



## Observational study

## Identifying characteristics of the most severely impaired chronic pain patients treated at a specialized inpatient pain clinic



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## HIGHLIGHTS

- The most complex chronic persistent pain (CPP) patients are offered in-hospital treatment.
- These patients documented a multitude of psychosocial signs and symptoms.
- They suffered from psychiatric comorbidity, poor physical-functioning and symptom-preoccupation.
- These obstacles to treatment must be focused on during pain rehabilitation.
- A specialist in psychiatry and sleeping disorder should amplify the team.

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## ABSTRACT

**Background and aims:** Patients suffering from chronic nonmalignant pain constitute a heterogeneous population in terms of clinical presentation and treatment results. Few data are available about what distinguishes different groups in this huge population of patients with chronic persistent pain (CPP). A subgroup that is poorly studied, consists of the most severely impaired chronic pain patients. At the Uppsala University Hospital Pain Clinic, there is a specialized department accepting the most complex patients for rehabilitation. In the endeavour to improve and evaluate treatment for this subgroup, a better understanding of the complex nature of the illness is essential. This prospective study aimed to describe the characteristics of this subgroup of patients with CPP.

**Methods:** Seventy-two consecutive patients enrolled in the Uppsala programme were evaluated. We collected data on demographics, type of pain and experienced symptoms other than pain using a checklist of 41 possible symptoms. Psychiatric comorbidity was assessed by a psychiatrist using a structured clinical interview. Quality of life (QoL), pain rating and medication/drug/alcohol usage were measured by validated questionnaires: SF-36, NRS, DUDIT and AUDIT. Concerning physical functioning and sick leave, a comparison was made with data from the Swedish Quality Register Registry for pain rehabilitation (SQRP).

**Results:** The cohort consisted of 61% women and the average age was 45 (range 20–70) years. For this cohort, 74% reported being on sick leave or disability-pension. In the SQRP 59% were on sick leave at the time they entered the rehabilitation programmes [1]. On average, the study-population reported 22 symptoms other than pain, to be at a high rate of severity. Patients treated in conventional pain-rehabilitation programmes reported a mean of 10 symptoms in average. Symptoms reported with the highest frequency (>80%), were lethargy, tiredness, headache and difficulties concentrating. Seventy-six percent were diagnosed with a psychiatric disorder. Sixty-nine fulfilled the criteria for depression or depression/anxiety disorder despite that most (65%) were treated with psychotropic medication. Alcohol/drug abuse was minimal. Seventy-one percent were on opioids but the doses were moderate (<100 mg) MEq. The pain rating was  $\geq 7$  (out of a maximum of 10) for 60% of the patients.

**Conclusion:** This study describes what makes the subgroup of pain patients most affected by their pain special according to associated factors and comorbidity. We found that they were distinguished by a high degree of psychiatric comorbidity, low physical functioning and extreme levels of symptom preoccupation/hypervigilance. Many severe symptoms

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additional to pain (e.g. depression/anxiety, tiredness, disturbed sleep, lack of concentration, constipation) were reported. The group seems hypervigilant, overwhelmed with a multitude of different symptoms on a high severity level.

**Implications:** When treating this complex group, the expressions of the illness can act as obstacles to achieve successful treatment outcomes. The study provides evidence based information, for a better understanding of the needs concerning these pain patients. Our result indicates that parallel assessment and treatment of psychiatric comorbidities and sleep disorders combined with traditional rehabilitation, i.e. physical activation and cognitive reorganization are imperative for improved outcomes.

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## 1. Introduction

Chronic pain is one of the most common health problems worldwide [2], and a common cause for patients consulting a doctor [1–3]. Impairment due to chronic pain leads to high levels of work absence and dramatically increases the consumption of health care. Pain imposes a huge financial and psychosocial burden on patients, their families and society [4,5]. Patients suffering from nonmalignant chronic pain are at risk for developing somatic and psychiatric co-morbidities [6–9]. Changes in lifestyle, associated with chronic pain (e.g. less physical activity, weight gain and sleep disturbance) leads to risk factors for fatal diseases and increased mortality [7,10].

Patients with chronic non-malignant pain constitute a heterogeneous population as to aetiology and clinical presentation [11]. Despite that, they are often treated as though they were a homogeneous group. Few data are available about what distinguishes different groups in the large population of CPP patients. This lack of data affects the ability to design treatment options for various groups. CPP can be complex, and there is an order from those least affected to those most affected by their pain, other symptoms and comorbidities. Evidence-based treatments addressing the requirements of the most severely impaired group of CPP patients have neither been established nor evaluated in Sweden (or elsewhere to our knowledge). The conventional multimodal rehabilitation programmes that focus on regaining physical function, psychosocial ability and return to work are well supported by science [12–16]. The target group for this kind of intervention is patients motivated to overcome their physical disabilities and quickly return to work. Through clinical experience, we know that there are groups of CPP patients not succeeding in these treatments. One of these groups comprises patients most affected by the pain.

Uppsala University Hospital runs a specialized inpatient pain rehabilitation unit that accepts this group of severely disabled patients with chronic pain syndromes. The intervention consists of a six-week multimodal, acceptance based, individualized programme starting with a one-week team-based evaluation of obstacles for physical and cognitive functioning as well as pharmacological treatment. The following four-week treatment programme are based on individualized exposure to avoided activities led by a psychologist and a physiotherapist/occupational-therapist/nurse in pair with the patient. The exposure is done in activity. This is a key component in the treatment since our group of patients are extremely avoiding. Another approach focus on reducing stress, tension and worry by using mindfulness. After six weeks, there is a follow-up week with focus on evaluation of the results of the treatment intervention.

The primary aim of this prospective study was to identify deeper characteristics of an almost intractable subgroup of patients with CPP. We try to form evidence based information concerning a group of the most complex pain patients. A future goal is to use this information to assess and improve interventions tailored to special needs of this group.

A further aim was to determine whether it was possible to identify any association between medications and reported symptoms.

The information presented includes demographic data, psychiatric comorbidity, the total burden of symptoms other than pain, quality of life (QoL), pain rating, type of pain, medication and alcohol/illicit drug use and abuse.

## 2. Methods

The study was performed in full accordance with the Declaration of Helsinki (1965 and later revisions).

The study was approved by the Regional Ethical Review Board in Uppsala, Sweden (Dnr 2010/182).

### 2.1. Patients setting and demographics

Seventy-two consecutive patients referred to a specialized inpatient pain rehabilitation programme at the Pain Clinic at Uppsala University Hospital, Sweden, were enrolled and gave informed written consent. No patients refused to participate and there were no drop-outs. The inclusion criteria that had to be met before entering the programme were; primary or secondary pain care, including multidisciplinary rehabilitation had failed to overcome chronic disability and hence severe functional limitations remained. The patients have severe functional limitations, with some entirely bedridden. Exclusion criteria were active alcohol/illicit drug abuse, psychosis or suicidal behaviour. At the pain clinic, patients with various diagnoses of CPP were accepted. They had a variety of diagnoses when they were referred to the clinic. They were diagnosed with mixed pain conditions musculoskeletal pain, fibromyalgia, widespread pain, abdominal pain, pelvic pain, facial pain, complex regional pain syndrome (CRPS), neuropathic pain of various origins, etc. All the patients had an extreme degree of chronic pain syndrome with physical, social and mental function limitations. This group of patients is at the extreme end of the spectrum of CPP patients, often considered “too complex for health care”.

### 2.2. Procedure

A prospective descriptive design was used. Information on symptoms, QoL, alcohol/drug use/abuse and pain rating were collected by validated self-assessment tools. Psychiatric disorders were diagnosed by a psychiatrist using a structured clinical interview. The survey was conducted during the patients first week in the unit. When possible, a comparison was done with data from the Swedish Quality Registry for Pain Rehabilitation (SQRP), a registry established in 1995 to compare the results among pain rehabilitation programmes in Sweden [17].

### 2.3. Assessment-tools and surveys

#### 2.3.1. Demographics

Data on age, sex and job status were obtained from patient medical records and the clinical interview.

### 2.3.2. Psychiatric co-morbidity

Psychiatric disorders were diagnosed by a psychiatrist using a structured clinical interview technique, all diagnoses were recorded according to 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10).

### 2.3.3. Symptom burden

Symptoms were assessed by a 41-item symptom survey checklist.

The survey is an empirically derived checklist of symptoms experienced by patients with complex chronic non-cancer pain. The 41 symptoms are listed and evaluated on an ordinal scale from 0 to 10, with 0 indicating no problems and 10 indicating severe problems. The survey has been developed and validated at the Copenhagen University Hospital, Denmark [18].

### 2.3.4. Quality of life

QoL was assessed using the Short Form-36 -instrument [19,20], a patient-reported survey of patient health. The instrument is a multi-purpose, short-form health survey consisting of 36 questions. The profiles measure physical functioning, social functioning, mental health, general health, vitality, pain and role limitations due to physical and emotional problems. There is also a summary of mental and physical components, measured as two separate indices. Each item of the SF-36 is scored on a weighted 0–100 scale. Patients were asked to answer items referring to symptoms with a recall of up to 4 weeks.

### 2.3.5. Mean pain intensity

Mean pain intensity during the previous 24-h was indicated by patients using an 11-point pain numerical rating scale (NRS) from 0–10, where 0 = no pain and 10 = the worst possible pain [21,22]. This scale has been shown to be valid and sensitive to change. A reduction of two points (or 30%) represented a clinically important difference [23].

### 2.3.6. Overall consumption of prescribed drugs

The total number of prescribed drugs for pain and other diagnoses was obtained from patient medical records.

### 2.3.7. Use of opioids

The patients prescribed opioids, if any, were obtained from their medical records. For comparison, all opioids were converted to morphine-equivalent doses (MEq) as per the EAPC (European Association for Palliative Care) conversion Table [24]. All opioids were given orally.

### 2.3.8. Use of benzodiazepines

Information about prescribed benzodiazepines and doses was obtained from the patient medical records. Benzodiazepine-use was monitored because of their known effects on cognitive ability [25]. The indication for drug treatment was recorded.

### 2.3.9. Use of alcohol and drugs

The Alcohol Use Disorder Identification Test (AUDIT) is a self-report questionnaire developed by WHO [26,27]. It is a 10-item screening instrument tool to detect hazardous and harmful alcohol consumption.

Three blood biomarkers indicative of alcohol use were analyzed: mean corpuscular volume (MCV), gamma glutamyl-transferase (GGT) and alanine aminotransferase (ALAT) [28].

Illicit drug abuse was assessed using the DUDIT (Drug Use Disorder Identification Test) [29].

**Table 1**

Demographic characteristics of the participants (N = 72).

| Variable            | N             |
|---------------------|---------------|
| <i>Demographics</i> |               |
| Age (in years)      |               |
| 20–30               | N = 7; 9.7%   |
| 31–40               | N = 19; 26.3% |
| 41–50               | N = 21; 29.1% |
| 51–60               | N = 17; 23.6% |
| 61–70               | N = 8; 11.1%  |
| Sex (%) female      | N = 44; 61.1% |
| Working or studying | N = 19; 26.3% |

## 3. Statistics

Data were analyzed with the statistical tool R [30]. An exploratory data analysis was performed using descriptive statistics and graphical tools. Correlations between numerical variables were compared using Spearman's correlation coefficient. For variables with missing data, correlations were compared, both by removing individuals with missing values and with sample averages imputed. Because the results did not differ, only the former values are reported here.

## 4. Results

### 4.1. Demographics

Seventy-two patients (44 women) were enrolled and screened. The mean age was 45 (range 20–70) years. Nineteen patients (26%) were working or studying (Table 1). In the Swedish registry for pain rehabilitation (SQRP, 2013) 41% of the patients were working or studying at the time they entered the rehabilitation programmes [17].

### 4.2. Psychiatric comorbidity

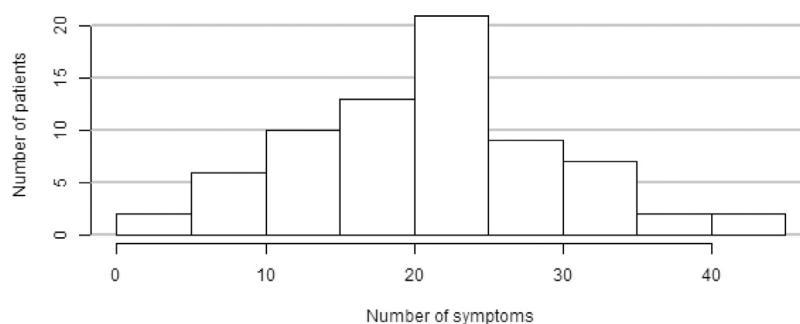
Fifty-five patients (76%) met the criteria of a psychiatric disorder, the most common diagnoses being depression (31 patients or 43%) and combined anxiety-depression disorder (19 patients or 26%). Two patients were diagnosed with post-traumatic stress disorder.

### 4.3. Total burden of symptoms

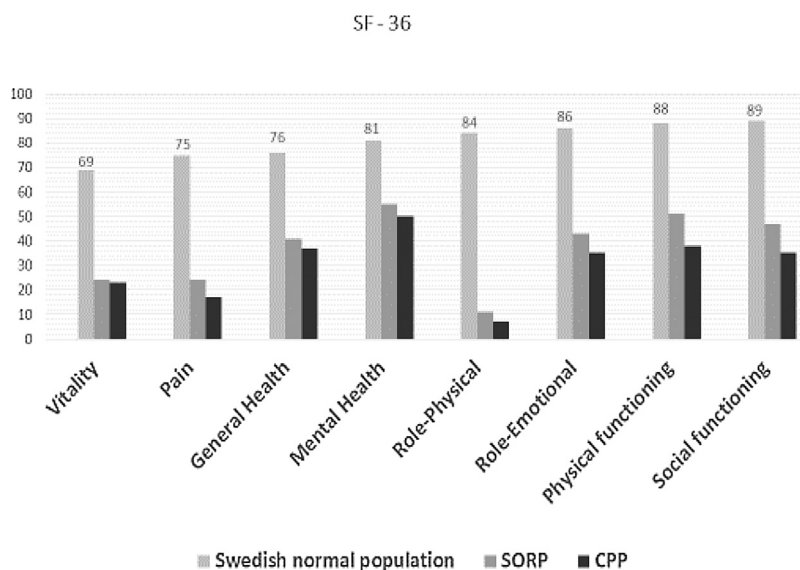
The patients reported a mean of 22/41 symptoms other than pain (Fig. 1). One patient reported the presence of all 41 symptoms. Symptoms reported with the highest frequency over (80%) were lethargy, tiredness, headache and difficulties concentrating. Three patients reported hallucinations (Table 3). Most of the symptoms were reported as severe. Twenty-seven symptoms had a severity-rating of >5/10. For example, sleeplessness had a severity-rating of 9.3 of 10 (see Table 3 for a more comprehensive view of severity-rating and frequency).

### 4.4. Quality of life

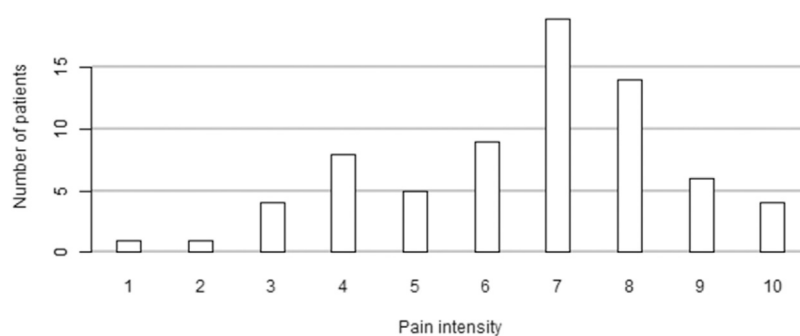
QoL as measured by the SF-36 was rated as poor (Fig. 2). The study-patients rated QoL worse than the patients in the Swedish registry (SQRP), but the difference was modest. The scores for both groups are near the bottom of the scale and because of an apparent “floor effect,” any comparison between the groups was judged not to be reasonable. Both groups of pain patients rated all indices in the SF-36 as extremely low when compared with the average of the Swedish population [20]. In the study group, there was variability between 6.6/100 for physical role-function and 49.3/100 for mental



**Fig. 1.** Total burden of symptoms other than pain. Number of symptoms possible was 41. Average number of symptoms was 22. Jonsson et al.,  $N = 72$ .



**Fig. 2.** SF-36. A comparison between the study group (CPP), Swedish normal population and patients in the Swedish Quality Registry for Pain Rehabilitation, 2013 (SORP),  $N = 72$ .



**Fig. 3.** Pain score on a scale from 0 to 10) as measured by the NRS at baseline. The mean pain intensity over the previous 24 h was rated. Sixty percent rated 7 or more,  $N = 71$ .

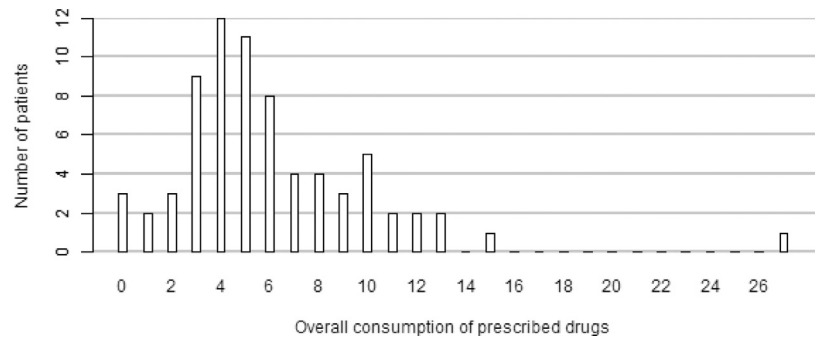
health. The SORP-group followed the same pattern with 11.0/100 for physical role-function and 55.0/100 for mental health.

#### 4.5. Mean pain intensity

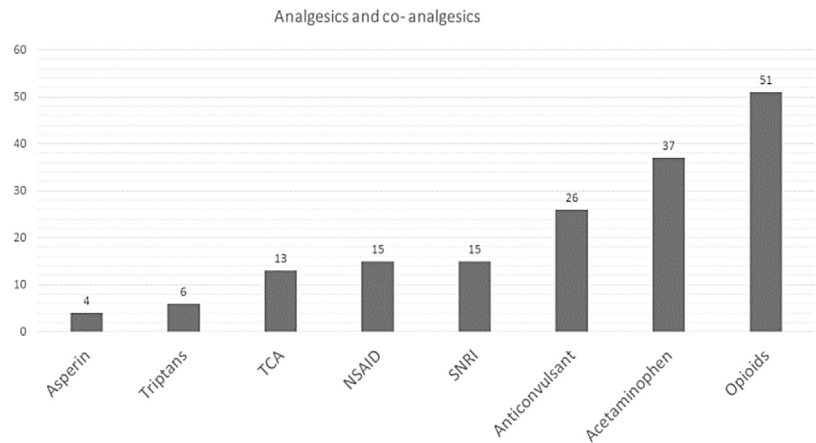
The mean pain intensity over the previous 24-h was rated on the NRS as 1–4 by 14 patients (20%), >4–7 by 14 patients (20%) and >7–10 by 43 patients (60%) (Fig. 3). One patient did not fill in the questionnaire. This NRS grouping is based on the impact that pain has on physical functioning and is described as mild (1–4), moderate (>4–7) or severe (>7–10) pain. This ranking is used for patients with non-malignant pain as well as cancer pain-patients [21,22].

#### 4.6. Overall consumption of prescribed drugs

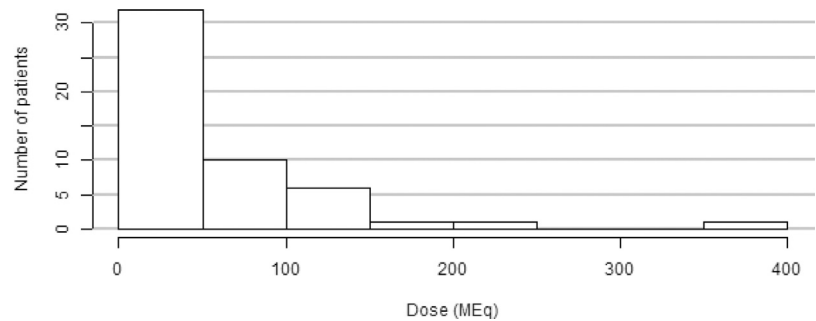
Sixty-nine patients (96%) were using prescribed drugs and, 43 (60%) of these were using five or more (Fig. 4). The most commonly prescribed analgesics were opioids (71%), followed by acetaminophen (paracetamol) (51%) and anticonvulsants (36%) (Fig. 5). Forty-five patients (65%) were using antidepressants, with 13 having more than one prescribed antidepressant. Antidepressant classes were SSRI (29%), SNRI (21%), tricyclic (18%) and others (12%). Antidepressants were prescribed for depression, anxiety, pain and insomnia. Medications for hypertension (8%) and diabetes (7%) were also recorded.



**Fig. 4.** Overall consumption of different prescribed drugs used on a daily basis, at the start of the treatment. Drugs used for different diagnoses were included. Sixty-nine patients/seventy-two used from 0 to 27 different drugs.



**Fig. 5.** Analgesics and co-analgesics used on a daily basis (N=72). Some patients used drugs from several classes. TCA – tricyclic antidepressants, NSAID – nonsteroidal anti-inflammatory drugs, SNRI – serotonin-norepinephrine reuptake inhibitors.



**Fig. 6.** Total opioid consumption, milligrams of morphine-equivalent doses (N=51). The doses were given orally. Patients were treated with 1–360 mg MEq. The majority 32/51 with doses under 50 mg MEq.

4.7. Use of opioids

Fifty-one patients (71%) were treated with opioids. Fourteen patients combined two types of opioids, there were no pattern in how the opioid were combined to each other. Seven types of opioid were used. Only nine patients had an average daily dose exceeding 100 mg MEq (Fig. 6 and Table 2). All opioids were given orally.

4.8. Use of benzodiazepines

Thirty patients (42%) were treated with benzodiazepines, all in modest doses. There were 11 patients treated with benzodiazepines with the indication anxiety; four with oxazepam, five with diazepam and one each with clonazepam and alprazolam. The doses for these patients were modest; with a majority low, 5 mg

**Table 2**

| Use of opioids.                                    |               |
|----------------------------------------------------|---------------|
| Opioids                                            | N             |
| Use of opioids                                     | N = 51; 70.8% |
| Top seven opioids                                  |               |
| Buprenorphine                                      | N = 17; 23.6% |
| Tramadol                                           | N = 13; 18.0% |
| Oxycodone                                          | N = 11; 15.2% |
| Morphine                                           | N = 10; 13.8% |
| Fentanyl                                           | N = 5; 6.9%   |
| Codeine                                            | N = 3; 4.1%   |
| Methadone                                          | N = 3; 4.1%   |
| Average daily dose, MEq (morphine-equivalent dose) |               |
| 1–49 mg MEq/day                                    | N = 32; 44.4% |
| 50–99 mg MEq/day                                   | N = 10; 13.8% |
| 100 mg+ MEq/day                                    | N = 9; 12%    |
| Combined two opioids                               | N = 14; 19.4% |



diazepam, and as highest 40 mg oxazepam. The other patients were treated with zolpidem or zopiclon for sleeping-disorder. Zolpidem in doses ranging between 5 and 10 mg and zopiclon 7.5 mg except one patient treated with 15 mg. Four patients were treated with benzodiazepines both day and night.

#### 4.9. Use of alcohol and illegal drugs

According to the AUDIT, only two patients (3%) reported the overuse/abuse of alcohol. Blood biomarkers indicative of alcohol abuse were all in the normal range. One patient admitted to the previous use of illegal drugs.

#### 4.10. Correlations

Correlations between symptoms clusters were calculated. The symptoms listed below were among those with the highest correlations, and are, based on clinical experience, believed to be truly correlated. That the numbers verify these relationships indicates that we have sufficient data to assume that the other correlations are true, i.e. there was no correlation between any of the symptoms and numbers or types of prescribed drugs.

Results were as follows; anxiety/depression ( $r=0.71$ ,  $p=10^{-11}$ ), anxiety/irritation ( $r=0.47$ ,  $p=5 \times 10^{-5}$ ), anxiety/stress ( $r=0.61$ ,  $p=2 \times 10^{-8}$ ), drowsiness/decreased energy ( $r=0.51$ ,  $p=5 \times 10^{-6}$ ), drowsiness/weakness ( $r=0.55$ ,  $p=10^{-6}$ ), drowsiness/stress ( $r=0.53$ ,  $p=2 \times 10^{-6}$ ), confusion/memory deficit ( $r=0.48$ ,  $p=10^{-5}$ ), confusion/headache ( $r=0.52$ ,  $p=10^{-6}$ ), confusion/stress ( $r=0.54$ ,  $p=10^{-6}$ ), and confusion/memory deficit ( $r=0.62$ ,  $p=9 \times 10^{-9}$ ).

### 5. Discussion

The most important findings in this study were the extreme burden of symptoms, other than pain, the high prevalence of psychiatric comorbidity and the low physical functioning that the group of severely impaired chronic pain patients reported (Table 3). Similar characteristics are reported in other groups of patients with CPP [31], but in the present study the problems were much more pronounced.

#### 5.1. The most severe and frequently occurring symptoms other than pain

The study group presented, on average, 22 (of 41) assessed symptoms, whereas previous studies on patients with non-malignant pain and in palliative care reported an average of 10 (of 41) symptoms [18,32,33]. The average number of symptoms present in the general population was 4 (of 41) [18]. The symptom severity rating in our study population was high (27/41 symptoms rated with a mean  $>5/10$ ). Sleeplessness was rated as the most severe symptom with an average score of 9.3/10 (Table 3).

Two clusters of symptoms, other than pain, stand out. The first cluster includes lethargy, tiredness, weakness, somnolence and insomnia; i.e. fatigue-related symptoms. The second cluster includes difficulties in concentrating and feelings of absentmindedness. These symptom clusters were reported by over 75% of the patients. To be able to choose the right rehabilitation interventions it is necessary to understand the cause of these symptoms. Are they caused by pain, by sleep disorder, by psychiatric comorbidity, a combination of these factors, or is there some other explanation? Tiredness and cognitive dysfunction are commonly attributed to depression and the comorbidity of depression and pain is estimated to be at least 50% in most studies [34,35]. In our group 69% met the criteria for depression or depression/anxiety disorder and 76% had a psychiatric diagnosis based on a psychiatric assessment. Tiredness and difficulties concentrating are also related to sleep disorder.

**Table 3**

Frequency and degree of symptom severity. Symptoms other than pain ( $N=72$ ).

| Symptom                    | Number | %    | Severity 0–10 |
|----------------------------|--------|------|---------------|
| Lethargic                  | 66     | 91.6 | 7.65          |
| Tired                      | 66     | 91.6 | 7.65          |
| Difficulties concentrating | 63     | 87.5 | 6.50          |
| Headache                   | 59     | 81.9 | 6.32          |
| Dry mouth                  | 58     | 80.5 | 6.62          |
| Weakness                   | 57     | 79.1 | 6.14          |
| Absentminded               | 57     | 79.1 | 5.91          |
| Somnolent                  | 54     | 75.0 | 5.28          |
| Irritated                  | 51     | 70.8 | 5.22          |
| Sleepless                  | 50     | 69.4 | 9.28          |
| Depressive                 | 50     | 69.4 | 5.50          |
| Dizzy                      | 49     | 68.0 | 4.73          |
| Sweating                   | 44     | 61.1 | 5.73          |
| Anxiety                    | 44     | 61.1 | 5.25          |
| Nausea                     | 44     | 61.1 | 4.68          |
| Weight gain                | 38     | 52.7 | 6.37          |
| Confused                   | 38     | 52.7 | 4.26          |
| Gassy stomach              | 37     | 51.3 | 4.92          |
| Stress                     | 36     | 50.0 | 5.33          |
| Constipated                | 35     | 48.6 | 6.29          |
| Visual disorder            | 34     | 47.2 | 5.20          |
| Stomach pain               | 34     | 47.2 | 5.62          |
| Dislike of food            | 33     | 45.8 | 6.79          |
| Worried                    | 33     | 45.8 | 5.39          |
| Aggressive                 | 33     | 45.8 | 4.84          |
| Nightmares                 | 31     | 43.0 | 5.13          |
| Itching                    | 28     | 38.8 | 5.54          |
| Palpitations               | 28     | 38.8 | 4.89          |
| Heart burn                 | 25     | 34.7 | 4.23          |
| Loss of hearing            | 19     | 26.3 | 4.79          |
| Aftertaste                 | 18     | 25.0 | 4.56          |
| Diarrhoea                  | 18     | 25.0 | 3.44          |
| Skin rash                  | 16     | 22.2 | 4.81          |
| Increased appetite         | 15     | 20.8 | 5.27          |
| Vomiting                   | 15     | 20.8 | 4.07          |
| Tinnitus                   | 14     | 19.4 | 6.00          |
| Weight loss                | 13     | 18.0 | 5.46          |
| Irregular menstruation     | 7      | 9.7  | 8.14          |
| Hiccups                    | 7      | 9.7  | 2.86          |
| Hallucinations             | 3      | 4.1  | 3.00          |

Almost 70% of our study group reported sleeplessness as a severe symptom (graded 9.3/10). In this group of severely impaired pain patients, it seems that parallel assessment and treatment of psychiatric comorbidities and sleep disorders are imperative for improved outcomes.

An interpretation is that the preoccupation of symptoms can be attributed to hypervigilance secondary to anxiety, and that experienced low physical role functioning is an expression of avoidance reinforces the importance of psychiatric co-morbidity.

Avoidance and high attention to symptoms interfere with the ability to be involved in education, mindfulness therapy and cognitive behavioural strategies used in most pain rehabilitation programmes [12] which is probably one of the primary reasons why the treatment interventions fail.

It is postulated that the high symptom load may be a sign of hypervigilance to bodily sensations [36]. The phenomenon of hypervigilance is closely related to anxiety and can be understood as an overreaction in the alarm-system that serves to ensure that the cognitive system is alert and in a state of readiness to detect high priority signals that have the potential to threaten survival [37]. Pain is a high priority signal. Hypervigilance, when understood as an expression of anxiety, will lead to individuals underestimating personal coping resources and also deactivation of motor responses, resulting in avoidance and a feeling of helplessness, which are commonly observed in the clinical setting [37–39]. Some studies have demonstrated that symptom preoccupation, as an expression of anxiety, is a psychological trait that is a predictor for the development of chronic pain [40]. The clinical experience of this group is

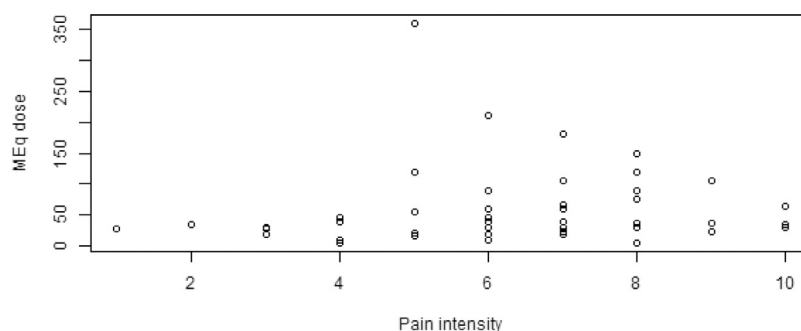


Fig. 7. Pain intensity on a 0–10 NRS scale vs. dose of opioids in milligrams morphine-equivalent doses (MEq).

that they have a pronounced physical inactivity and avoidance. This is also reflected in the results from the SF-36 in which the patients reported physical role-functioning as the lowest parameter.

### 5.2. Psychiatric comorbidity

Sixty-five percent of our patients were treated with antidepressants but still 69% fulfilled the criteria for depression or depression/anxiety disorder, suggesting a lack of treatment follow-up for depression in this group of patients with psychiatric comorbidity. The findings in this study indicate that psychiatric comorbidity, extreme levels of symptom preoccupation with non-pain symptoms, e.g. perceived cognitive dysfunction and tiredness and low physical functioning are much more pronounced for the subgroup of extreme disabled pain patients than for other CPP patients.

### 5.3. Quality of life

Low quality of life is one of the main reason why patients will be offered a multimodal pain rehabilitation [31]. As could be expected, the study group reported low QoL as evaluated by the SF-36. They presented levels inferior to patients reporting to the Swedish registry SQRP taking part of conventional rehabilitation. The scores for both groups are near the bottom of the scale and because of an apparent “floor effect,” any comparison between the groups was judged not to be reasonable. The SF-36 does not seem to be an adequate tool to distinguish between subgroups of pain patients. Both groups reported their QoL far below the average of the healthy Swedish population [20].

### 5.4. Pain

Pain rating was high in our study population: 60% of the patients reported a NRS score of  $\geq 7$ , which is classified as severe pain [41,42]. High pain levels have been correlated to low physical functioning [22]. In our study the participants reported physical role functioning as the lowest (6.6/100) of the eight domains of the SF-36 scores. This correlates well with the high NRS scores [22], indicating that low physical functioning is closely linked to the experience of high pain levels. One interpretation of this finding is that low physical functioning aggravates the pain through inactivity and because of lower participation in social and everyday life activities.

### 5.5. Use of opioids, alcohol and illicit drugs

The opioid-doses were moderate compared with what has been reported in other studies of chronic pain populations [31,43–45]. No correlation was found between type or quantity of opioid and any of the symptoms reported. Most surprisingly was the lack of correlation between the opioid dose and pain score (Fig. 7).

The incidence of alcohol/illicit drug use/abuse was low, like findings in other groups of patients with CPP [46]. One bias for the low frequency can be that ongoing alcohol and drug abuse is one of the few exclusion criteria for participation in the programme.

## 6. Strength of this study

This study was done in a clinical setting, where we collected prospective consecutive data from 72 participants. The patients have a complicated disease and they are complicated to describe. This is probably why it is seldom done. We have tried to do so in order to find new treatment options so this group do not have to be “too complicated to healthcare”, in the future.

## 7. Limitations and weakness of this study

The study does have some weaknesses. First, the total number of patients included is relatively small. Second, because the programme has broad and rather nonspecific inclusion criteria and few exclusion criteria, the heterogeneity of the population, making analysis with somatic variables difficult.

This is one of a few studies highlighting the characteristics of the most impaired pain patients. Patients are often treated with the same group-based multimodal interventions, despite that clinically there are subgroups of patients needing different treatment modalities. It is not only for pharmacological interventions that it is important to identify potential responders, but also for multidisciplinary rehabilitation programmes. An understanding of what characterizes different subgroups of patients with CPP and how to improve treatment for different groups would translate into clinical benefit for the patient.

## 8. Conclusion

This study provides evidence based information of the subgroup of pain patients most effected by their pain and referred to our specialized inpatient pain clinic. They are distinguished by a high degree of psychiatric comorbidity, low physical functioning and extreme levels of symptom preoccupation with non-pain symptoms. The patient group seems hypervigilant, overwhelmed with a multitude of different symptoms on a high severity level. The most prominent, experienced by over 80% were fatigue-related symptoms and cognitive dysfunction.

**Implications:** When treating this group, their heavy symptom burden, e.g. tiredness, sleep loss, concentration-deficit can act as obstacles to achieve successful treatment outcomes. In the design of new evidence-based treatment-options our results support the idea that a psychiatrist and a physician with expertise in sleep-disorders should be part of the treatment team together with a pain-rehabilitation specialist. Careful assessment of the co-complaints is needed to achieve improvement.

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## Ethical issues

The study was performed in full accordance with the Declaration of Helsinki (1965 and later revisions). The study was approved by the Regional Ethical Review Board in Uppsala, Sweden (Dnr 2010/182). The patients included in the study were informed and gave written informed consent.

## Conflict of interest

No conflicts of interest.

## Authors' contribution

EBH and LS oversaw and participated in all data collection, TG and EBH designed the protocol, and wrote the manuscript, RK and SB provided technical and interpretational advice and edited the manuscript and MT analyzed the data and performed the statistical analyses. All authors approved the final manuscript.

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