Ingeborg Torvik Gotaas
Frida Øygard

Chronic Pelvic Pain: Assessment, Treatment and Outcomes

Data from a Tertiary Multidisciplinary Pain Center for Chronic Pain

Master's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences

◼ NTNU
NORWEGIAN UNIVERSITY OF
Science and Technology

Ingeborg Torvik Gotaas
Frida Øygard

Chronic Pelvic Pain: Assessment, Treatment and Outcomes

Data from a Tertiary Multidisciplinary Pain Center for Chronic Pain

Master's thesis in Medicine
Supervisor: Cecilie Therese Hagemann
Co-supervisor: Mona Stedenfeldt
July 2020

Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences

NTNU

Norwegian University of
Science and Technology

Abstract

Objective

Chronic pelvic pain (CPP) is a common, complex and burdensome pain condition. Our knowledge on etiology and optimal management is limited. For chronic pain patients in general, multidisciplinary management have shown to be effective, and current research indicates that it also is beneficial for CPP patients. However, few evaluations have been done. Due to its resource-demanding nature, evaluations of multidisciplinary management are desirable and necessary, from both a resource distribution and patient perspective. Existing research underlines the need to further investigate the role of multidisciplinary management, factors impacting its efficacy and early identification of CPP patients who may benefit from such management.

In the present study, the overall purpose was to increase knowledge regarding assessment, treatment and self-reported outcomes of patients consulting a tertiary multidisciplinary pain center for CPP. The specific aims were to compare CPP and chronic non pelvic pain (CNPP) patients in relation to the distribution of received assessment and treatment consultations; the assessment status (assessment completed versus not completed); and the assessment strategy received (multidisciplinary versus non-multidisciplinary). In addition, we wanted to compare post versus pre-changes in health-related quality of life and reported impression of change between CPP patients and CNPP patients. Further, among the CPP patients to investigate how patients' impression of change was associated with received assessment and treatment consultations or not; having completed assessment or not; and having received multidisciplinary or non-multidisciplinary assessment; patient background characteristics at baseline; and pre-consultation (baseline) symptom scores. Finally, to describe and compare between CPP and CNPP patients the use of pain medications.

Methods

This is a prospective cohort designed study, using patient self-reported outcomes and health providers' information from Norwegian tertiary multidisciplinary pain centers for chronic non-malignant pain (CNMP). Patient self-reported information was collected through web-based questionnaires one month prior and one year after the initial consultation. Pre-consultation data included background characteristics, symptom scores and quality of life, whereas post-consultation data involved quality of life and personal impression of change.

Health care providers' information encompassed (up to) four patient consultations and was retrieved from each of the local quality registries.

Results

Out of 934 CNMP patients consenting to be recorded at one of the three tertiary multidisciplinary pain centers at baseline, 687 (74 %) patients answered the self-report package at one year follow-up. Out of the 687 patients, 84 (12 %) had a CPP diagnosis. Among CNMP patients, 52 % received assessment consultations only (no treatment), whereas 48 % received both assessment and treatment consultations; 78 % had not completed their assessment; and 42 % received multidisciplinary assessment. No significant differences were found between the CPP and CNPP patients in regard to the assessment and treatment characteristics investigated. Regarding quality of life, for the CPP group, there were no changes in any of the domain scores after one year follow-up, nor were there any differences between the CPP patients and CNPP patients regarding mean score changes in any of these domains. However, at one year follow-up, a larger proportion of the CPP patients than of the CNPP patients reported feeling better, since as many as 36 (43 %) of the CPP patients had a global impression of improvement after one year, as in contrast to only 154 (26 %) in the CNPP category (p<0.01). For CPP patients, those having status as "completed assessment" by one year follow-up, reported to a larger degree a worsening of their condition (p=0.02). Further, there was a borderline significant difference regarding CPP patients' gender (p=0.09), with a higher proportion of women than men reporting feeling "better", and reporting "no to subclinical insomnia" at baseline was associated with patients reporting feeling "better" at one year follow-up (p=0.04). Also, among the CPP patients, a borderline statistically significant finding concerned the mean number of years patients had lived with pain, where patients that reported feeling "better" had a mean of 5.8 years with pain, while those with poorer Patient Global Impression of Change (PGIC) ratings at one year follow-up, had a mean of 9.3 years (p=0.12). CPP patients had used or were still using pain modifying medications to a larger extent than the CNPP patients (p=0.01), and selective serotonin reuptake inhibitors (SSRI)/serotonin-norepinephrine reuptake inhibitors (SNRI), pregabalin, benzodiazepines, Z-hypnotics and opioids were all more frequently used.

Conclusion

The present study indicates that CPP patients may benefit from management in a multidisciplinary pain center, possibly even more than CNPP patients. However, reporting

clinical insomnia, possibly male gender, having completed their assessment at the pain center and larger number of years with pain may be negatively associated with the CPP patient's outcome after one year. But, further studies with better registrations and specifications on actual treatment details from health personnel are needed to increase our understanding of factors that may impact patient outcomes.

Sammendrag

Bakgrunn

Kroniske bekkensmerter (CPP) er en vanlig, kompleks og ofte belastende smertetilstand. Det er begrenset kunnskap om tilstandens etiologi og den optimale håndteringen av bekkensmertepasienter. For kroniske smertetilstander generelt, har tverrfaglige tilbud vist seg å være effektive, og forskning indikerer at slike tilbud også kan være nyttige for bekkensmertepasienter. Det er imidlertid få studier som har evaluert bekkensmertepasienters nytte av slik utredning og behandling. Ettersom tverrfaglige tilbud er tids- og ressurskrevende, er evaluering nødvendig, både fra et pasientperspektiv og et samfunnsøkonomisk perspektiv. Eksisterende forskning understreker behovet for å evaluere nytteverdien av et tverrfaglig tilbud, faktorer som kan påvirke dets effektivitet, samt tidlig identifisering av bekkensmertepasienter som kan dra nytte av et slikt tilbud.

Formålet med studien var å øke kunnskapen om utredning, behandling og selvrapporterte utfall blant bekkensmertepasienter som fikk helsehjelp fra et regionalt, tverrfaglig smertesenter. Vi ønsket å sammenligne kroniske bekkensmertepasienter med andre kroniske smertepasienter (CNPP), vedrørende andel som; mottok utredning- og behandlingskonsultasjoner; hadde fullført utredning i løpet av ett år; og som mottok tverrfaglig kontra ikke-tverrfaglig utredning. I tillegg ønsket vi å sammenligne pasientenes opplevelse av helserelatert livskvalitet før og etter, og global opplevelse av endring (Patient Global Impression of Change, PGIC) etter ett år. Videre ville vi undersøke hvordan bekkensmertepasienters globale opplevelse av endring, var assosiert med andel som mottok utredning- og behandlingskonsultasjoner; andel som hadde fullført utredning i løpet av ett år; andel som mottok tverrfaglig kontra ikke-tverrfaglig utredning; pasientenes bakgrunnskarakteristika før oppstart, samt pasientenes symptomskårer før oppstart og ved ett års oppfølging. Avslutningsvis ønsket vi å beskrive og sammenligne bruk av smertestillende medikamenter blant bekkensmertepasienter og andre kroniske smertepasienter.

Metode

En prospektiv kohortstudie basert på pasientrapportert og behandlerregistrert informasjon fra tre, regionale, tverrfaglige smertesentre i Norge. Pasientrapporterte data ble samlet inn via nettbaserte spørreskjema en måned før og ett år etter første konsultasjon ved smertesenteret. Før-konsultasjonsdata omfattet bakgrunnskarakteristika, symptomskårer og livskvalitet, mens

etter-konsultasjonsdata omfattet livskvalitet og global opplevelse av endring. Behandlerregistrert informasjon inneholdt opplysninger fra (opp til) fire konsultasjoner per pasient, og ble hentet ut fra lokale kvalitetsregistre ved hvert senter.

Resultater

Blant 934 samtykkende pasienter i studien, besvarte 687 (74 %) pasienter spørreskjema ved ett års oppfølging. Av disse, hadde 84 (12 %) pasienter kroniske bekkensmerter. Blant alle kroniske smertepasienter, mottok 52 % utredning (ingen behandling), mens 48 % mottok både utredning og behandling; 78 % hadde ikke fullført utredning i løpet av ett år; og 42 % mottok tverrfaglig utredning. Det var ingen signifikante forskjeller mellom bekkensmertepasienter og andre smertepasienter med hensyn til nevnte utrednings- og behandlingskarakteristika. Vedrørende helserelatert livskvalitet, var det ingen endringer i domeneskårer blant bekkensmertepasientene ved ett års oppfølging, og heller ikke forskjell mellom bekkensmertepasienter og andre smertepasienter. Det var imidlertid en forskjell mellom pasientgruppene når det gjaldt global opplevelse av endring, hvor en større andel bekkensmertepasienter rapporterte forbedring. Hele 36 (43 %) bekkensmertepasienter følte seg «bedre» etter ett år, i motsetning til 154 (26 %) av andre smertepasienter (p<0,01). Videre, for bekkensmertepasienter, var opplevelse av forverring assosiert med å ha fullført utredning i løpet av ett år (p=0,02). Opplevelse av forbedring var grensesignifikant assosiert med å være kvinne (p=0,09), signifikant assosiert med rapportering av «ingen til subklinisk insomni» før oppstart (p=0,04) og grensesignifikant assosiert med antall år med smerter, hvor pasienter som opplevde forbedring hadde gjennomsnittlig 5,8 år med smerter, mens de som opplevde forverring hadde hatt smerter i gjennomsnittlig 9,3 år (p=0,12). Bekkensmertepasienter brukte smertestillende medikamenter i større grad enn andre smertepasienter (p=0,01), hvor selektive serotoninreopptakshemmere (SSRI)/serotonin- og noradrenalinreopptakshemmere (SNRI), pregabalin, benzodiazepiner, Z-hypnotika og opioider alle ble hyppigere anvendt.

Konklusjon

Denne studien indikerer at kroniske bekkensmertepasienter kan dra nytte av utredning og behandling i et tverrfaglig smertesenter, muligens i enda større grad enn andre kroniske smertepasienter. For bekkensmertepasientene kan det imidlertid virke som at rapportering av klinisk insomni, muligvis mannlig kjønn, det å ha fullført utredning i løpet av ett år, samt

mange år med smerter, kan være assosiert med negative pasientrapporterte utfall etter ett år. Flere studier med bedre og mer spesifikk registrering av behandlingsdetaljer og behandlerinformasjon er nødvendig for å øke forståelsen av hvilke faktorer som kan påvirke pasientenes utfall.

Acknowledgements

Keywords

Table of contents

Abbreviations

CPP	Chronic pelvic pain
CNPP	Chronic non-pelvic pain
CNMP	Chronic non-malignant pain
PRO	Patient reported outcomes
CFQ	Chalder Fatigue Questionnaire
HSCL-25	Hopkin Symptom Checklist
ISI	Insomnia Severity Index
PCS	Pain Catastrophizing Scale
HRQoL	Health-related quality of life
PGIC	Patient Global Impression of Change
HUS	Haukeland University Hospital
STOH	St. Olavs University Hospital
UNN	University Hospital of North Norway
ICD	International Classification of Diseases
IASP	The International Association for the Study of Pain
GP	General practitioner

Introduction

Chronic pelvic pain (CPP) is described as a common, but complex pain condition, affecting 2 – 27 % of the population (1-6). The varying prevalence can be explained by diverse study populations and different CPP definition used. The definition used in this study is from the European Association of Urology (EAU) guidelines: "CPP is chronic or persistent pain perceived in structures related to the pelvis. It is often associated with negative cognitive, behavioral, sexual and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynaecological dysfunction" (7). This definition encompasses both conditions with well-defined classical pathology (chronic secondary pain, see theory chapter), like cancer, and those with no obvious underlying pathology (chronic primary pain).

Our knowledge on etiology and optimal ways of diagnosing and treating CPP is limited (1, 8). In many cases, there is not a distinct cause or single explanation to the chronic pain condition. What is more, often no such explanatory cause even exists. Consequently, the patients are thrown back and forth between professionals to find this imagined single "root of all evil". This complicated picture can also lead to difficulties providing adequate patient treatment. CPP is associated with a series of negative impacts, ranging from poor health-related quality of life among affected patients, reduced work productivity and socioeconomic costs (9). Self-reported data from CPP patients admitted to Norwegian multidisciplinary pain centers supports this (10). In this recent study, comparable to other pain patients visiting the center, only 34 % of the CPP patients were actively working or attending an educational program; 86 % reported fatigue, 51 % scored above the cut off point for anxiety symptoms, and 40 % scoring above the cut off point for clinical insomnia. As many as 77 % of the CPP patients scored above the cut off point for depressive symptoms, and the CPP patients tended to have less widespread pain, however more catastrophizing than other chronic pain patients. Irrespective of the location of pain, all of the pain patients scored significantly lower on health-related quality of life compared to the general Norwegian population. It is therefore of great value, both for the affected men and women and the society in general, to provide as efficient and cost-effective treatment as feasible (11).

There are several different treatment strategies of CPP. A well-recognized pain treatment approach emphasizes the simultaneous integration of somatic, psychological, and social aspects of the treatment. The biopsychosocial model (see Theory chapter) is an important

cornerstone for the personalized pain treatment, and include concepts of mental therapy methods like patient education and psychotherapy (e.g. behavioural therapy) – in addition to medical/biological treatment like pharmacotherapy (NSAIDs, anticonvulsants, antidepressants, opioids, hormonal therapy etc.) and physical therapy (e.g. exercise, manual therapy, electrical stimulation, acupuncture, etc.). Conservative therapies as mentioned above can often provide significant symptom relief and improved quality of life. Interventional and surgical methods (such as ablative procedures, sacral neuromodulation, neurolysis, hysterectomy, vulvar, vestibular surgery, resection, and prostatectomy) can be used in some conservative treatment-resistant cases. However, the described holistic approach, and the interdisciplinary teamwork are essential for facilitating a patient-centered rehabilitation, where the goal should be to relieve the symptoms, to help the patient toward self-management and to improve the quality of life of the patient (12).

Although studies have shown promising results of multidisciplinary treatment, more knowledge is needed. Prior research on treatment of CPP have mainly been centered around single modality efficacy, differences between various therapies, and identifying risk factors and comorbidities in CPP patients. Studies that examine the synergistic effect of therapies are lacking (13, 14).

For chronic pain conditions in general, multidisciplinary treatments have shown to be effective. Several studies have demonstrated that multidisciplinary interventions have higher effectiveness compared with single-multidisciplinary treatments, standard medical treatment or no treatment, and that combining therapies have an impact on reducing pain and improving functional status (15-17). Current research on the management of CPP support these findings, and are indicative of that such multidisciplinary treatment programs also are effective in treating CPP (18-22). The existing studies on synergistic effects of therapies, report of variability in treatment outcomes and multifactorial variables impacting outcomes of multidisciplinary treatment. Existing studies underline the need for further research to increase our understanding of the role of a multidisciplinary approach, and factors impacting and predicting its efficacy (23). Future research should aim at validating factors which mediate treatment response, to examine whether these factors are modifiable, and the possibility of early identification of CPP patients who may benefit from multidisciplinary management (18, 24-27).

Purpose and aim

In the present study, the overall purpose was to increase knowledge regarding assessment, treatment and self-reported outcomes of patients consulting a tertiary multidisciplinary pain center for CPP.

The specific aims were to compare CPP and CNPP patients in relation to the distribution of received assessment and treatment consultations; the assessment status (assessment completed versus not completed); and the assessment strategy received (multidisciplinary versus non-multidisciplinary). In addition, we wanted to compare post versus pre-changes in health-related quality of life and reported personal impression of change between CPP patients and CNPP patients. Further, among the CPP patients to investigate how patients' impression of change was associated with received assessment and treatment consultations or not; having completed assessment or not; and having received multidisciplinary or non-multidisciplinary assessment; patient background characteristics at baseline; and pre-consultation (baseline) symptom scores. Finally, to describe and compare between CPP and CNPP patients the use of pain medications.

Theory

Etiology and pain theories

For the understanding of chronic pain conditions in general, a biopsychosocial framework is commonly assumed, where chronic pain is considered to be of multifactorial origin, with biological pain mechanisms, psychological and social factors contributing to the pain experience (28). Presently, for the biological pain mechanisms, three main categories are suggested. These are nociceptive, neuropathic and nociplastic pain (24, 29, 30). Nociceptive pain is induced by an injurious stimulus that causes tissue damage. Neuropathic pain appears due to a lesion or disease of the somatosensory nervous system. Nociplastic pain, a rather new term and theory adapted from the research on widespread pain (30), refers to neurophysiological alterations causing pain in the absence of tissue damage or evidence of pathology in the somatosensory nervous system, and involves changes described as the phenomenon of central sensitization. A patient's pain may be caused by one primary mechanism, or two or more mechanisms simultaneously (29-31). In the following we will describe more deeply these pain mechanisms and connect them to CPP.

Peripheral (nociceptive)	Peripheral Neuropathic	Central neuropathic or "centralized" pain
■ Inflammation or mechanical damage in tissues ■ NSAID, opioid responsive ■ Responds to procedures ■ Classic examples ■ Osteoarthritis ■ Rheumatoid arthritis ■ Cancer pain	■ Damage or dysfunction of peripheral nerves ■ Responds to both peripheral and central ly acting pharmacological therapies ■ Classic examples ■ Diabetic neuropathic pain ■ Post-herpetic neuralgia	■ Characterized by central disturbance in pain processing (diffuse hyperalgesia/allodynia) ■ Responsive to neuroactive compounds altering levels of neurotransmitters involved in pain transmission ■ Classic examples ■ Fibromyalgia ■ Irritable bowel syndrome ■ TMJD ■ Tension headache

Figure 1. Mechanistic characterization of pain (32).

Furthermore, nociceptive pain can be classified into somatic and visceral nociceptive pain. Nociceptive visceral pain can be caused by organ distension, spasms, hemorrhage, inflammation, mesentery traction, neoplasm and endometriosis (1). Visceral pain is often described as diffuse and dull aching. It may be associated with referred pain, which occurs at a dermatome supplied by the same nerve root as the affected viscera, for example pain caused by the endometrial shedding and cervical dilation during menstruation could be felt as lumbar pain. Inflammatory pain can be regarded as a type of nociceptive pain, and is, not surprisingly, a result from inflammatory processes. Inflammation is a common cause of CPP (1). Many inflammatory mediators are associated with CPP, and the cross-sensitization phenomenon may be an important mechanism, where repeated pain impulses from a specific organ may lead to false pain sensation from the adjacent organ supplied by the same dorsal root ganglion (1). For example, pain from the uterus in dysmenorrhea, often is companied by symptoms of irritable bowel or painful bladder.

Neuropathic pain, usually described as a burning and tingling sensation, arises from abnormal neural activity secondary to damage or disease in the somatosensory nervous system itself (29, 33). This type of pain rarely involves nociceptive stimulation. Neuropathic pain may be further subdivided into central and peripheral neuropathic pain, depending on the localization of the lesion or disease. Pelvic structures are innervated by the somatic (T12-S5) and visceral (T10-S5) nervous system, which are organized in complex anatomical and neurobiological

networks. The main autonomic neuronal center of the pelvis is the hypogastric plexus, while the pudendal nerve is the major somatic nerve. Injury or affection of these structures, for example compression of the pudendal nerve during prolonged labor or straining with stools, may lead to chronic pain in the innervated regions.

Neuropathic pain may also play an important role in chronic post-surgical pain (a type of chronic secondary pain). The definition of chronic post-surgical pain is pain persisting for at least two months, developed after a surgical procedure, where other causes have been excluded (34). The pain physiology of chronic post-surgical pain is suggested to be a continuum of both nociceptive and neuropathic pain. The tissue injury, an inflammatory response or visceral pain may cause nociceptive pain initially, and then neuropathic pain is developing by a primary lesion in the peripheral or central nervous system (CNS).

Nociplastic pain arises from altered nociception despite no obvious finding of actual or threatened tissue damage causing the activation of peripheral nociceptors, nor evidence of disease or lesions of the somatosensory system causing the pain (30). We know that any pain experience involves the CNS, and that pain can be generated and maintained by the CNS itself, regardless of where the pain is perceived to originate (33). Nociplastic pain conditions are due to deranged nociceptive processing, most likely within the CNS, such as enhanced central excitability or diminished central inhibition, or both, often referred to as central sensitization (31). This may lead the CNS to continue receiving pain signals, even after removal of the triggering lesion. The main clinical symptoms of central sensitization include cutaneous hyperalgesia, when pain is triggered by a smaller stimulus than normal, cutaneous allodynia, defined as pain from a non-painful stimulus, and the presence of myofascial trigger points, where pain sensations lead to secondary, painful contraction of the skeletal muscles in the pain areas. These phenomena are significantly higher among CPP patients compared to controls (1).

Development of central alterations of nociceptive processing, is associated with the experience of chronic pain and may be true for many chronic pain conditions (35). Different neuroimaging techniques, like functional MRI, corroborates the existence of CNS alterations among chronic pain patients. Through neuroimaging, a detailed description of brain structure and function is allowed, and neurobiological alterations can be detected. Alterations include cerebral changes in regional gray matter volume, chemistry and regional connectivity.

Neuroimaging studies of women with CPP, with and without endometriosis, give an example of this (36). Among women with CPP, neuroimaging showed alterations in gray matter volume in key pain regulatory regions of the brain, and increased concentrations of excitatory neurotransmitters. These alterations were present in patients with pelvic pain regardless of which endometriosis stage the women suffered. Additionally, women with endometriosis, but without pelvic pain, did not show changes in regional gray matter volume. This suggest that alterations in brain physiology may be specific to the chronic pain state, rather than being caused by peripheral pathology (36). Moreover, CNS dysfunction itself can lead to changed adjacent organ function resulting in symptoms such as rectal dysfunction, diarrhea and constipation, as well as urinary frequency or retention, which are commonly associated with CPP (35).

These (bio)mechanistic terms are descriptors of putative contributors to the experience of chronic pain. It is nevertheless important to emphasize the role which psychological and social factors play in the development and maintenance of chronic pain conditions. The biopsychosocial model gives an established and well-recognized understanding of this. Through the biopsychosocial approach, pain and disability are explained by a multidimensional, dynamic interaction between physiological, psychological and social factors that reciprocally influence each other (37). The biopsychosocial model describes how risk and vulnerability on one side, and resilience and protective factors on the other, can influence an individual's probability of developing chronic and complex pain syndromes, and how this probability also will be affected by the person's genetic and acquired experience as well as psychological status and sociocultural influences (38).

Meta analyzes and systematic reviews indicates that patients with chronic pain have higher levels of psychological complaints, such as anxiety (both general and pain related), somatization, depression and other negative emotions compared to controls without pain conditions (39). Psychological morbidity is often understood as a result of the chronic pain. However, several studies suggest that psychological premorbidity is a risk factor for developing chronic pain, and can further affect the long term outcome of the pain condition (37).

CPP is associated with several gynecological and non-gynecological conditions, such as endometriosis, adenomyosis, bladder pain syndrome, adhesions, irritable bowel syndrome and

musculoskeletal problems (36). It can often be challenging to point out a specific diagnosis in patients with CPP, as the symptoms patients experience, may be caused by one condition or organ system alone, or as a result of an interplay between various conditions and organ systems. The relevant organ systems include the urological, gynecological, gastrointestinal, neurological, endocrinological, psychological and musculoskeletal systems (see Table 1). Moreover, even when pathology is identified, pain can persist despite the patient having received specific treatment targeting the diagnosed pathology (ending with a diagnosis of chronic secondary visceral pain) (35). As a consequence, CPP may be best viewed as an end symptom with multiple possible etiologies, each contributing to the end result of chronic pain (40).

Table 1. System based etiologies of chronic pelvic pain (36).

Gynecologic	Endometriosis, adenomyosis, ovarian remnant, pelvic congestion/pelvic venous insufficiency, pelvic inflammatory disease, ovarian cysts, uterine leiomyomas, tubal pathology (hydrosalpinx, pyosalpinx), adhesive disease
Neurologic	Nerve entrapment/irritations/impingement, disc herniation, postherpetic neuralgia, visceral sensitivity
Gastrointestinal	Irritable bowel syndrome, inflammatory bowel disease, chronic appendicitis
Urologic	Bladder pain syndrome/interstitial cystitis, urethritis
Musculoskeletal	Fibromyalgia, abdominal wall myalgias, pelvic floor tension myalgias, sacroiliac joint dysfunction, symphysis pubis pain, coccydynia
Psychological	Anxiety/depression, somatization disorders, psychosexual dysfunction, sexual abuse, post-traumatic stress disorder

Pain classification

The IASP and ICD-11 classification of pain divides chronic pain into chronic primary and chronic secondary pain. Chronic primary pain is defined as "pain in one or more anatomical regions, that persists or recurs for longer than 3 months, and is associated with significant emotional distress or functional disability, and that cannot be better accounted for by another diagnosis" (28). In this approach, chronic primary pain is regarded as a disease by itself, where the pain is the only or leading complaint (41). The category of chronic primary pain is further subdivided into chronic widespread pain, complex regional pain syndromes, chronic primary headache and orofacial pain, chronic primary visceral pain and chronic primary musculoskeletal pain.

Contrarily, chronic secondary pain syndromes are connected to other diseases as the underlying cause, for which pain may initially be interpreted as a symptom. The subgroups of chronic secondary pain are chronic cancer-related pain, chronic postsurgical or posttraumatic pain, chronic neuropathic pain, chronic secondary headache or orofacial pain, chronic secondary visceral pain and chronic secondary musculoskeletal pain (41). Chronic pelvic pain is a collective term that include several conditions of which each, depending on the etiology, can be classified into every subgroup of both chronic primary and chronic secondary pain.

Given the complex nature of chronic pain, the symptoms are commonly a consequence of the interplay between various organ systems and biological pain mechanisms, psychological and social factors, and may be best viewed as a multifactorial dysfunction, rather than one independent disease with one single cause. This explains the necessity of a multidisciplinary approach for management of CPP (1). Nociceptive, neuropathic and nociplastic pain may not respond equally well to various treatment strategies, thus, the understanding of underlying mechanisms will help to guide treatment choices aimed at these mechanisms. Additionally, management requires knowledge of the interplay between the pelvic organ function and neuro-functional anatomy, as well as the social and psychological aspects of CPP (42).

Treatment levels and the tertiary multidisciplinary pain centers

In Norway, the first line of treatment for chronic pain is handled by the primary health care, where the general practitioner (GP) plays a significant role. The GP will try to identify and take care of any treatable conditions and pathology, and cooperates with other professions in the primary health service like physiotherapists, nurses, psychologists and manual therapists. If the patient does not achieve sufficient pain control from the treatment given in the primary care, the GP is likely to refer the patient to a secondary health care outpatient clinic (like for example a gynecological or gastrointestinal outpatient clinic). Depending on the patient history and clinical findings, the patient will be further investigated (by biochemical tests, imaging and/or endoscopy/laparoscopy) and get treatment for the possible somatic underlying disorder at this second level in a hospital unit, as for example, referred to surgery, to physical therapy or admitted back to the GP again. If the uni-/bimodal or specific treatment does not improve the patients pain situation, the patient is likely to be referred to a pain clinic or a tertiary health care multidisciplinary pain center.

Several studies indicate that CPP patients may benefit from assessment and treatment in a multidisciplinary pain center (18-21). The International Association for the Study of Pain (IASP) assembled a task force, who in 1990 developed the Guidelines for Desirable characteristics of Pain Treatment Facilities. In 2009, a new IASP task force created the Recommendations for Pain Treatment Services. The IASP recommends that interdisciplinary pain centers should offer a diversity of health care providers with expertise in pain management. Furthermore, the staff should have enough professional broadness to comprehensively address the interconnected aspects of the biopsychosocial model of pain. The professions at a pain center should include physicians, mental health professionals (e.g. clinical psychologist, psychiatrists), physical therapists and nurses. The IASP emphasizes that the clinicians from the different specialties should work together in the same space and communicate with each other on a frequent and scheduled basis. Care is delivered in a programmed and coordinated manner, and the assessment and treatment should be patient-centered, up-to-date, evidence-based and safe. The treatment should aim to improve pain and pain management, as well as improving the patient's physical, psychological, and work and social role functioning (43).

In Norway, there are four regional multidisciplinary pain centers: St. Olavs University hospital, Haukeland University Hospital (HUS), University Hospital North Norway (UNN) and Oslo University Hospital (OUS). The incoming referrals to the pain centers are evaluated by an interdisciplinary admission team at each center. Of all referrals for chronic pain conditions, 60-75 % are considered to meet the eligible criteria to be admitted to the multidisciplinary pain centers (44).

When the interdisciplinary admission team have found a referral to be eligible, the team decides if the patient will be offered an evaluation from either 1) a multidisciplinary team involving a minimum of three different professions, of whom at least one of them is a psychologist in addition to a physician or 2) other treatment strategies like a physician alone (an anesthesiologist, a physical medicine specialist, a GP with special education in pain medicine, a neurologist, or at two of the centers, a gynecologist), a psychologist alone, a

physiotherapist (general, manual therapist, or psychomotor) alone, or one or two of these groups together.
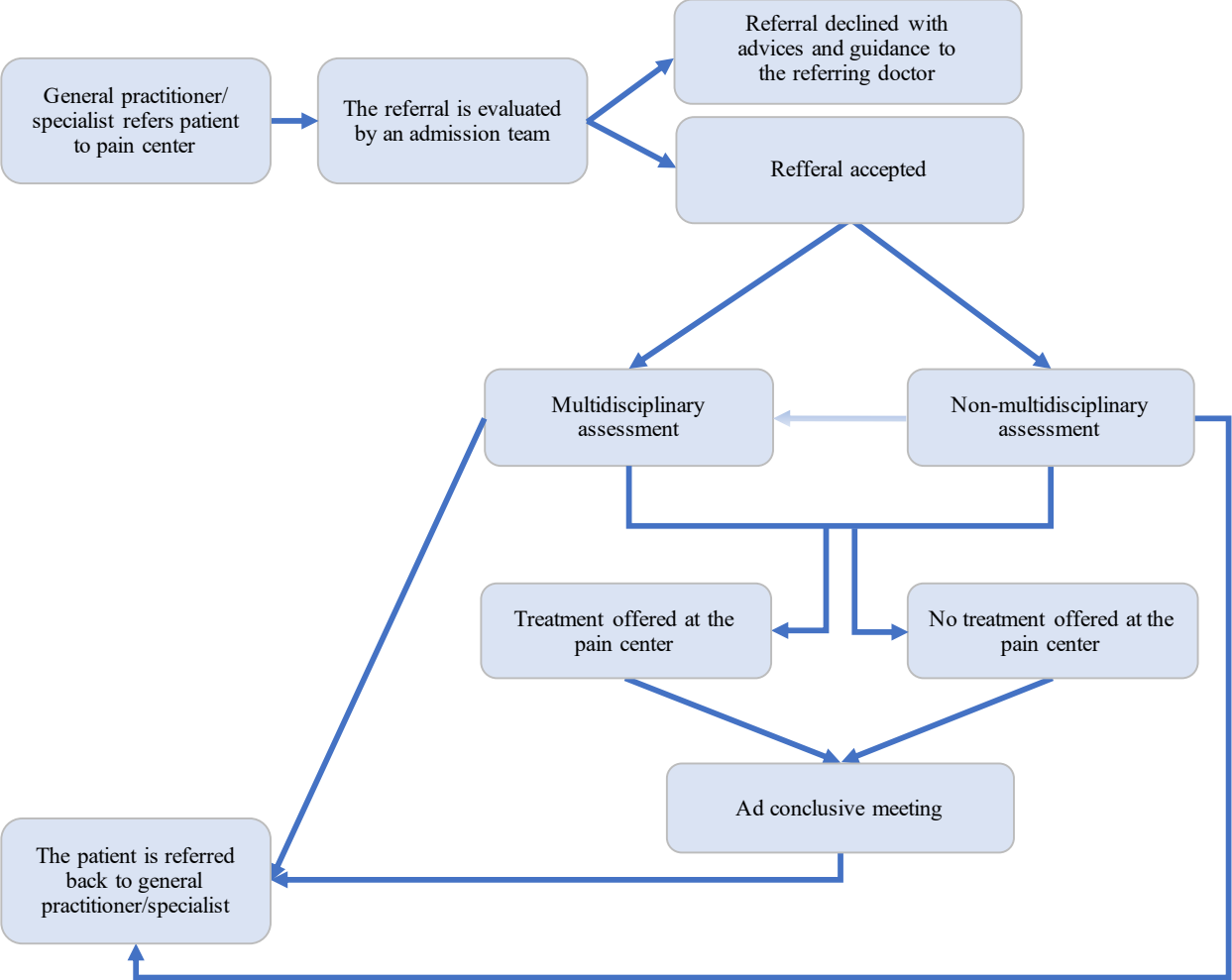
Figure 2. General patient pathway at the pain centers, based on Stedenfeldt and Halsteinli's (44) comparative description of four multidisciplinary pain centers in Norway.

The treatment offered at the pain centers can be offered as individual- or group-treatment. All the Norwegian tertiary pain centers offer both types of treatment. However, the group treatment's content, frequency and duration offered at the different centers are varying. When the treatment in the pain center has come to an end, there is an individual meeting with all the therapists involved.

Materials and methods

Design and setting

This is a prospective cohort designed study, including patients aged 17 years and older with chronic non-malignant pain (CNMP) who were found to meet the eligible criteria for receiving health care services from one of three multidisciplinary pain centers in Norway: St. Olavs University hospital (STOH), Haukeland University Hospital (HUS) and University Hospital of North Norway (UNN). CNMP was defined, in accordance with IASP, as any painful condition persisting for at least three months and not being related to cancer disease or its treatment (41).

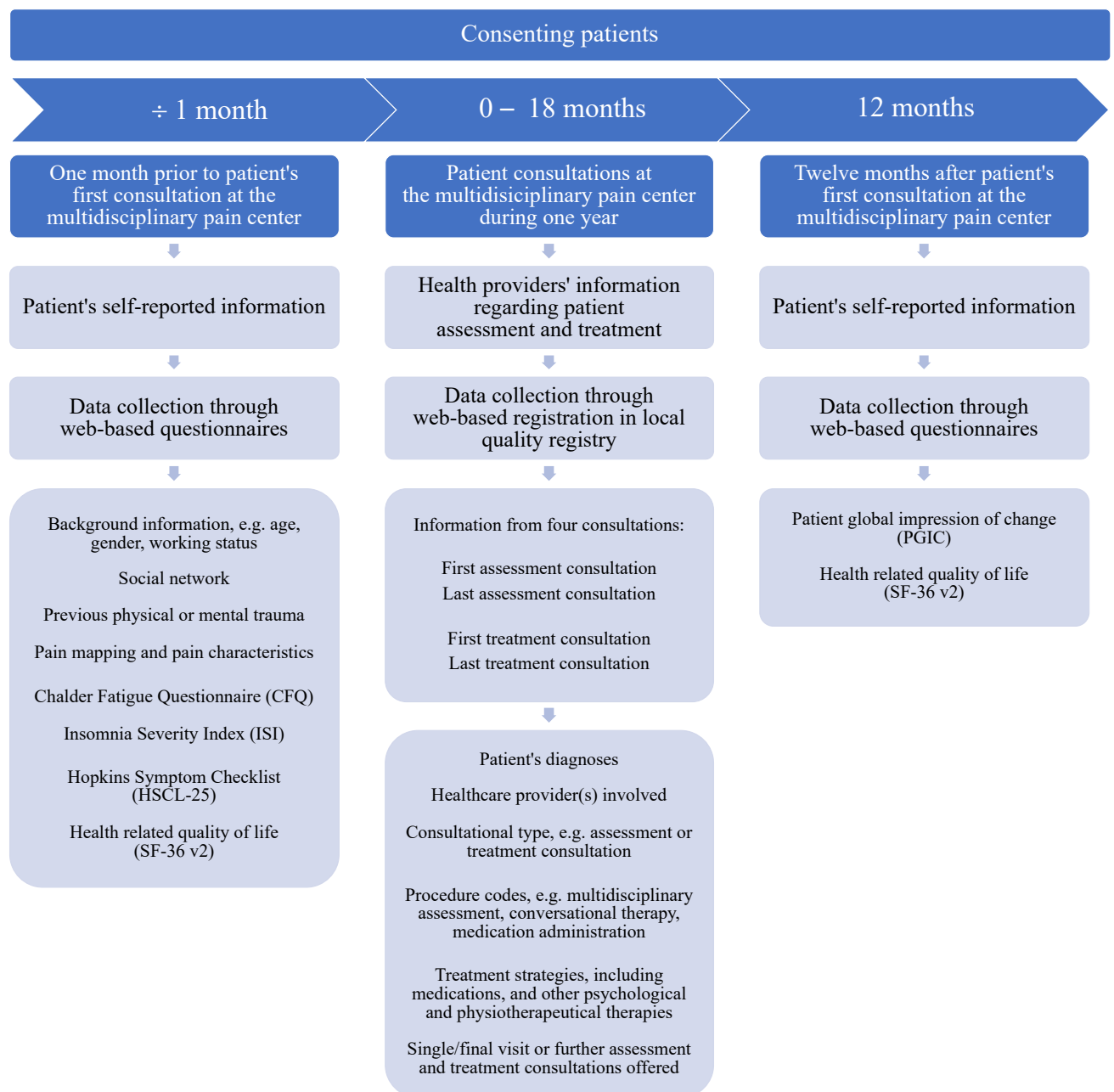| Consenting patients		
÷ 1 month	0 – 18 months	12 months
One month prior to patient's first consultation at the multidisciplinary pain center	Patient consultations at the multidisiciplinary pain center during one year	Twelve months after patient's first consultation at the multidisciplinary pain center
Patient's self-reported information	Health providers' information regarding patient assessment and treatment	Patient's self-reported information
Data collection through web-based questionnaires	Data collection through web-based registration in local quality registry	Data collection through web-based questionnaires
Background information, e.g. age, gender, working status Social network Previous physical or mental trauma Pain mapping and pain characteristics Chalder Fatigue Questionnaire (CFQ) Insomnia Severity Index (ISI) Hopkins Symptom Checklist (HSCL-25) Health related quality of life (SF-36 v2)	Information from four consultations: First assessment consultation Last assessment consultation First treatment consultation Last treatment consultation	Patient global impression of change (PGIC) Health related quality of life (SF-36 v2)
	Patient's diagnoses Healthcare provider(s) involved Consultational type, e.g. assessment or treatment consultation Procedure codes, e.g. multidisciplinary assessment, conversational therapy, medication administration Treatment strategies, including medications, and other psychological and physiotherapeutical therapies Single/final visit or further assessment and treatment consultations offered	

Figure 3. Collected data for this study at different time points.

Study data were collected during the period from 01.01.2017 to 01.03.2018, and included patient self-reported information and health providers' information from patient consultations at the three, tertiary multidisciplinary pain centers (see Figure 3). Patient self-reported information was collected through web-based questionnaires that each patient answered one month prior (pre-consultation) and one year after (post-consultation) receiving the initial consultation at the respective pain center. Pre-consultation information included background characteristics, symptom scores and quality of life, whereas post-consultation information involved two questionnaires assessing quality of life and patient impression of change, respectively. Health care providers' information were collected through three identical local, web-based quality registries at the digital platform named CheckWare®, and encompassed information from four patient consultations. To ensure the cohort design, patients had to have answered the patient impression of change questionnaire at one year follow-up to be included in the study.

Ethical approval was obtained from the Regional committee for medical and health research Ethics (number 2018/634). Only patients consenting to use their answers and collected health care provider data, were included.

ICD-10 diagnoses

Included patients were categorized according to their coded pain condition, those having CPP and those having chronic non-pelvic pain (CNPP) (10). Categorizing was based on patients' primary and secondary ICD-10 diagnoses, registered by the health care provider at the pain center in the course of the first and the last assessment consultation, and first and last treatment consultation (Figure 3).

ICD-10 diagnoses classified as chronic pelvic pain are listed in the Table 2. Patients not having been diagnosed with any of the ICD-10 diagnoses considered as CPP, were regarded as having CNPP.

Table 2. ICD-10 diagnoses classified as chronic pelvic pain for the purpose of this study.

- R10.2 Pelvic and perineal pain
- R10.3 Pain localized to other parts of lower abdomen
- R10.4 Other and unspecified abdominal pain
- M25.55 Generalized arthralgia in pelvic- and thigh region
- M53.3 Coccygodynia
- M54.17 Radiculopathy, lumbosacral region
- M79.15 Myalgia hip/thigh region
- M79.65 Pain in thigh
- M79.8 Other specified soft tissue diseases, pelvic floor myalgia
- N80.9 Endometriosis
- N94.1 Dyspareunia
- N94.8 Vulvodynia
- K36 Other specified appendicitis, chronic appendicitis
- K50.9 Mb. Crohn
- K51 Ulcerative colitis
- K58 Irritable colon with obstipation and esophagitis
- K59.4 Proctalgia Fugax
- K60.1 Rectal pain after chronic fissure/crack/hemorrhoids
- K92.9 Unspecified digestive system disease
- T91.9 Sequelae of unspecified injury of neck and trunk
- S.39.9 unspecified injury to abdomen, lower back and pelvic
- Visceral sensitizing

Measures

Patient reported background characteristics and pre-consultation symptom scores

The first time point of data collection was one month prior to patient's first consultation at the respective multidisciplinary pain center (see Figure 3). Each patient answered a battery of web-based questionnaires via a web-link sent to the patient's mobile phone. Patients were asked to report their year of birth, their gender, education level and working status. The patients were also asked if they had experienced a traumatic event, such as early death of family members, accident(s), abuse or violence, as well as a question regarding their social

network. Several self-reported questionnaires concerning the patients' symptoms were also filled out at the same time point. Symptoms assessed included fatigue (Chalder Fatigue Questionnaire, CFQ), insomnia (Insomnia Severity Index, ISI), depressive and anxiety symptoms (Hopkins Symptom Checklist-25, HSCL-25) and characteristics of pain. Health-related quality of life was also assessed, using the Short Form 36 questionnaire (SF-36 v2®) (further described below). As referred to in the introduction, patient characteristics and pre-consultation symptom scores, as well as thorough descriptions and details about the questionnaires, have been explored in another graduate thesis within the same working group (10), and this study will be partly based on the results from this.

Health care provider's evaluations

Information from health care providers at the pain centers were registered at each consultation. However, CheckWare®, was configured to collect data only at four distinct time points during each patient's clinical course (see Figure 3). The clinical registration included patients' primary and secondary ICD-10 diagnoses, kind of health care provider involved (physician/mental health provider/physiotherapist/nurse), consultation type (assessment or treatment), procedure codes (multidisciplinary assessment, conversational therapy, medication administration), treatment strategies (including medications, psychological and physiotherapeutical therapies), and single visit or further appointments offered (that is if the assessment/treatment at the pain center was completed or not).

Multidisciplinary assessment

Multidisciplinary assessment was defined as assessment carried out by at least two distinct health care professions. This could be any combination of a physician, mental health care professional, physiotherapist and nurse. The mental health care professional could be a psychologist, a psychiatrist or a cognitive-behavioral therapist within the acceptance and commitment therapy (ACT) approach. Patients had to meet at least two disciplines within the frames of the first and last assessment consultation to be regarded as having received multidisciplinary assessment. Sequential multidisciplinary assessment, where patients for example met a physician at first assessment consultation, and a psychologist and physiotherapist at the last, was encompassed by this definition. In addition to the criteria of assessment by at least two different health care professions, at least one of the two registered

15

assessment consultations had to be checked off as "multidisciplinary assessment" in the health provider's information registration.

Patient reported outcomes (PRO)

Health-related quality of life (SF-36 v2®)

Patients answered the Norwegian version of the Short Form 36 questionnaire (SF-36 v2®) one month before and one year after their first consultation at one of the multidisciplinary pain centers. The SF-36 is a generic health survey, assessing different aspects of mental health, physical health and social functioning. It consists of 36 items, grouped into eight domains, encompassing physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE) and mental health (MH) (45). For every patient, item scores were transformed into eight domain scores, each ranging from 0-100, where worst is 0 and best is 100. The SF-36 is a widely used patient reported outcome measure for health-related quality of life (HRQoL), shown to be sensitive to changes in health status, and has been validated through previous international and Norwegian studies (46-48). The minimal clinically important difference (MCID, that is the smallest difference that patients perceive as beneficial) in score of SF-36 between two time measurements varies in different studies between 3 and 5 score points (49, 50). For this study, we defined the MCID to be +/- 3 score points, where a negative sign on the change score implies worsening and a positive sign means improvement.

Patient Global Impression of Change (PGIC)

The Patient Global Impression of Change (PGIC) is a single-item, self-report question, used to assess the extent to which patients' overall health status had changed over the past year since their first consultation at one of the multidisciplinary pain centers. Patients answered on a seven-point Likert scale, ranging from 1 = very much worse, to 7 = very much improved (4 = no change). Answers were recategorized into three main categories of "worse" (1 – 3), "no change" (4) and "improvement" (5 – 7). PGIC ratings have demonstrated to be associated with clinically important change in pain intensity among patients with various pain conditions, as well as correlating with other outcome measures (51, 52).

Analyses

The collected study data was converted into an SPSS file for analyses purposes. The statistical processing was performed in the IBM SPSS Statistic 25 computer software. Categorical data are presented as frequencies and percentages and compared using the Pearson χ^2 test or the Fisher's exact test. For the comparisons of continuous variables, independent and dependent samples t-test were used. Associations were examined by the Pearson χ^2 test and the one-way analysis of variance (ANOVA). A p-value less than 0.05 was considered statistically significant.

Results

A total of 1314 CNMP patients were admitted to one of the three multidisciplinary pain centers and answered the battery of web-based questionnaires between January 1st, 2017 and Mars 1st, 2018. Altogether, 934 of these patients consented to their data being collected into a local quality registry one month before the first consultation, and 687 (74 %) of those patients answered the PGIC questionnaire at one year follow-up. Out of the 687 patients, 84 (12 %) had a CPP diagnosis. A flowchart of included patients and distribution regarding assessment type is presented below. In total, 35 patients were not registered as with any health care professional during the selected assessment consultations (see Figure 4).

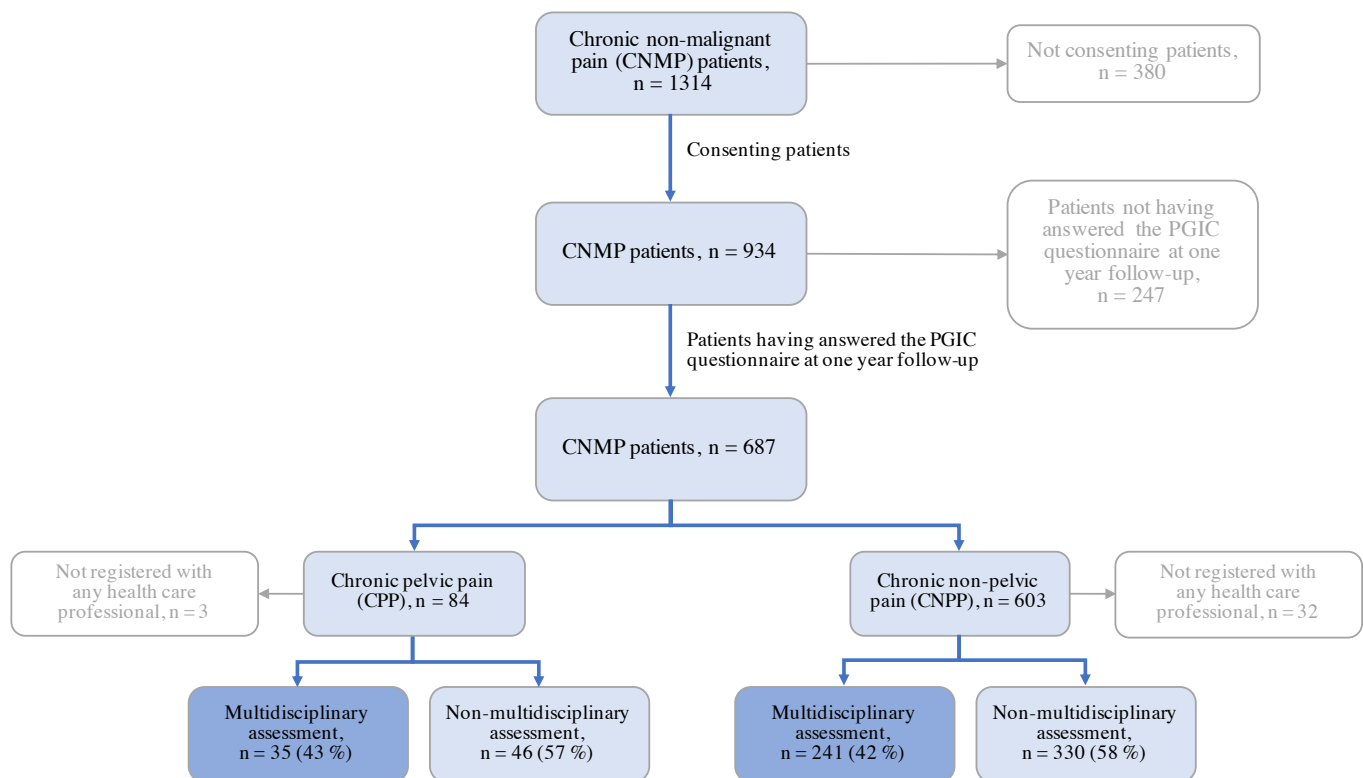*Figure 4: Flowchart of admitted CNMP patients at the three regional pain centers (St. Olavs hospital (STO), Haukeland University hospital (HUS) and University hospital of North Norway (UNN)) between January 1st and March 1st, 2018. The chart shows how admitted CNMP patients were further included in the study, the number of patients in the CPP and CNPP subgroups, and how many received multi- and non-multidisciplinary assessment.*

Assessment and treatment characteristics

Among all the 687 CNMP patients included in this study, 354 (52 %) patients received assessment consultations only (no treatment), whereas 333 (48 %) received both assessment- and treatment consultations (i.e. having received treatment). Among those receiving assessment consultations *only*, a total of 116 (33 %) had completed their assessment by one year follow-up. Among the 333 patients who received *both* treatment and assessment consultations, 30 (10 %) had completed their assessment. Altogether, of patients with available registry data regarding assessment and treatment status at one year follow-up, 146 (22 %) patients were registered as having completed their assessment, whereas 512 (78 %) patients were registered as without completed assessment.
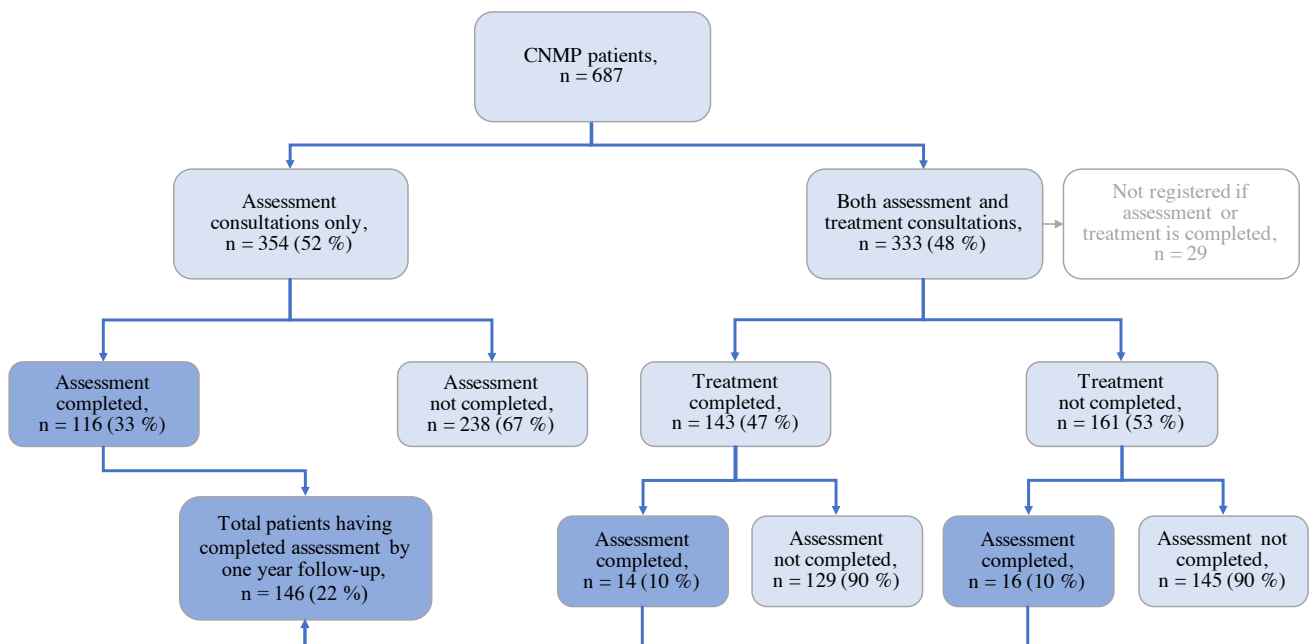

Figure 5: Flowchart illustrating the distribution of CNMP patients at the three regional pain centers between January 1st and March 1st, 2018, regarding patients that received assessment consultations alone (no treatment) versus patients that received both assessment and treatment consultations, as well as the proportions of CNMP patients registered with completed assessment and treatment consultations by one year follow-up.

Table 3 shows the distribution of CPP and CNPP patients having received assessment consultations only (no treatment) versus both assessment and treatment consultations, and the distribution of patients' assessment status at one year follow-up. There were no statistically significant differences when comparing the patient categories regarding neither the proportions of patients having received assessment consultations only versus both assessment and treatment consultations (p=0.60), nor the proportions of patients registered as having completed their assessment versus not completed, by one year follow up (p=0.61).

Among all CNMP patients, 276 (42 %) patients received multidisciplinary assessment. In the CPP group, 35 (43 %) received multidisciplinary assessment, whereas 241 (42 %) of the CNPP patients received such assessment, see Figure 4 and Table 3. There was no statistically significant difference between the CPP and CNPP patient category regarding the proportion of patients having received multidisciplinary assessment (p=0.86).

Table 3: Assessment and treatment consultations received, assessment status at one year follow up and assessment strategy, by patient category (chronic pelvic pain (CPP) versus chronic non-pelvic pain (CNPP)) among 687 patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

	Total N=687 n (%)	CPP N=84 n (%)	CNPP N=603 n (%)	p
Assessment and treatment consultations, n=687				0.60[a]
Assessment consultations only (no treatment received)	354 (51.5)	41 (48.8)	313 (51.9)	
Assessment and treatment consultations (treatment received)	333 (48.5)	43 (51.2)	290 (48.1)	
Assessment status, n=658				0.61[a]
Assessment completed	146 (22.2)	20 (24.4)	126 (21.9)	
Assessment non-completed	512 (77.8)	62 (75.6)	450 (78.1)	
Assessment strategy, n=652				0.86[a]
Multidisciplinary assessment	276 (42.3)	35 (43.2)	241 (42.2)	
Non-multidisciplinary assessment	376 (57.7)	46 (56.8)	330 (57.8)	

[a]*Pearson χ^2 test*

Patient reported outcomes (PRO)

Health-related quality of life (SF-36 v2®)

Table 4 displays mean scores at baseline, at one year follow-up, as well as mean change for each of the eight domains of health-related quality of life, for CPP and CNPP patients separately. For the CPP group, there were neither any clinically, nor any statistically significant changes in the scores in any of the eight domains. However, for the CNPP group, even if some of the decreases in mean scores between baseline and follow-up were statistically significant, the decreases in mean scores were all less than the 3 points (which is defined as the "minimal clinically important difference" (MCID) (49, 50) for this study).

Table 4: Mean scores at baseline and one year follow-up, and mean score changes, in the eight domains of health-related quality of life, by patient category (chronic pelvic pain (CPP) and chronic non-pelvic pain (CNPP)) among 687 patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

| | | CPP N=84 | | | | | CNPP N=603 | | | |
| | | Baseline | Follow-up | Change | | | Baseline | Follow-up | Change | |
	(n)	Mean (SD)	Mean (SD)	Mean (SD)	p	(n)	Mean (SD)	Mean (SD)	Mean (SD)	p
Physical Functioning	52	40.6 (10.8)	39.6 (10.7)	-1.0 (6.7)	0.28[b]	391	39.9 (9.8)	39.0 (10.0)	-0.9 (7.3)	**0.02[b]**
Role Physical	57	30.7 (9.3)	29.9 (8.4)	-0.9 (7.8)	0.41[b]	413	31.3 (9.4)	30.9 (9.8)	-0.4 (9.4)	0.38[b]
Bodily Pain	61	30.6 (6.5)	31.6 (7.2)	0.9 (6.0)	0.22[b]	440	30.2 (6.6)	30.8 (7.3)	0.6 (7.2)	0.09[b]
General Health	57	35.5 (10.7)	35.1 (10.2)	-0.4 (8.9)	0.73[b]	426	37.5 (10.3)	35.0 (9.9)	-2.6 (8.6)	**<0.01[b]**
Vitality	60	33.9 (9.5)	34.3 (10.8)	0.4 (8.6)	0.71[b]	434	34.4 (9.5)	34.1 (9.9)	-0.3 (9.1)	0.52[b]
Social Functioning	61	34.0 (12.7)	34.6 (12.0)	0.6 (12.3)	0.73[b]	434	34.6 (11.9)	34.3 (12.4)	-0.2 (11.7)	0.70[b]
Role Emotion	55	41.2 (14.1)	38.2 (15.1)	-3.0 (16.4)	0.18[b]	413	42.6 (13.9)	40.2 (15.0)	-2.4 (15.7)	**<0.01[b]**
Mental Health	61	44.7 (10.9)	43.0 (11.8)	-1.8 (9.8)	0.17[b]	434	44.4 (10.8)	43.1 (12.2)	-1.2 (10.7)	**0.02[b]**

[b]*Dependent samples t-test*

In Table 5 the mean score changes in the eight domains of health-related quality of life (from baseline to one year follow-up) are compared between the two patient categories (CPP versus CNPP). There were no statistically significant differences between the CPP patients and CNPP patients regarding mean score changes in any of the eight domains. Figure 6 illustrates that the mean changes in SF-36 domain scores for the two patient groups are largely overlapping.

Table 5: Mean score changes in the eight domains of health-related quality of life from baseline to one year follow up, compared between patient categories (chronic pelvic pain (CPP) versus chronic non-pelvic pain (CNPP)) among 687 patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

	CPP N=84		CNPP N=603		
	(n)	Mean change (SD)	(n)	Mean change (SD)	p
Physical Functioning	52	-1.0 (6.7)	391	-0.9 (7.3)	0.95[c]
Role Physical	57	-0.9 (7.8)	413	-0.4 (9.4)	0.10[c]
Bodily Pain	61	0.9 (6.0)	440	0.6 (7.2)	0.27[c]
General Health	57	-0.4 (8.9)	426	-2.6 (8.6)	0.96[c]
Vitality	60	0.4 (8.6)	434	-0.3 (9.1)	0.56[c]
Social Functioning	61	0.6 (12.3)	434	-0.2 (11.7)	0.38[c]
Role Emotion	55	-3.0 (16.4)	413	-2.4 (15.7)	0.76[c]
Mental Health	61	-1.8 (9.8)	434	-1.2 (10.7)	0.72[c]

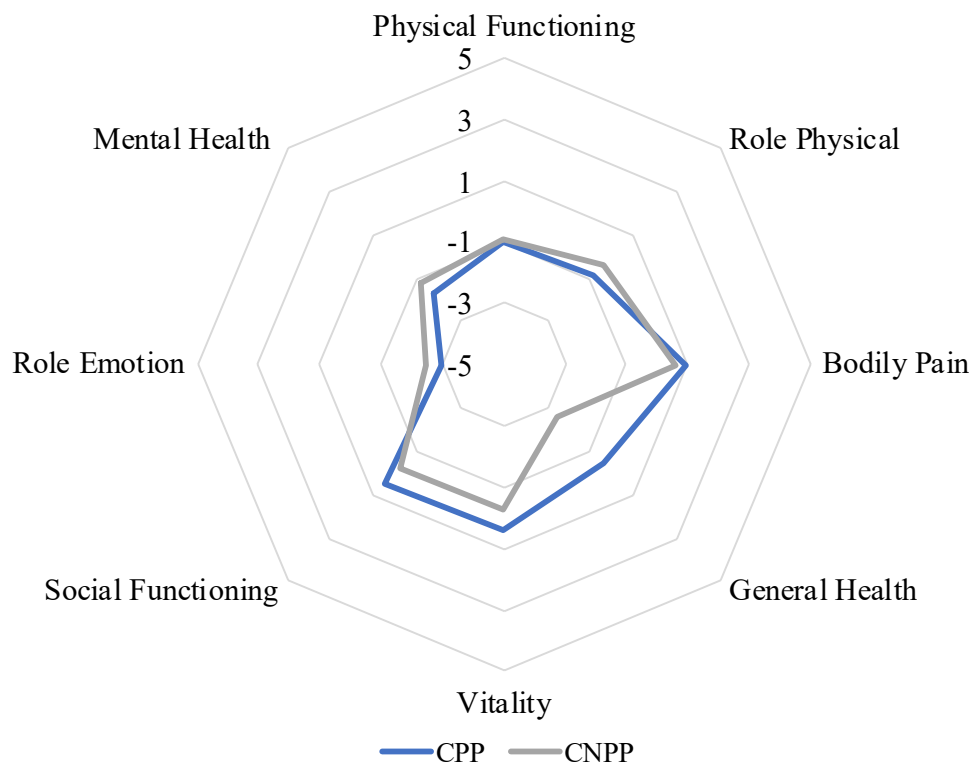[c]*Independent samples t-test*

Figure 6: Comparison of mean score changes from baseline to one year follow-up in the eight health-related quality of life domains, between 84 chronic pelvic pain (CPP) patients and 603 chronic non-pelvic pain (CNPP) patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

Patient Global Impression of Change (PGIC)

Table 6 presents Patient Global Impression of Change (PGIC) ratings, ranging from "better", "no change" and "worse", among all the CNMP patients. As many as 36 (43 %) of the CPP patients had a global impression of improvement after one year, as in contrast to 154 (26 %) in the CNPP category (p<0.01).

Table 6: "Patient Global Impression of Change" (PGIC) ratings at one year follow up, by patient category (chronic pelvic pain (CPP) versus chronic non-pelvic pain (CNPP)) among 687 patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

	Total N=687 n (%)	CPP N=84 n (%)	CNPP N=603 n (%)	p
Better	190 (27.7)	36 (42.9)	154 (25.5)	**<0.01[a]**
No change	252 (36.7)	23 (27.3)	229 (38.0)	
Worse	245 (35.6)	25 (29.8)	220 (36.5)	

[a]*Pearson χ^2 test*

Patient Global Impression of Change (PGIC) and associations among the CPP patients

Assessment and treatment characteristics of the CPP patients

In Table 7, assessment characteristics and PGIC ratings among CPP patients at one year follow-up are presented. When comparing the PGIC ratings of CPP patients who had completed versus those who had not completed their assessment, there was a statistically significant difference (p=0.02) in PGIC ratings, where patients that had completed their assessment had poorer PGIC ratings. Assessment status and strategy did not influence the PGIC ratings.

Table 7: Assessment and treatment consultations received, assessment status, and assessment strategy versus "Patient Global Impression of Change" (PGIC) ratings at one year follow up, among the 84 chronic pelvic pain (CPP) patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

	Better N=36 n (%)	No change N=23 n (%)	Worse N=25 n (%)	p
Assessment and treatment consultations, N=84				0.21[a]
Assessment consultations only (no treatment received)	18 (50.0)	8 (34.8)	15 (60.0)	
Assessment and treatment consultations (treatment received)	18 (50.0)	15 (65.2)	10 (40.0)	
Assessment status, n=82				**0.02[a]**
Assessment completed	8 (22.2)	2 (9.7)	10 (43.5)	
Assessment non-completed	28 (77.8)	21 (91.3)	13 (56.5)	
Assessment strategy, n=81				0.58[a]
Multidisciplinary	17 (48.6)	8 (34.8)	10 (43.5)	
Non-multidisciplinary	18 (51.4)	15 (65.2)	13 (56.5)	

[a]*Pearson χ^2 test*

CPP patients' background characteristics

The CPP patients' background characteristics reported at baseline and associations with PGIC ratings one year later are listed in Table 8. There were no statistically significant associations between the CPP patient characteristics at baseline and PGIC ratings, except for a borderline significant difference regarding patients' gender, with a higher proportion of women than men reporting feeling "better" at one year follow-up.

Table 8: Patient background characteristics reported at baseline and associations with "Patient Global Impression of Change" (PGIC) ratings at one year follow-up, among 84 chronic pelvic pain (CPP) patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

	Better N=36 Mean (SD)	No change N=23 Mean (SD)	Worse N=25 Mean (SD)	p
Age, n=81	44.6 (15.8)	45.7 (11.7)	43.9 (15.0)	0.91[d]
	n (%)	n (%)	n (%)	
Gender, n=83				0.09[a]
Women	30 (83.3)	15 (65.2)	14 (58.3)	
Men	6 (16.7)	8 (34.8)	10 (41.7)	
Education, n=83				0.60[a]
Primary education, high school or eqivalent	21 (60.0)	14 (60.9)	18 (72.0)	
Higher education	14 (40.0)	9 (39.1)	7 (28.0)	
Working status, n=84				0.72[a]
Actively working/student/military	13 (36.1)	6 (26.1)	8 (32.0)	
Not actively working/student/military	23 (63.9)	17 (73.9)	17 (68.0)	
Applied for disability pension, n=83				0.25[a]
Yes	12 (33.3)	11 (47.8)	6 (25.0)	
No	24 (66.7)	12 (52.2)	18 (75.0)	
Experience of previous traumatic event(s), n=84				0.82[a]
Yes	19 (52.8)	12 (52.2)	15 (60.0)	
No	17 (47.2)	11 (47.8)	10 (40.0)	
Social network (do you have a close friend to talk to?), n=82				0.67[a]
Yes	26 (72.2)	16 (72.7)	15 (62.5)	
No	10 (27.8)	6 (27.3)	9 (37.5)	
Comorbidities, n=84				0.79[a]
None	13 (36.1)	7 (30.4)	10 (40.0)	
≥1	23 (63.9)	16 (69.6)	15 (60.0)	

[a]Pearson χ^2 test, [d]One-way ANOVA

CPP patients' pain characteristics and symptom scores

In Table 9, pain characteristics and symptom scores reported at baseline and their associations with PGIC ratings at one year follow-up among CPP patients, are summarized. The only statistically significant finding was regarding insomnia and insomnia severity. Reporting no clinical significant insomnia to subclinical insomnia at baseline, was associated with better

PGIC ratings at one year follow-up (p=0.04). Also, a borderline statistically significant finding concerned the mean number of years patients had lived with pain, where patients that reported feeling better had a mean of 5.8 years with pain, while those with poorer PGIC ratings at one year follow-up, had a mean of 9.3 years (p=0.12).

Table 9: Pain characteristics and symptom scores reported at baseline and associations with "Patient Global Impression of Change" (PGIC) ratings at one year follow-up, among 84 chronic pelvic pain (CPP) patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

	Better N=36 Mean (SD)	No change N=23 Mean (SD)	Worse N=25 Mean (SD)	p
Years with pain, n=80	5.8 (6.0)	9.0 (9.6)	9.3 (6.2)	0.12[d]
Strongest pain last week (0-10), n=83	7.2 (1.5)	7.2 (1.7)	7.5 (1.3)	0.67[d]
Average pain last week (0-10), n=80	5.2 (1.6)	5.3 (1.2)	5.8 (1.3)	0.37[d]
How much does the pain bother you? (0-10), n=84	7.5 (2.1)	7.7 (1.5)	8.2 (1.6)	0.34[d]
	n (%)	**n (%)**	**n (%)**	
Widespread pain, n=84				0.17[a]
No	31 (86.1)	15 (65.2)	19 (76.0)	
Yes[f]	5 (13.9)	8 (34.8)	6 (24.0)	
Chronic fatigue (CFQ), n=84				0.49[a]
No fatigue to moderate fatigue	20 (55.6)	12 (52.2)	17 (68.0)	
Severe fatigue[g]	16 (44.4)	11 (47.8)	8 (32.0)	
Insomnia (ISI), n=83				**0.04[a]**
No clinical significant to subclinical insomnia	19 (52.8)	19 (82.6)	12 (50.0)	
Moderate to severe clinical insomnia[h]	17 (47.2)	4 (17.4)	12 (50.0)	
Symptoms of anxiety (HSCL-25), n=82				0.18[a]
Without symptoms	16 (44.4)	15 (68.2)	11 (45.8)	
With symptoms[i]	20 (55.6)	7 (31.8)	13 (54.2)	
Symptoms of depression (HSCL-25), n=82				0.87[a]
Without symptoms	9 (25.0)	6 (27.3)	5 (20.8)	
With symptoms[i]	27 (75.0)	16 (72.7)	19 (79.2)	

[a]*Pearson χ^2 test,* [d]*One-way ANOVA,* [f]*Defined and calculated according to the ACR 1990 criteria (10),* [g]*cut off ≥ 9,* [h]*cut off ≥ 15,* [i]*cut off ≥ 1.75.*

Pharmacological pain management

Descriptive statistics of the pain modifying medication use among CPP versus CNPP patients are listed in Table 10 below. A larger proportion of the CPP patients (77 %) had used or was still using medications, compared to CNPP patients (63 %) (p=0.01). There were only borderline statistically significant differences between the patient categories in regard to the number of medications that had been or was being used (p=0.13). However, there were differences in the types of medications in use. Antidepressant SSRI (selective serotonin reuptake inhibitors) and SNRI (serotonin-norepinephrine reuptake inhibitors), pregabalin, benzodiazepines, Z-hypnotics and opioids were all used to a larger extent by the CPP patients than by CNPP patients, see Table 10 for details.

Table 10: Pharmacological pain management for one year, by patient category (chronic pelvic pain (CPP) versus chronic non-pelvic (CNPP)) among 687 patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018.

	CPP N=84 n (%)	CNPP N=603 n (%)	p
Use of medications	65 (77.4)	380 (63.0)	**0.01[a]**
Number of medications			0.13[a]
1	13 (20.0)	121 (31.8)	
2	24 (35.9)	132 (34.7)	
≥ 3	28 (43.1)	127 (33.4)	
Type			
Paracetamol	39 (46.4)	235 (39.0)	0.19[a]
NSAIDs	22 (26.4)	138 (22.9)	0.50[a]
TCA	11 (13.1)	75 (12.4)	0.87[a]
SSRI/SNRI	13 (15.5)	30 (5.0)	**<0.01[a]**
Gabapentin	8 (9.5)	33 (5.5)	0.14[a]
Pregabalin	12 (14.3)	38 (6.3)	**< 0.01[a]**
Benzodiazepines	9 (10.7)	30 (5.0)	**0.03[e]**
Z-hypnotics	11 (13.1)	39 (6.5)	**0.03[a]**
Opioids	41 (48.8)	196 (32.5)	**<0.01[a]**

[a]Pearson χ^2 test, [e]Fisher's exact test

Table 11: Key findings.

Study population
▪ Among 934 CNMP patients recorded at baseline, 687 (74 %) answered the PGIC questionnaire at one year follow-up. Out of the 687 patients, 84 (12 %) had a CPP diagnosis

Assessment and treatment characteristics
▪ Among CNMP patients, by one year follow-up, 52 % received assessment consultations only (no treatment), whereas 48 % received both assessment and treatment consultations; 78 % had not completed their assessment; and 42 % received multidisciplinary assessment.
▪ There were no significant differences between the proportions of CPP and CNPP patients having received assessment only versus both assessment and treatment; having completed their assessment versus not completed assessment; and having received multidisciplinary versus non-multidisciplinary assessment

Patient reported outcomes
▪ For CPP patients, at one year follow-up, there were neither any clinically nor statistically significant changes in any of the HRQoL-domains from baseline. The CNPP patients had statistically significant changes in some HRQoL-domains, but these were not clinically significant
▪ A significantly greater proportion of CPP patients (43 %) had an impression of improvement after one year compared to CNPP patients (26 %)
▪ CPP patient's impression of feeling worse at one year follow-up, was associated with having a status of "assessment completed" by one year follow-up
▪ CPP patient's impression of feeling better at one year follow-up, was borderline significantly different regarding CPP patients' gender, with a higher proportion of women than men reporting feeling "better"
▪ CPP patient's impression of feeling better at one year follow-up, was associated with having "no to subclinical insomnia" at baseline
▪ CPP patient's impression of change was borderline different concerning the mean number of years with pain, where patients reporting feeling "better" had a mean of 5.8 years with pain, while those with poorer PGIC ratings at one year follow-up, had a mean of 9.3 years

Pharmacological pain management
▪ A larger proportion of CPP patients had used or was still using pain medications compared to CNPP patients
▪ There were differences regarding types of medications in use, where SSRI/SNRI, pregabalin, benzodiazepines, Z-hypnotics and opioids all were used to a larger extent by CPP patients than by CNPP patients

Discussion

The results from this prospective cohort designed study suggested that CPP patients may benefit from management in a multidisciplinary pain center. Our primary outcome measures were assessed at one year follow-up, and concerned patient's health-related quality of life (HRQoL) and patient's global impression of change (PGIC). In the analysis of HRQoL, there were no changes in any of the domain scores after one year follow-up for the CPP group, and there were no differences between the CPP patients and CNPP patients regarding mean score changes in any of these domains. However, at one year follow-up, a larger proportion of the CPP patients than the CNPP patients reported feeling better, where as many as 36 (43 %) of the CPP patients had a global impression of improvement after one year, as in contrast to only 154 (26 %) in the CNPP category.

Rather surprisingly, for CPP patients, those whom had status as "assessment completed" by one year follow-up, reported to a larger degree a worsening of their condition. However, there was a borderline significant difference regarding CPP patients' gender, with a higher proportion of women than men reporting feeling "better", and reporting "no to subclinical insomnia" at baseline was associated with CPP patients reporting feeling "better" at one year follow-up. Also, among the CPP patients, patients that reported feeling "better" had a mean of 5.8 years with pain, while those with poorer PGIC ratings at one year follow-up, had a mean of 9.3 years. CPP patients had used or was still using pain modifying medications to a larger extent than other chronic pain patients, and SSRI/SNRI, pregabalin, benzodiazepines, Z-hypnotics and opioids were all more frequently used.

For the CPP patients, we found neither any clinical, nor any statistically significant changes between mean baseline and follow-up scores in any of the eight SF-36 domains, assessing the patients' HRQoL. Likewise, when comparing the CPP and CNPP patients regarding the mean score changes in the HRQoL-domains, there were no differences between the two patient groups. In a recent randomized controlled trial (22) compared structured group-based multimodal physical therapy at the National Competence Service for Incontinence and Pelvic Disorders (NKIB, University Hospital of Northern Norway) with primary-care physical therapy for women with CPP. Similar to our study and findings, the 62 included patients did not report any significant changes in HRQoL (measured byEQ-5D) at one year follow-up. However, a common feature for both these studies, is the relatively small sample size. In our study, only 84 CPP patients were included, and most of these had not yet completed their

assessment or treatment. The SF-36 consists of 100 points and as many as eight domains, and may be a tool that may benefit from larger study populations to uncover changes. Hence, this may partly explain the minimal changes in SF-36 domain scores for both these studies.

A recent study from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) research network (53) investigated how physical (SF12 PCS), mental (SF-12 MCS) and condition (that is, disease) specific (Genitourinary Pain Index, GUPI) HRQoL by one year of follow-up, correlated with patient characteristics and symptoms (both in relation to urologic chronic pelvic pain syndrome, UCPPS, and non-UCPPS-related symptoms) reported at baseline. Clemens and colleagues performed in this study a clustering procedure to the three longitudinal HRQoL scores to classify the overall HRQoL for each patient as worsening, stable or improving over the 12 months course of the treatment. They found that physical and mental HRQoL improved in 22-25 % of the patients, was stable in 45-50 % and worsened in about 30 %. Condition-specific HRQoL, however, improved in 47 %, and was stable/worsened in 53 %. For our study, although SF-36 has been shown in previous studies to be sensitive to detect changes in health status in a general population, this instrument would probably have been more reliable if combined with a disease-specific questionnaire when assessing a specific population of patients, as in accordance with the results of the MAPP-study.

What is important to point out regarding our study, is that we only compared the baseline and follow-up mean scores in each of the eight SF-36 domains. As we did not find any significant SF-36 mean score changes, neither for the CPP or CNPP group separately, nor for the comparison of mean score changes between CPP and CNPP patients, and due to the relatively small sample size, we chose to refrain from using the SF-36 score changes for further analyses in this study.

Compared to Norwegian general population data, HRQoL for both the CPP and CNPP patients are considerably lower (see Figure 7). The spider diagram below illustrates how similar the CPP and the CNPP patients scored on the eight HRQoL domains at follow-up, and how poor their HRQoL is compared to the Norwegian general population. In a 20 year old American study (54), HRQoL of patients with bipolar disorder was compared to the HRQoL of patients with chronic back pain and of the general population. They found that patients with bipolar disorder had lower HRQoL compared to the general population. Bipolar patients

had, however, better SF-36 scores in areas of physical and social functioning than the chronic back pain patients, but similar impairment of mental health. The fact that the chronic pain patients already have such a poor HRQoL, may partly explain why their mean SF-36 scores do not change by one year follow-up.
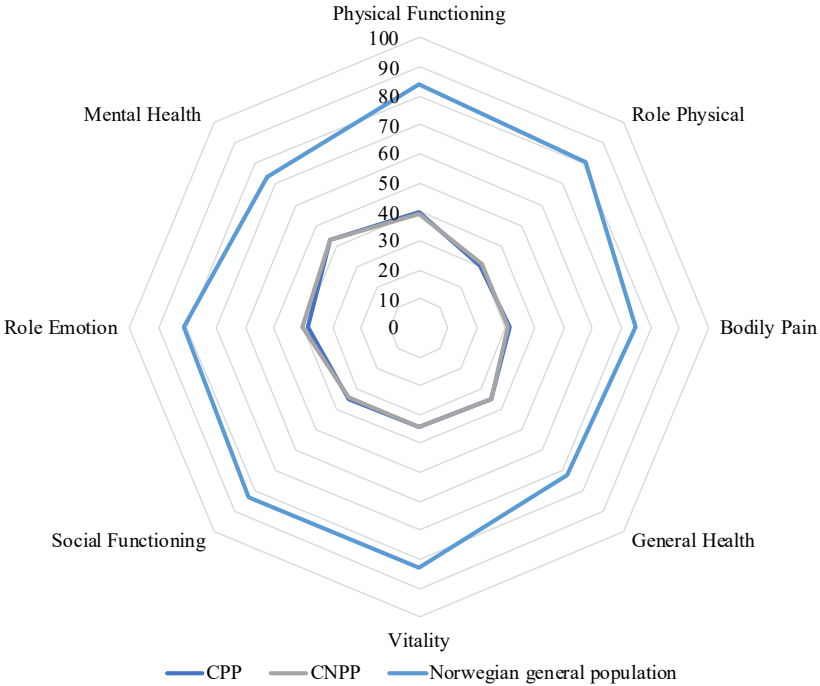

Figure 7: Mean scores in the eight domains of health-related quality of life by patient category (chronic pelvic pain (CPP) and chronic non-pelvic pain (CNPP)) among 687 patients attending one of the tertiary pain centers during the period from January 1st, 2017 to March 1st, 2018. The two groups' mean scores at one year follow-up are compared to the mean scores of the Norwegian general population.

Furthermore, despite a potential treatment effect (that is, that a proportion of the patients actually felt better after attending pain center), it may take longer than a year to see changes in such variables, as QoL is not a quick fix. The SF-36 is not able to assess change in health status over shorter periods of time due to the time frame in which questions are asked, and the results may have been impacted by a too short follow-up period. As we saw, half of the patients referred to the pain centers had suffered with pain for more than six years (22), and this may influence patients' possibility to change their QoL. The mentioned MAPP Research Network recently proclaimed that a new study is underway, where participants will be followed for a longer time-period (up to 3 years). Moreover, like mentioned in the Introduction and Theory chapter, chronic pain patients often have a compound clinical picture, with higher levels of anxiety, somatization, depression and other negative emotions

than people without chronic pain conditions (39). Chronic pain patients may therefore be especially challenging to help towards a change.

In an eleven-year-old Swiss study Angst et. al. (55) prospectively assessed 2 cohorts of chronic pain patients admitted either to an interdisciplinary inpatient pain management program, or to a standard inpatient rehabilitation at the same clinic. In this study, they found that the interdisciplinary intervention was favorable for the patients when discharged from the clinic. This was especially so for their main outcome, which in contrast to our study was "pain" (MPI pain severity) and, to a lesser extent, the coping with the pain, and physical and social function in a quality of life instrument. Despite these promising first results on some of these QoL measurements, at 6-month follow-up after discharge, these effects had disappeared, corresponding to a greater loss of improvements in the interdisciplinary pain management program group compared with the standard rehabilitation group, especially regarding the functional and affective outcomes. They concluded, however, that patients who are severely affected by chronic pain may benefit from interdisciplinary, inpatient pain management programs, especially when focusing on operant and cognitive behavioral therapies. Moreover, they may benefit even further when they are offered subsequent, individually tailored outpatient care (55). However, the interdisciplinary management in this Swiss study (55) was an intensive inpatient program (more than 100 hours of therapy during a period of 4 weeks, consisting of different types of medical care, physiotherapy and psychotherapy), as opposed to the multidisciplinary outpatient assessment we have studied. An intensive inpatient program may require a different patient type than an outpatient clinic. It is nevertheless possible to imagine that, like the study of Angst et. al. (55), our tertiary pain center patients might have experienced an initial improvement, only to deteriorate after a certain amount of time, and consequently their HRQoL came back to status quo. However, we only measured HRQoL before the first assessment and at one year follow-up.

For our second primary outcome measure, (PGIC), we found a significant difference in PGIC ratings between CPP-patients and CNPP-patients, where as many as 43 % of the CPP patients had an impression of improvement, compared to only 26 % in the CNPP group. This difference is striking, and despite the minimal change in HRQoL, as discussed above. One of our following questions is naturally "what is it about the CPP patients that made them feel better than the CNPP patients after one year?".

As mentioned earlier, the baseline characteristics of CNMP patients (both CPP and CNPP patients) attending one of the three tertiary pain centers have already been described (10). The group of CPP patients tended to have less self-reported pattern of chronic widespread pain (CWP) than other chronic pain patients. One could assume that complaints of widespread pain at baseline may play a role on the impression of change after one year follow-up at the centers. As shown in Table 9, we found that only 14 % of those feeling better one year after had CWP, although the difference did not reach significance. The mentioned 2020 MAPP study (53) also found that larger degree of widespread pain (and non-urological pain) predicted a poorer general physical and mental HRQoL outcome. Likewise, an earlier study from the same research network, found that presence of widespread pain seemed to be a risk factor for more complex pain and poorer outcomes related to urologic symptoms in both men and women (53, 56). Being aware that HRQoL is not totally comparable to our chosen PRO of "impression of change" (PGIC rating), these common findings may indicate that CPP patients' better PGIC ratings might have been mediated through the effect of lower degree of widespread pain than among the CNPP patients. However, again due too low sample size, we did not control for mediators or confounders in our statistical analyses.

On the other hand, the group of CPP patients in our study tended to have more catastrophizing thoughts at pre-consultation (10). One may imagine that the higher level of catastrophizing thoughts among the CPP patients at baseline rather negatively would influence the outcome of these patients one year later, although changing such thoughts should be a meaningful treatment goal possible to reach through typical multidisciplinary treatment which include a psychologist. This has been shown in a British study by Scott and McCracken (57), using PGIC ratings following a 4-weeks interdisciplinary acceptance and commitment therapy (ACT) treatment program for chronic pain. Here, they found that improving the "acceptance of pain" during treatment may play an important role in patients' posttreatment impressions of change. It is possible that the catastrophizing of the CPP patients have been thoroughly addressed in our Norwegian pain centers, which might have led to higher acceptance of pain, and hence, may be part of the explanation behind the better PGIC ratings among CPP patients. However, in a prospective cohort from 2018, Allaire and colleagues (14) concluded that higher pain catastrophizing at baseline was associated with greater chronic pelvic pain severity at 1 year. Another prospective 12-months follow-up study (58) of patients with chronic pelvic pain syndrome (CPPS) from 2018, also found that psychological symptoms, especially anxiety and depressive symptoms, were risk factors for continuing pain and urinary

symptoms through treatment and for a lasting impaired quality of life in these patients. They concluded that depressive and anxiety symptoms should be examined as early as possible in patients with CPPS, and if positively diagnosed, these symptoms should be especially targeted as part of a biopsychosocial oriented treatment rationale.

Further, our study protocol did not include measurements of pain after one year. In accordance with this choice, PGIC ratings appear to be influenced to a greater degree by patients' experienced improvements in physical activities and mood rather than by improvements of pain, as demonstrated by Scott and McCracken in a study from 2015 (57). They here pointed out that in the context of the interdisciplinary ACT-based treatment that was studied in this case, the apparently lesser role of change in pain within the overall impression of change shown contrasted with outcome measures from pharmacological trials. In such trials, the change in pain appears as the predominant predictor for that outcome (59, 60). They stated that the type of intervention and its aims may drive which domains contribute the most to global impression ratings. Changes in pain intensity were however assessed in a French study from 2018, where Perrot and colleagues (61) found that reports of feeling "much improved" or "very much improved" on PGIC, was associated with pain relief. Hence, PGIC may still be contemplated as a useful and indicative measure also in studies of chronic pain patients. However, as the abovementioned study investigated the effect of a capsaicin cutaneous patch, on peripheral neuropathic pain, and hence, a pharmacological intervention, the different intervention and clinical patient population type may not be comparable, and thus maybe not be generalizable for all chronic (pelvic) pain patients.

In our study, we found that having completed the assessments at one of the pain centers by one year follow-up, was associated with poorer PGIC ratings among the CPP patients. In the abovementioned British study by Scott and McCracken (57), as many as 79 % of patients who completed the treatment program, reported minimal improvement or more. A reason for this negative outcome on the global impression of change, might be that the patients that have completed their assessment may be disappointed or exhausted after having gone through yet another assessment leading no further. Having completed assessment, does not necessarily mean that the patient and the health care professionals involved have had a satisfying or straightforward answer, nor any treatment for the patient's pain problem. The guarantee of health care, meaning the right to receive medical help within a maximum amount of waiting time, applies only to the assessment, and not to the further treatment that is given (or not).

Therefore, although the *assessment* is carried out by a given time period (to avoid exceeded waiting time), there is no guarantee for the extent and quality of the *treatment* that may follow, which also can affect the patient's impression of change. The European Association of Urology (EAU) discussed in an article (7) their own 2012 guidelines on CPP, and emphasized the dilemma of carrying out too many (invasive) investigations versus the risk of failure to detect a treatable cause of the pain and possibly serious disease. They pointed out the importance of addressing the patients' worries and to collaborate with the patient to make an assessment- and treatment plan acceptable to both the therapists and patients. One possible reason for the differences in PGIC ratings in our study, may be that the patients who had already completed their assessment, may have felt that the investigations went too quickly, and maybe the patients did not fully agreed with the terminated management plan in the specialist health care.

Rather surprisingly, we did not find any differences in PGIC ratings among patients having received multidisciplinary versus non-multidisciplinary assessment. It is likely to assume that the assessment strategy at the pain centers may be selected according to the patient's background factors, their history, main complaints, and of course their motivation for the respective type of assessment. A patient that is motivated for a specific clinical pathway may be more likely to feel improvement if met by health care assessment suiting their needs or wishes (62). The patients admitted to a regional pain center may be even more complex than most pain patients, as the tertiary pain center is "the last bastion" of the health care system for pain conditions.

When it comes to multidisciplinary treatment, which is not included in our study, the earlier mentioned Norwegian study of Nygaard et. al. (22), found that the patients receiving group based multimodal physical therapy reported a significantly larger reduction in mean pelvic pain intensity than patients receiving only primary care physical therapy. The intervention group also showed greater improvements in respiratory patterns and pain-related fear of movements, however, no significant differences were observed between the groups for the other secondary outcomes. They did not find the differences in pain relief that they expected, and could not conclude that the group-based intervention including body awareness therapy, patient education, and cognitive techniques was clinically better than primary-care physical therapy for women with CPP.

In relation to CPP patients' background characteristics reported at baseline, there were only a borderline significant association to CPP patients' gender. Female patients tended to feel improvement to a relatively larger degree than male patients. This is also an interesting finding, rousing curiosity on whether and why it could seem that women may benefit more than men of management on a tertiary pain center. In our study, there was a significantly higher prevalence of severe fatigue among women with CPP compared to men with CPP (10). A possible hypothesis derived from this, might be that women and men differ in clinical phenotypes, that can be treated differently (63). Women may be more susceptible to the multimodal management, like for example the psychotherapy offered by the pain centers. Men, on the other hand might appreciate more unimodal, "straightforward" ways of management, like surgery or medications. What is more, we found a significant association regarding degree of insomnia, where reporting no clinical significant insomnia to subclinical insomnia at baseline, was associated with better PGIC ratings at one year follow-up. Different from our findings, the earlier mentioned MAPP study (53), found that higher baseline mental HRQoL, female gender and greater baseline depression and stress, were associated with lower probability of improvement in mental HRQoL. However, stress and depression are common causes (and consequences) of insomnia, and these findings point "by proxy" in the same direction as our findings, and insomnia could be a possible point of attack regarding the treatment of CPP patients. It may therefore be useful to reveal and address insomnia as early as possible in the management of patients with CPP.

Further, among the CPP patients who reported feeling "better" after one year, a borderline statistically significant finding concerned the mean number of years patients had lived with pain, where patients that reported feeling "better" had a mean of 5.8 years with pain, while those with poorer PGIC ratings at one year follow-up, had a mean of 9.3 years. This could indicate that CPP patients should be identified and handled as early as possible, to increase the change of improvement. In contrast to our findings, Landmark and colleagues (64) did a population based study in 2012 to characterize the persistence of pain in the Norwegian general population, to validate recall measures against longitudinal reporting of pain. They found that pain reporting seems to be stable over time, especially if a cutoff point at the level of moderate or more severe pain is reported. However, the Norwegian study was based on a random sample of participants from the general population (the HUNT 3 study in Norway), and the study did not assess the participants' healthcare seeking or any kind of merging against medical records, thereby lacking information on relevant modifying interventions.

Despite attempts of treating the patients, and even so in highly specialized multidisciplinary pain centers, moderate to severe pain might be more resistant to change and hence, more likely to persist over time. However, we failed to demonstrate any association between moderate-severe pain at baseline with a poor PGIC-outcome at one year follow-up among CPP patients, and an important explanation to this is the different study population we had compared to population data. Nevertheless, as the moderate-severe pain seems to be somewhat resistant to change, it may also be more difficult for these patients to feel better after one year.

When comparing the use of pain modifying medications between the CPP patients and CNPP patients, we found that a larger proportion of CPP patients had used or was still using medications compared to CNPP patients. What is more, there were also differences regarding types of medications in use, where both the non-addictive preparations like antidepressant SSRI/SNRI and pregabalin (but not gabapentin), and the addictive preparations like benzodiazepines, z-hypnotics and opioids were all used to a larger extent by CPP patients than by CNPP patients. In a German study (65) investigating the somatic and psychosocial determinants of CPP symptom severity and quality of life, it was shown that together with presence of depressive symptoms and pain catastrophizing, the intake of pain modifying medication significantly predicted increased CPP symptom severity. On the other side, a high usage of pharmacotherapy can also indicate a higher symptom burden in the first place, and therefore a higher probability of symptom severity over time. The wide use of medications among CPP patients may be one of the explanations to why these patients seem less susceptible to multidisciplinary assessment. However, a measuring tool describing if the pharmacological treatment was under escalation or stepping down would be useful to get a more nuanced picture.

The current study has several strengths. One of them concerns the use of a prospective cohort study design, with baseline self-report information preceding the PROs by more than a year for a substantial number of patients. Hence, reducing the influence of recall-bias into our results. In addition, it was possible to assess multiple associations and outcomes at the same time, making it a comprehensive set of data, in which both patients' self-reported data and health providers' information were collected. Furthermore, validated questionnaires with approved psychometric properties like the SF-36 and PGIC have been used. Especially SF-36 has been and is still used in many clinical trials, and thus makes the present study easier to

compare with other studies. Another valuable benefit of this study is that the project is done in a regular clinical setting. It represents different parts of the country, increasing the probability of generalizability of the results. The high number of total CNMP patients included in this study is also an important strength.

Although this study encompasses information from a large group of CNMP patients, one of its limitations concerns the relatively low number of CPP patients. For this study, CPP patients were classified on clinician-based ICD-10 diagnose codes, and this may have led to loss of potential CPP cases. Additional tools could have been used to identify more CPP patients, like the 25-pain site self-report body diagram, where patients may mark the pelvic region as a painful area, and adding this could have led to different results or outcomes. Surprisingly, as many as 20 % of the CNMP patients at baseline were classified as having CPP (10), compared to only 12 % in our study at one year follow-up. This means, that a larger proportion of the CPP patients was lost to follow-up than of the CNPP patients. In addition, low sample size in many of the comparisons, could lead to type II errors, and may explain the borderline findings regarding CPP patients' gender and years of pain.

Secondly, collected data was based on self-reported inquiries, and even if prospectively examined, the baseline data may be exposed to recall bias, as well as under- and over-reporting of symptoms and information. Moreover, even though data was *collected* in a standardized way, it is likely that the surveys of the health care provider's evaluations were not *answered* in a standardized way. Among others, there were differences in health-care providers' registration of "multidisciplinary assessment", which led us to manually recoding of this variable. Also, some systematic errors in the CheckWare calculation of SF-36 domains were discovered (and the case numbers consequently excluded), which may indicate a possibility for other yet undetected weaknesses in the data set.

Another limitation is the number of patients that were excluded; 380 non-consenting patients at baseline; and 247 patients at one year follow-up due to lack of PGIC response. Moreover, as many as 512 (75 %) patients had not finished assessment by one year follow-up. The drop-out and attrition of patients and the fact that many patients were not completely assessed, possibly because of missing information, could have influenced outcomes and study results. What is more, the proportions of CPP patients receiving multidisciplinary assessment (43 %), is maybe lower than one would expect from such specialized tertiary regional

multidisciplinary pain centers (44). It is, after all, the benefits from such multidisciplinary assessments that are the reasons for referrals in most cases. Yet, this being the true numbers, multidisciplinary consultations are demanding when it comes to human resources, as it is per our definition two or more professions involved. However, a partly explanation may once again be due to inadequate registration (by health personnel in a busy clinical working mode) in CheckWare.

One important point of future research could be a similar study, but with a larger study population and longer follow-up time, to investigate if the SF-36 scores and PGIC ratings would present with the same distribution after for example 18 months or 24 months – or even over several years. Also, it may be beneficial if some of the measures retrieved from patient's self-reported information on baseline also were retrieved after six months and after one year. That is the Numerous Rating Scale (NRS) or another pain differential and/or impact score, the Chalder Fatigue Questionnaire (CFQ), Hopkins Symptom Checklist (HSCL-25) and Insomnia Severity Index (ISI). It would especially be useful to compare the NRS on baseline and after one year, and to interpret this together with PGIC and SF-36. Also, a more comprehensive registration of the detailed treatment offered each patient, not only regarding multidisciplinary assessment, should follow. Last, but not least, more studies are needed to investigate if, and in this case, why CPP patients in multidisciplinary pain centers use more pain modifying medications than CNPP patients, as well as randomized controlled trials on the effect of each medication among CPP patients.

Conclusion

The present study indicates that CPP patients may benefit from management in a multidisciplinary pain center, possibly even more than CNPP patient. At one year follow-up, there were no changes in HRQoL among CPP patients. However, CPP patients reported feeling better at one year follow-up compared to CNPP patients. CPP patients did not have impression of change according to them receiving multidisciplinary assessment versus non-multidisciplinary, but surprisingly, CPP patients who had status as "assessment completed" by one year follow-up, reported to a larger degree a worsening of their condition. Low levels of insomnia at baseline were associated with CPP patients reporting feeling "better". Disappointingly, CPP patients had used or was still using pain modifying medications to a larger extent than the CNPP patients.

This study reveals more need for future research on this topic, like further studies to draw an inference on whether (and perhaps why) CPP patients may benefit from such management. Further, to investigate and identify optimal assessment and treatment strategies for CPP patients, and to increase our understanding of factors that may impact patient outcomes. This study lack important information on treatment details offered, and hence, future studies should address this more comprehensively.

References

1. Yosef A, Ahmed AG, Al-Hussaini T, Abdellah MS, Cua G, Bedaiwy MA. Chronic pelvic pain: Pathogenesis and validated assessment. Middle East Fertility Society Journal. 2016;21(4):205-21.

2. Ahangari A. Prevalence of chronic pelvic pain among women: an updated review. Pain physician. 2014;17(2):E141-7.

3. Latthe P, Latthe M, Say L, Gulmezoglu M, Khan KS. WHO systematic review of prevalence of chronic pelvic pain: a neglected reproductive health morbidity. BMC Public Health. 2006;6:177.

4. Zondervan KT, Yudkin PL, Vessey MP, Dawes MG, Barlow DH, Kennedy SH. The prevalence of chronic pelvic pain in women in the United Kingdom: a systematic review. Br J Obstet Gynaecol. 1998;105(1):93-9.

5. Ayorinde AA, Macfarlane GJ, Saraswat L, Bhattacharya S. Chronic pelvic pain in women: an epidemiological perspective. Womens Health (Lond). 2015;11(6):851-64.

6. Ferris JA, Pitts MK, Richters J, Simpson JM, Shelley JM, Smith AM. National prevalence of urogenital pain and prostatitis-like symptoms in Australian men using the National Institutes of Health Chronic Prostatitis Symptoms Index. BJU Int. 2010;105(3):373-9.

7. Engeler DS, Baranowski AP, Dinis-Oliveira P, Elneil S, Hughes J, Messelink EJ, et al. The 2013 EAU guidelines on chronic pelvic pain: is management of chronic pelvic pain a habit, a philosophy, or a science? 10 years of development. European urology. 2013;64(3):431-9.

8. Stein SL. Chronic pelvic pain. Gastroenterol Clin North Am. 2013;42(4):785-800.

9. Mathias SD, Kuppermann M, Liberman RF, Lipschutz RC, Steege JF. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. Obstet Gynecol. 1996;87(3):321-7.

10. Eliesen J, Hagemann CT, Stedenfeldt M. Patient consulting a tertiary, multidisciplinary pain clinic for chronic pelvic pain. Trondheim: Norwegian University of Science and Technology; 2020.

11. Cheong YC, Smotra G, Williams A. Non-surgical interventions for the management of chronic pelvic pain. Cochrane Database Syst Rev. 2014(3).

12. Vural M. Pelvic pain rehabilitation. Turk J Phys Med Rehabil. 2018;64(4):291-9.

13. Bartley JM, Carrico DJ, Gilleran JP, Sirls LT, Peters KM. Chronic pelvic pain in women: common etiologies and management approach recommendations. Clinical Practice. 2013;10(1):89-102.

14. Allaire C, Williams C, Bodmer-Roy S, Zhu S, Arion K, Ambacher K, et al. Chronic pelvic pain in an interdisciplinary setting: 1-year prospective cohort. American journal of obstetrics and gynecology. 2018;218(1):114.e1-.e12.

15. Scascighini L, Toma V, Dober-Spielmann S, Sprott H. Multidisciplinary treatment for chronic pain: a systematic review of interventions and outcomes. Rheumatology (Oxford). 2008;47(5):670-8.

16. Allegrante JP. The role of adjunctive therapy in the management of chronic nonmalignant pain. Am J Med. 1996;101(1a):33s-9s.

17. Kamper SJ, Apeldoorn AT, Chiarotto A, Smeets RJ, Ostelo R, Guzman J, et al. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. Cochrane Database Syst Rev. 2014(9).

18. Aboussouan A, Martincin K, Huffman K. (534) Chronic pelvic pain is effectively treated in an interdisciplinary chronic pain rehabilitation program. The Journal of Pain. 2016;17(4).

19.   Shoskes DA, Nickel JC, Kattan MW. Phenotypically directed multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome: a prospective study using UPOINT. Urology. 2010;75(6):1249-53.

20.   Kames LD, Rapkin AJ, Naliboff BD, Afifi S, Ferrer-Brechner T. Effectiveness of an interdisciplinary pain management program for the treatment of chronic pelvic pain. Pain. 1990;41(1):41-6.

21.   Miller-Matero LR, Saulino C, Clark S, Bugenski M, Eshelman A, Eisenstein D. When treating the pain is not enough: a multidisciplinary approach for chronic pelvic pain. Arch Womens Ment Health. 2016;19(2):349-54.

22.   Nygaard AS, Rydningen MB, Stedenfeldt M, Wojniusz S, Larsen M, Lindsetmo RO, et al. Group-based multimodal physical therapy in women with chronic pelvic pain: A randomized controlled trial. Acta Obstet Gynecol Scand. 2020.

23.   Sewell M, Churilov L, Mooney S, Ma T, Maher P, Grover SR. Chronic pelvic pain - pain catastrophizing, pelvic pain and quality of life. Scand J Pain. 2018;18(3):441-8.

24.   Yosef A, Allaire C, Williams C, Ahmed AG, Al-Hussaini T, Abdellah MS, et al. Multifactorial contributors to the severity of chronic pelvic pain in women. Am J Obstet Gynecol. 2016;215(6):760.e1-.e14.

25.   Baranowski AP. Chronic pelvic pain. Best Pract Res Clin Gastroenterol. 2009;23(4):593-610.

26.   Twiddy H, Lane N, Chawla R, Johnson S, Bradshaw A, Aleem S, et al. The development and delivery of a female chronic pelvic pain management programme: a specialised interdisciplinary approach. British journal of pain. 2015;9(4):233-40.

27.   Daniels JP, Khan KS. Chronic pelvic pain in women. 2010;341.

28.   Nicholas M, Vlaeyen JWS, Rief W, Barke A, Aziz Q, Benoliel R, et al. The IASP classification of chronic pain for ICD-11: chronic primary pain. Pain. 2019;160(1):28-37.

29.   International Association for the Study of Pain. IASP Pain Terminology. Washington: International Association for the Study of Pain; 2017 [updated 2014 December 14; cited 2020 March 08]. Available from: https://www.iasp-pain.org/terminology?&navItemNumber=576.

30.   Kosek E, Cohen M, Baron R, Gebhart GF, Mico J-A, Rice ASC, et al. Do we need a third mechanistic descriptor for chronic pain states? Pain. 2016;157(7):1382-6.

31.   Chimenti RL, Frey-Law LA, Sluka KA. A Mechanism-Based Approach to Physical Therapist Management of Pain. Phys Ther. 2018;98(5):302-14.

32.   Clauw DJ. Diagnosing and treating chronic musculoskeletal pain based on the underlying mechanism(s). Best Practice & Research Clinical Rheumatology2015. p. 6-19.

33.   Origoni M, Leone Roberti Maggiore U, Salvatore S, Candiani M. Neurobiological mechanisms of pelvic pain. Biomed Res Int. 2014;2014:903848.

34.   Hagemann CT, Kirste UM. Assessment of persistent pelvic pain after hysterectomy: Neuropathic or nociceptive? Scand J Pain. 2016;11:127-9.

35.   Simpson LR, Mahmood T. Medical and surgical management of chronic pelvic pain. Obstetrics, Gynaecology & Reproductive Medicine. 2017;27(1):14-21.

36.   Carey ET, As-Sanie S. New developments in the pharmacotherapy of neuropathic chronic pelvic pain. Future science OA. 2016;2(4):Fso148.

37.   Edwards RR, Dworkin RH, Sullivan MD, Turk DC, Wasan AD. The Role of Psychosocial Processes in the Development and Maintenance of Chronic Pain. J Pain. 2016;17(9 Suppl):T70-92.

38.   Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. Psychol Bull. 2007;133(4):581-624.

39.   Burke AL, Mathias JL, Denson LA. Psychological functioning of people living with chronic pain: a meta-analytic review. Br J Clin Psychol. 2015;54(3):345-60.

40.   As-Sanie S. Causes of chronic pelvic pain in nonpregnant women. *UpToDate* [Internet]. 2020 January 26 [cited 2020 March 10]. Available from: https://www.uptodate.com/contents/causes-of-chronic-pelvic-pain-in-nonpregnant-women?search=chronic%20pelvic%20pain&topicRef=5467&source=see_link.

41.   Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). Pain. 2019;160(1):19-27.

42.   Possover M, Andersson KE, Forman A. Neuropelveology: An Emerging Discipline for the Management of Chronic Pelvic Pain. Int Neurourol J. 2017;21(4):243-6.

43.   International Association for the Study of Pain. Pain Treatment Services. Washington: International Association for the Study of Pain; 2009 [cited 2020 March 06]. Available from: https://www.iasp-pain.org/Education/Content.aspx?ItemNumber=1381.

44.   Stedenfeldt M, Halsteinli V. Organisering og drift av tilbud til pasienter med langvarige smertetilstander: En komparativ beskrivelse av fire smertesentre i Norge Trondheim: Regionalt senter for helsetjenesteutvikling, St. Olavs Hospital; 2018 [updated 2018 April 04; cited 2020 March 06]. Available from: https://stolav.no/seksjon-avdeling/Documents/Rapport evaluering smertesentre - delprosjekt 1 - organisering og drift - versjon 1.0.pdf.

45.   Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992;30(6):473-83.

46.   Loge JH, Kaasa S, Hjermstad MJ, Kvien TK. Translation and Performance of the Norwegian SF-36 Health Survey in Patients with Rheumatoid Arthritis. I. Data Quality, Scaling Assumptions, Reliability, and Construct Validity. J Clin Epidemiol. 1998;51(11):1069-76.

47.   Hemingway H, Stafford M, Stansfeld S, Shipley M, Marmot M. Is the SF-36 a valid measure of change in population health? Results from the Whitehall II Study. BMJ. 1997;315(7118):1273-9.

48.   Ware JE, Kosinski M, Dewey JE, Gandek B. SF-36 health survey: manual and interpretation guide: Quality Metric Inc.; 2000.

49.   Badhiwala JH, Witiw CD, Nassiri F, Akbar MA, Jaja B, Wilson JR, et al. Minimum Clinically Important Difference in SF-36 Scores for Use in Degenerative Cervical Myelopathy. Spine (Phila Pa 1976). 2018;43(21):E1260-e6.

50.   Steinhaus ME, Iyer S, Lovecchio F, Khechen B, Stein D, Ross T, et al. Minimal Clinically Important Difference and Substantial Clinical Benefit Using PROMIS CAT in Cervical Spine Surgery. Clin Spine Surg. 2019;32(9):392-7.

51.   Farrar JT, Young JP, Jr., LaMoreaux L, Werth JL, Poole RM. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain. 2001;94(2):149-58.

52.   Gagnon CM, Scholten P, Atchison J. Multidimensional Patient Impression of Change Following Interdisciplinary Pain Management. Pain Pract. 2018;18(8):997-1010.

53.   Clemens JQ, Stephens-Shields AJ, Newcomb C, Rodriguez LV, Lai HH, Bradley CS, et al. Correlates of 1-Year Change in Quality of Life in Patients with Urologic Chronic Pelvic Pain Syndrome: Findings from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network. J Urol. 2020:101097JU0000000000001080.

54.   Arnold LM, Witzeman KA, Swank ML, McElroy SL, Keck PE, Jr. Health-related quality of life using the SF-36 in patients with bipolar disorder compared with patients with chronic back pain and the general population. J Affect Disord. 2000;57(1-3):235-9.

55.   Angst F, Verra ML, Lehmann S, Brioschi R, Aeschlimann A. Clinical effectiveness of an interdisciplinary pain management programme compared with standard inpatient

rehabilitation in chronic pain: a naturalistic, prospective controlled cohort study. J Rehabil Med. 2009;41(7):569-75.

56. Naliboff BD, Stephens AJ, Lai HH, Griffith JW, Clemens JQ, Lutgendorf S, et al. Clinical and Psychosocial Predictors of Urological Chronic Pelvic Pain Symptom Change in 1 Year: A Prospective Study from the MAPP Research Network. J Urol. 2017;198(4):848-57.

57. Scott W, McCracken LM. Patients' impression of change following treatment for chronic pain: global, specific, a single dimension, or many? J Pain. 2015;16(6):518-26.

58. Dybowski C, Löwe B, Brünahl C. Predictors of pain, urinary symptoms and quality of life in patients with chronic pelvic pain syndrome (CPPS): A prospective 12-month follow-up study. Journal of Psychosomatic Research. 2018;112:99-106.

59. Geisser ME, Clauw DJ, Strand V, Gendreau RM, Palmer R, Williams DA. Contributions of change in clinical status parameters to Patient Global Impression of Change (PGIC) scores among persons with fibromyalgia treated with milnacipran. Pain. 2010;149(2):373-8.

60. Hudson JI, Arnold LM, Bradley LA, Choy EH, Mease PJ, Wang F, et al. What makes patients with fibromyalgia feel better? Correlations between Patient Global Impression of Improvement and changes in clinical symptoms and function: a pooled analysis of 4 randomized placebo-controlled trials of duloxetine. J Rheumatol. 2009;36(11):2517-22.

61. Perrot S, Lantéri-Minet M. Patients' Global Impression of Change in the management of peripheral neuropathic pain: Clinical relevance and correlations in daily practice. Eur J Pain. 2019;23(6):1117-28.

62. Vincent AM, Stewart JA, Egloff N, Grosse Holtforth M. Motive Satisfaction in Chronic Pain Patients: Does It Improve in Multidisciplinary Inpatient Treatment and, if so, Does It Matter? J Clin Psychol Med Settings. 2020.

63. Hosier GW, Doiron RC, Tolls V, Nickel JC. The X-Y factor: Females and males with urological chronic pelvic pain syndrome present distinct clinical phenotypes. Can Urol Assoc J. 2018;12(6):E270-e5.

64. Landmark T, Romundstad P, Dale O, Borchgrevink PC, Kaasa S. Estimating the prevalence of chronic pain: validation of recall against longitudinal reporting (the HUNT pain study). Pain. 2012;153(7):1368-73.

65. Piontek K, Ketels G, Albrecht R, Schnurr U, Dybowski C, Brunahl CA, et al. Somatic and psychosocial determinants of symptom severity and quality of life in male and female patients with chronic pelvic pain syndrome. J Psychosom Res. 2019;120:1-7.