)	3 (2-5)	4 (2-6)	5 (4-7)	7 (4-8)	3 (2-5)
Health status, (median IQR)	90 (80-95)	80 (70-90)	80 (75-88)	70 (50-80)	50 (30-64)	82.5 (70-90)
Baseline patient characteristics						
Age (y), median (IQR)	45 (35-53)	43 (35-52)	47 (38-54)	46 (38-55)	46 (41-63)	46 (35-57)
Female, %	60	78	63	79	57	68
First consultation, %	21	14	14	14	15	32
Physical activity, yes %	69	68	70	70	57	77
Pain intensity, median (IQR)	3 (0-4)	4 (2-5)	3 (2-5)	5 (4-6)	5 (5-7)	4 (2-6)
No previous episodes, %	33	13	10	7	14	14
NP history baseline >5 years, yes %	48	71	64	75	92	47

[1]Presented as median of individual mean pain intensity, [2]Presented as standard deviation from individual mean pain intensityPain intensity from NRS: the 11-point numerical rating scale (19), Recovery expectations from "In your view, how large is the risk that your current pain may become persistent?" (0-10, 0= no risk, 10=very large risk) and psychosocial risk factors: Örebro Screening Questionnaire (0-100) (24, 28), HSCL-10: Hopkins Symptom Checklist measuring emotional stress (0-4) (23), NDI: Neck Disability Index (0-50) measuring disability (21), Health status (0-100) (39), NP: Neck pain.

3.2 Associations between visual trajectories and classification into SMS-based patterns

Figure 4 shows the frequency of the SMS-based patterns for each of the visual trajectories (numbers in Supplementary Table S3). The majority (75%) of the patients selecting a Single episode visual trajectory were classified as Episodic and 18% as Single episode/Recovery. Sixty-eight percent of patients selecting an Episodic visual trajectory were classified as Episodic, with most of the remaining (31%) classified as Minor to Moderate Persistent fluctuating. For patients selecting the Mild ongoing visual trajectory, 49% were classified Mild or Minor Persistent fluctuating, and 39% were classified as Severe or Moderate Episodic. The majority of patients selecting a Fluctuating or Severe ongoing visual trajectory were classified as Persistent fluctuating (80% and 100%, respectively) and 19% of those selecting Fluctuating pattern were classified as Severe Episodic. None of the patients selecting the Mild ongoing, Fluctuating or Severe ongoing trajectories were classified as Single episode/Recovery on SMS.

Figure 4 Relationship between the five Visual trajectories and the 1-year SMS-based patterns



3.3 1-year questionnaire data

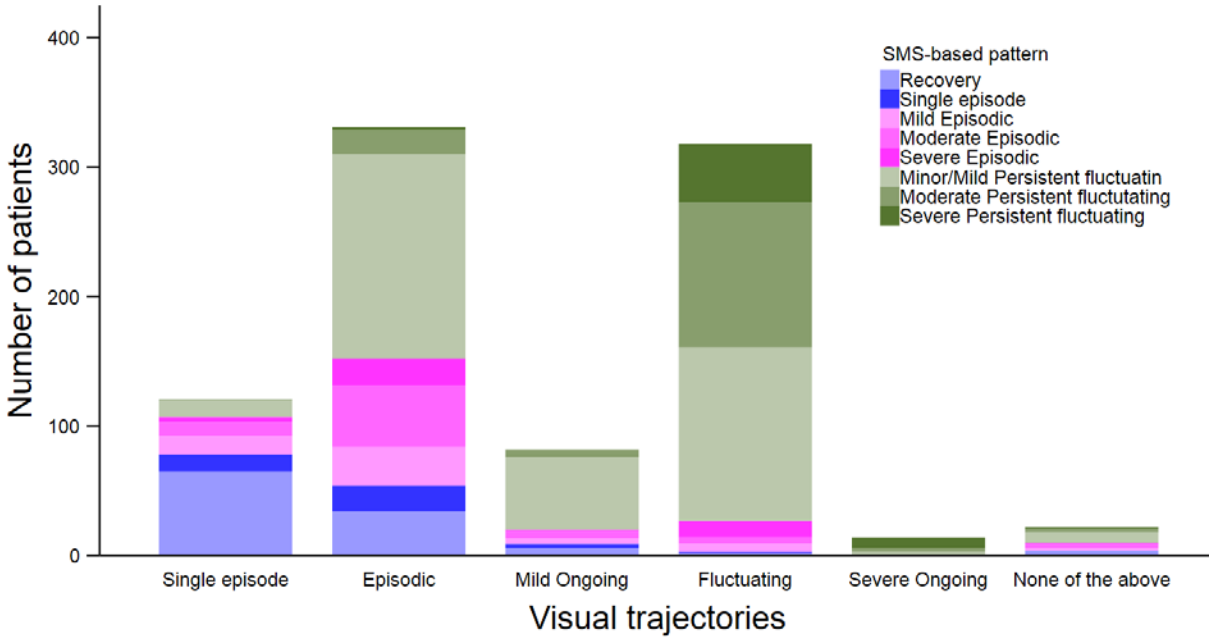
The data reported for symptoms, disability and psychosocial factors showed an increase in severity from those selecting the Single episode visual trajectory to the Severe Ongoing visual trajectory (Table 1). Patients selecting Episodic or Mild ongoing visual trajectories and classified as Episodic with SMS data were almost similar in both clinical course and patient characteristics (Table 2). This group of patients was different from patients selecting Single episode visual trajectory and classified as Episodic (less pain and less bothered) and patients selecting Fluctuating visual trajectory and classified as Episodic (more pain and more bothered). Similar associations were found in patients selecting Episodic or Mild ongoing visual trajectory but classified as Persistent fluctuating. There were few differences between patients selecting

Episodic and Mild ongoing visual trajectory, but they had less pain-free weeks, higher pain intensity and longer painful periods compared to patients selecting Episodic or Mild ongoing visual trajectory and classified as Episodic.

3.4 Visual trajectory selection and last quarter SMS-based classification

The main differences between comparing visual trajectories to the 1-year or the last quarter SMS-based classification, was that patients selecting Single episode visual trajectory were more often recovered in the last quarter but had reported episodes of pain previously during the full year (Figure 5, numbers in Supplementary Table S4). Also, most (77%) of the patients selecting the Mild ongoing visual trajectory were classified as Persistent based on SMS data in the last quarter, whereas this was the case for only 57% when considering the full year (Supplementary Table S3 and S4). In contrast, 68% of patients selecting the Episodic visual trajectory were classified as Episodic using SMS during the full year, but only 30% were classified as SMS-based Episodic in the last quarter.

Figure 5 Relationship between the five Visual trajectories and the last quarter SMS-based patterns



All patients who selected the Single episode visual trajectory and were classified as Single episode/Recovery (18%, n=22) for the full year (Figure 4), had their single episode of pain in the last quarter of follow-up (Table 3). Fifty-two (48%) of the remaining 99 (82%) patients having selected Single episode visual trajectory were also classified as single episode in the last quarter (Episodic in the full year). For patients classified as Episodic the full year, there was an increase in the number classified as Persistent fluctuating in the last quarter (going from Single episode to Fluctuating visual trajectory).

Table 2 Weekly SMS-based details and patient characteristics by patients' selected visual trajectory and their 1-year classified Episodic or Persistent fluctuating pattern

	Visual trajectory				Visual trajectory		
	Single episode	**Episodic**	**Mild Ongoing**	**Fluctuating**	**Episodic**	**Mild Ongoing**	**Fluctuating**
		Episodic SMS-based pattern				**Persistent fluctuating SMS-based pattern**	
Number, n	91	225	35	65	104	47	253
Weekly SMS-based details							
Total number of days with pain, median (IQR)	100 (81-118)	122 (103-146)	134 (112-172)	154 (130-208)	183 (154-210)	211 (176-268)	273 (221-352)
Proportion (%) of weeks, median (IQR)							
Minor pain (<2)	80 (67-90)	61 (46-78)	60 (43-76)	44 (33-56)	17 (8-29)	10 (0-24)	2 (0-8)
Mild pain (≥2<4)	13 (6-24)	21 (13-31)	21 (13-39)	22 (14-33)	41 (28-55)	52 (33-71)	29 (12-44)
Moderate pain (≥4<6)	4 (2-8)	8 (4-20)	8 (2-16)	17 (12-25)	25 (14-37)	25 (13-37)	35 (23-47)
Severe pain intensity (≥6)	0 (0-2)	2 (0-6)	2 (0-4)	6 (4-19)	8 (2-16)	2 (0-8)	19 (6-41)
Mean pain intensity, median (IQR)[1]	0.6 (0.3-1.1)	1.4 (0.9-2.0)	1.4 (0.9-1.9)	2.1 (1.6-3.0)	2.7 (2.3-3.4)	3.0 (2.4-3.5)	4.3 (3.4-5.1)
Longest pain-free period (weeks), median (IQR)	19 (10-28)	8 (5-14)	7 (5-13)	7 (5-9)	2 (1-2)	1 (0-2)	0 (0-1)
No pain last four weeks, %	67	33	20	15	0	0	0
Number of pain-free periods, median (IQR)	1 (0-2)	2 (1-3)	1 (1-2)	2 (1-3)	1 (0-2)	0 (0-1)	0 (0-0)
Longest painful period (weeks), median (IQR)	4 (3-9)	7 (4-11)	9 (4-12)	9 (6-14)	16 (10-28)	16 (10-39)	26 (13-50)
Stable SMS-based pattern, yes %	25	44	46	58	99	100	100
1-year patient characteristics							
Pain intensity, median (IQR)	0 (0-0)	0 (0-2)	1 (0-3)	3 (0-5)	3 (2-5)	3 (2-4)	4 (3-6)
Recovery expectations, median (IQR)	1 (0-2)	4 (2-7)	5 (2-8)	8 (5-10)	7 (4.5-9)	7 (5-10)	9 (7-10)
Örebro screening questionnaire, median (IQR)	17 (11-25)	27 (19-34)	27 (21-39)	37 (30-49)	35 (28-44)	34 (26-40)	47 (40-55)
HSCL-10, median (IQR)	1.1 (1.0-1.5)	1.3 (1.1-1.6)	1.3 (1.1-1.5)	1.4 (1.2-1.8)	1.5 (1.2-1.7)	1.5 (1.2-1.9)	1.6 (1.3-2.0)
NDI, median (IQR)	2 (1-4)	6 (3-9)	6 (4-9)	12 (8-15)	9 (6-12)	8 (5-13)	15 (11-19)
Baseline patient characteristics							
Pain intensity, median (IQR)	3 (1-4)	3 (2-5)	2 (1-4)	4 (3-6)	4 (3-6)	4 (3-5)	5 (4-6)
Proportion of patients with positive change score[2], %							
NDI	43	30	23	31	22	21	13
Örebro screening questionnaire	40	27	29	23	19	13	29
HSCL-10	25	20	31	29	20	13	18
Recovery expectation	63	52	31	26	38	30	26

[1]Presented as median of individual mean pain intensity,[2]Positive change score: patients in the cohort's 80th percentile for change in score between baseline and 1-year.

Pain intensity from NRS: the 11-point numerical rating scale (19), Recovery expectations from "In your view, how large is the risk that your current pain may become persistent?" (0-10, 0= no risk, 10=very large risk) and psychosocial risk factors: Örebro Screening Questionnaire (0-100) (24, 28), HSCL-10: Hopkins Symptom Checklist measuring emotional stress (0-4) (23), NDI: Neck Disability Index (0-50) measuring disability (21), Health status (0-100) (39).

Table 3 Visual trajectory and SMS-based classification for 1-year versus last quarter

		Last quarter SMS-based pattern			
Visual trajectory	1-year SMS-based pattern	Single episode/Recovery	Episodic	Persistent fluctuating	Total
Single episode	Single episode/Recovery	22 (100)	0	0	22
	Episodic	56 (62)	29 (32)	**6 (6)**	91
	Persistent fluctuating	0	0	8 (100)	8
Episodic	Single episode/Recovery	2 (100)	0	0	2
	Episodic	52 (23)	97 (43)	**76 (34)**	225
	Persistent fluctuating	0	1 (1)	103 (99)	104
Mild ongoing	Single episode/Recovery	0	0	0	0
	Episodic	9 (26)	11 (31)	**15 (43)**	35
	Persistent fluctuating	0	0	47 (100)	47
Fluctuating	Single episode/Recovery	0	0	0	0
	Episodic	3 (5)	24 (37)	**38 (58)**	65
	Persistent fluctuating	0	0	253 (100)	253
Severe ongoing	Single episode/Recovery	0	0	0	0
	Episodic	0	0	0	0
	Persistent fluctuating	0	0	14 (100)	14
Neither	Single episode/Recovery	2 (100)	0	0	2
	Episodic	2 (20)	6 (60)	2 (20)	10
	Persistent fluctuating	0	0	10 (100)	10

Note: Patients with a 1-year episodic SMS-based pattern and last quarter persistent fluctuating SMS-based pattern are marked in bold

4. Discussion

The visual trajectories reflected the descriptors of the clinical course of pain captured by weekly SMS measures on a group level. Patients seemed to a large extend to recall both the pain variation and intensity dimensions of their neck pain. Patients' selection of the visual trajectories also appears to form groups that differ on other symptoms and patient characteristics. However, there were large variations in symptoms and characteristics within each visual trajectory and overlap rather than leaps between the trajectories. Thus, we cannot at this point conclude that the visual trajectories fully reflect the experienced course of NP. However, our results support that the visual trajectories and the SMS-based classifications are related on a group level.

4.1. Clinical course and characteristics of patients in the different visual trajectories

Patients selecting Severe ongoing and Fluctuating visual trajectories reported the highest pain intensity and few to no pain-free weeks throughout the follow-up year. Hence, these two visual trajectories seem to be selected by patients with the highest disability and psychosocial risk factors, and with very low expectations of recovery. In addition, the large majority of these patients were classified as Persistent fluctuating throughout the follow-up year. However, we had only 14 patients selecting the Severe ongoing visual trajectory. They reported no pain-free weeks, more than half of

their reported weeks were with severe pain, and all were classified as Persistent fluctuating. These are the only patients we can be certain had selected a visual trajectory that mostly reflected their clinical course. Still, a few of these patients reported some weeks with mild pain.

In contrast, only 18% of the patients selecting the Single episode visual trajectory actually reported only one single episode of pain during the 1-year follow-up (classified as Single episode/Recovery pattern). They typically reported several short episodes of pain on SMS throughout the follow-up year. Furthermore, one of these episodes most often occurred within the last quarter. One could thus hypothesize that recall bias plays a role in patients with few and short pain episodes, as such short episodes are less likely to be remembered over time (40). Since these participants had high expectations of recovery and were mostly pain-free with negligible scores on symptoms and distress, one may suggest that their episodes are more tolerable and thus not easily recalled. The only comparable study by Dunn et al (15) had three visual trajectories, illustrating single episode, few episodes and no or only little pain. These three trajectories were selected by patients having little pain and were negligibly affected. Thus, it is likely that the Single episode visual trajectory used in our study is sufficient. Even though our patients selecting Single episode visual trajectory typically have more than one single episode of pain during 1 year, it still is a group with a mild course of pain and little affliction.

The patients selecting the Episodic and Mild ongoing visual trajectories were comparable on most parameters, in particular: they reported mild to no pain most weeks, interspersed with flare-ups of pain that varied greatly in duration. The painful episodes also varied in intensity among patients in both visual trajectories, but weeks with severe pain were rarely reported. In addition, patients in both the Episodic and Mild ongoing visual trajectories scored moderate to low on all health-related factors. There are several possible explanations for these similarities. First, previous studies show that steady pain with minimal fluctuations is rare (9, 10), and a large group of patients with episodic pain report painful episodes lasting longer than three months (14). Second, patients consider pain intensity ≤3 on NRS as a satisfactory state (41). This could explain the similar patient characteristics in the Episodic and Mild ongoing visual trajectories, despite Episodic patients having had twice as many pain-free weeks as those selecting Mild ongoing. Third, some patients might simply not recall pain-free periods in a course mostly characterized by mild pain intensity, nor the duration of painful and pain-free periods (40, 42-44). Nevertheless, the importance of periods with minor/no pain needs further examinations.

A group of patients did not select a visual trajectory reflecting their observed clinical course. The visual trajectories are not simply a measure of pain, but more likely includes aspects of the pain experience, and have been shown to carry prognostic information as well as been related to

expectation of pain (15-17). The SMS-based classifications, on the other hand, are based on pain intensity measures and have a temporal aspect. Pain intensity is both subjective and complex, and thus likely not an adequate or complete measure of affliction related to pain (45-48). It is generally accepted that pain scores are not easily compared between individuals. Moreover, recent studies have shown that pain intensity is not a good outcome measure compared to other health constructs (49). It is therefore likely that the differences found between the visual trajectories and the SMS-based classification patterns reflects some of these factors.

4.2. Strengths and weaknesses

The strength of this study is the large cohort and the good response rate. We have used descriptors and definitions for SMS-based patterns based on weekly measures over 1 year, which can easily be repeated constructed as they are on previous published recommendations (5). This has allowed us to identify the large variation in individuals' course of pain over time, which are not found in studies that use two to three measurements during a 1-year follow-up time (50, 51). In addition, we included patients with neck pain, regardless of the time for pain onset and treatment duration. It is therefore likely that our findings reflect a general distribution of the visual trajectories of neck pain patients in chiropractic practice. We included the options, "Do not know" and "Neither", for responders who did not recognize any of the visual trajectories, and these answer-alternatives accounted for only 2% of our participants. It is therefore doubtful that we have missed relevant information regarding the understanding of the trajectories.

The weaknesses of the study are that the visual trajectories used have not been validated, and there are no studies for direct comparison. However, there is evidence of face, criterion, and construct validity of similar visual trajectories (15). We did not include an extra visual trajectory questionnaire especially for the last quarter. Hence, we can only hypothesize on recall bias and its effect on the selection of Single episode and Episodic trajectories, and these results must be interpreted with care. Furthermore, the differences in NDI (function), HSCL-10 (emotional distress) and Örebro (psychological risk factors) between the visual trajectories were often below proposed minimal clinical important differences (30, 52), and conclusions regarding difference between the trajectories should be interpreted more as trends. Based on results from previous studies using latent class analyses (5, 11, 12), Dunn et al included two visual trajectories "Gradual improvement" and "Gradual worsening" (15). Even though these were selected by only 5% (improvement) and 4% (worsening) of their patients, we cannot exclude that these might be relevant for neck pain patients in chiropractic care.

4.3. Clinical implications and future indications

In clinical practice, the visual trajectories are likely more applicable than frequent measures over time. The visual trajectories can be useful as a communication tool between patient and clinician regarding the course and prognosis of neck pain. They are simple to implement and seem easy to understand for patients and clinicians. The visual trajectories can potentially be used in clinic as a measure of pain history, but also as a picture of patients' condition and illness perception here and now. Patients with similar observed clinical course have different recall of their neck pain experience, and it would be of interest to understand more regarding the factors that influence this difference in recollection. Based on our study and a very recent study showing that similar visual trajectories are relatively stable over time (53), the visual trajectories have potential for use in prognostic research. Both as a substitute to frequent measures, and in combination with other factors in prediction models and phenotypes for prediction and/or subgrouping. However, our descriptive study indicates that both the visual trajectory pattern questionnaire and the SMS-based pattern definitions need more refinement. Future studies should explore the differences between patients selecting a visual trajectory that closely matches their SMS-based clinical course pattern, and patients selecting visual trajectories more "positive" or more "negative" than their classified pattern.

Conclusions

The visual trajectories used in this study generally reflect the patients' clinical course defined by SMS data on group level. However, it is not a perfect match. This can be due to recall bias, but just as likely, that a patient's experienced course of pain is not based on pain intensity alone. Our findings suggest that the visual trajectories and SMS-based classifications may capture different elements of the pain experience. The visual trajectories most likely represent pictures that encompass features of the patients' course of pain, individual level of pain tolerance, and clinical condition at the time of reporting. Therefore, they cannot be seen as a proxy for SMS-tracking of pain intensity over 1 year. Rather, visual trajectories may be a suitable tool to attain a broader picture for prediction of NP or stratification of NP patients.

List of abbreviations

SMS = Short Messaging Services

NRS = Numeric Rating Scale

NDI = Neck Disability Index

HSCL-10 = Hopkins Symptom Checklist

NPQ = Nordic pain questionnaire

MIC = minimal important change

SD = Standard Deviation

IQR = Inter-Quartile Range

NP = Neck pain

Declarations

Ethics approval and consent to participate: The study was approved by The Norwegian Regional Committees for Medical and Health Research Ethics (2015/89). All procedures followed were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 1983. Participants were asked for and gave a written informed consent, authorizing the use of demographic and clinical data collected as part of this study. Following standard practice in Norway there was no compensation received for participation by neither patients nor clinicians.

Consent for publication: Written informed consent for publication of their clinical details was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Availability of data and materials: The datasets generated and/or analyzed during the current study are not publicly available due to data protection policies but are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Author contributions: All authors were involved in developing the design of the study. Pernille Irgens and Birgitte Lawaetz Myhrvold prepared and cleaned the data. Pernille Irgens did the statistical analysis. Pernille Irgens, Hilde Stendal Robinson and Nina Køpke Vøllestad wrote the first draft. All authors contributed by reviewing previous versions of the manuscript and improving the final version.

Pernille Irgens and Birgitte Lawaetz Myhrvold had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Written permission was from all persons named in the acknowledgment.

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Supplementary files

File S1

Imputation of the weekly SMS data before classification

We imputated missing values on the weekly pain intensity measures from SMS in three stages as follows: (1) we replaced missing responses in week 52 by the values reported in week 51, (2) one-week and two-week gaps between weeks with the same pain intensity, were replaced with that same value; (3) patients who after steps 1 and 2 had less than 26 complete responses out of 52 were excluded from the analysis and categorized as missing.

Classification into patterns and subgroups

The original definitions used in this study were based on conclusions drawn from a collaborative group on the clinical course of LBP (Kongsted et al., 2016), and translated into four variation patterns and tested on a LBP cohort (Kongsted et al., 2017): Ongoing, Fluctuating, Episodic and Single episode patterns. Patients in the Ongoing pattern should have a variation in pain intensity that did not exceed ±1 from the mean value each week. For the Fluctuating pattern, patients should have no consecutive four-week or more pain-free, and variation from the mean pain had to exceed ±1. Patients in the Episodic pattern should have pain-free periods of minimum four consecutive weeks between periods with pain. The definition of an episode was based on previously suggested definitions by de Vet et al (de Vet et al., 2002) and later upheld by a Delphi study (Stanton et al., 2011) and tested on a LBP cohort (Eklund et al., 2016), where an episode of LBP is defined as a period of pain lasting more than 24 hours, preceded and followed by at least four pain free weeks. Patients with a Single episode could have only one episode lasting 1-2 weeks during the study period. In addition, the Single episode could not be at the end of the study period. Findings and subsequent suggestions from two previous studies using the original definitions (Irgens et al., 2020; Kongsted et al., 2017) resulted in the following alterations in the

patterns. The two studies found that very few patients fit into the Ongoing and Single episode variation patterns. Also, Ongoing and Fluctuating patterns were very similar, where persistent pain was rarely completely steady in pain intensity (Irgens et al., 2020). We therefore combined the Ongoing and Fluctuating variation patterns into one pattern called Persistent pattern. In addition, patients classified in the Minor subgroups of Ongoing, Episodic and Single episode shared similar demographic, psychosocial and functional characteristics. These patients were only negligibly affected by their pain, and their pain intensity was also below what is considered clinically significant (<2 on NRS) (Kovacs et al., 2008; Pool et al., 2007). As a result, all patients with maximum pain intensity <2 were included in a new pattern called Recovery. However, patients in the Minor Persistent fluctuating subgroup were significantly more affected by their pain than the other three minor subgroups and were not included in the Recovery pattern. Details of the definitions of each pattern used in this study are shown in Methods S2.

File S2 *Definitions of the SMS-based patterns*

Pattern label		Variation pattern	Intensity
Recovery	Recovery	Pain that is either Episodic or Single episode, or where mean intensity equals zero	**Maximum** intensity <2
Single episode	Severe single episode	One episode lasting 1 - 2 weeks (which are not the first or the last week of measurement)	**Maximum** intensity ≥6 No restriction on mean intensity
	Moderate single episode	One episode lasting 1 - 2 weeks (which are not the first or the last week of measurement)	**Maximum** intensity ≥4 and <6 No restriction on mean intensity
	Mild single episode	One episode lasting 1 - 2 weeks (which are not the first or the last week of measurement)	**Maximum** intensity ≥2 and <4 No restriction on mean intensity
Episodic	Severe episodic	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.	**Maximum** intensity ≥6 No restriction on mean intensity
	Moderate episodic	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.	**Maximum** intensity ≥4 and <6 No restriction on mean intensity
	Mild episodic	Pain-free periods of min. 4 weeks in a row between weeks with pain. Four weeks or more without pain in the beginning or end of the course does not indicate a new episode.	**Maximum** intensity ≥2 and <4 No restriction on mean intensity
Persistent fluctuating	Severe persistent	No pain-free 4-weeks periods	**Mean** intensity ≥6 No restrictions on maximum intensity
	Moderate persistent	No pain-free 4-weeks periods	**Mean** intensity ≥4 and <6 No restrictions on maximum intensity
	Mild persistent	No pain-free 4-weeks periods	**Mean** intensity ≥2 and <4 No restrictions on maximum intensity
	Minor persistent	No pain-free 4-weeks periods	**Mean** intensity <2 No restrictions on maximum intensity

Table S3 Association between the Visual trajectories and the 1-year SMS-based patterns

	1-year SMS-based pattern distribution, (n%)											
	Recovery	Single episode			Episodic			Persistent fluctuating				
Visual trajectory		Severe	Moderate	Mild	Severe	Moderate	Mild	Severe	Moderate	Mild	Minor	Total
Single episode	14 (12)	2 (2)	0	6 (5)	36 (30)	37 (31)	18 (15)	0	0	7 (6)	1 (1)	8 (7)
Episodic	1 (<1)	0	0	1 (<1)	143(43)	61(18)	21(6)	1 (<1)	17 (5)	73 (22)	13 (4)	104 (31)
Mild ongoing	0	0	0	0	20 (24)	12 (15)	3 (4)	0	7 (9)	32 (39)	8 (10)	47 (57)
Fluctuating	0	0	0	0	59 (19)	6 (2)	0	30 (9)	113 (36)	105 (33)	5 (2)	253 (80)
Severe ongoing	0	0	0	0	0	0	0	7 (50)	6 (43)	1 (7)	0	14 (100)
Neither	0	0	0	2 (9)	6 (27)	3 (14)	1 (5)	1 (5)	4 (18)	5 (23)	0 (0)	10 (45)
Total	15 (2)	2 (<1)	0	9 (1)	264 (30)	119(13)	43 (5)	39 (4)	147 (17)	223 (25)	27 (3)	436 (49)

Table S4 Association between the Visual trajectories and the last quarter SMS-based patterns

	1-year SMS-based pattern distribution, (n%)											
	Recovery	Single episode			Episodic			Persistent fluctuating				
Visual trajectory		Severe	Moderate	Mild	Severe	Moderate	Mild	Severe	Moderate	Mild	Minor	Total
Single episode	65 (53)	0	1 (1)	12 (10)	4 (4)	11 (9)	14 (12)	0	1 (1)	5 (4)	8 (7)	65 (53)
Episodic	34 (10)	4 (1)	7 (2)	9 (3)	21 (6)	47 (14)	30 (9)	2 (1)	19 (6)	106 (32)	52 (16)	34 (10)
Mild ongoing	6 (7)	1 (1)	1 (1)	1 (1)	1 (1)	6 (7)	4 (5)	0	6 (7)	36 (44)	20 (24)	6 (7)
Fluctuating	2 (1)	1 (<1)	0	0	13 (4)	5 (2)	6 (2)	45 (14)	112 (35)	111 (35)	23 (7)	2 (1)
Severe ongoing	0	0	0	0	0	0	0	8 (57)	3 (21)	3 (21)	0	0
Neither	4 (18)	0	0	0	1 (5)	3 (14)	2 (9)	1 (5)	3 (14)	6 (27)	2 (9)	4 (18)
Total	111 (12)	6 (1)	9 (1)	22 (2)	41 (5)	72 (8)	56 (6)	56 (6)	144 (16)	267 (30)	105 (12)	111 (12)

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