The long-term outcome of interdisciplinary treatment in patients with chronic musculoskeletal pain on level of disability

The long-term outcome of interdisciplinary treatment in patients with chronic musculoskeletal pain on level of disability, a longitudinal observational study.

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"ONDERGETEKENDE

Daan Bauke Uilkema,

Bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld."

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ABSTRACT

Rationale: Chronic musculoskeletal pain (CMP) can lead to increasing level of disability and other limitations in daily functioning and participation. Evidence of the long-term outcome of interdisciplinary treatment on level of disability in patients with CMP is scarce and a responder analyses were not conducted.

Aim: The aim of the present study was to measure the long-term outcome of interdisciplinary treatment on level of disability in patients with CMP and to calculate the responder rate.

Methods: Data were recorded routinely at admission, discharge, and at three, six and 12 months' follow up for all consecutive patients referred to a rehabilitation program between July 1st, 2017 and December 31st, 2018. The interdisciplinary treatment program consisted of Pain Neuroscience Education, Cognitive Behavioural Therapy, Graded Activity, individual therapy by a psychologists and physical therapists and goal setting and (mid-term) evaluation with coordinator and physiatrist. Assessments included the Pain Disability Index (PDI), Beck's Depression Inventory (BDI), Checklist Individual Strength (CIS) and Tampa Scale of Kinesiophobia (TSK). Mixed-model analysis was used to analyze changes over time and responder analysis was used to measure the responder rate.

Results: 628 patients were included in this study [mean age 44.2 (standard deviation 12.0) years], 460 (73.2%) of whom were women. Data from 484 (77.1%), 26 (4.1%), and 35 (5.6%) patients was available respectively at discharge, three- and six months follow-up. No data was available at 12 months' follow-up. The level of disability showed significant improvement between admission and discharge (p=0.000), and three months follow-up (p=0.008). The responder rate for the different patient groups stratified in PDI scores at baseline was respectively 51.5%, 52.8% and 53.7%.

Conclusion: Patients with CMP showed a significant improvement on level of disability directly after discharge and was maintained until three months after discharge. Over half of the patients with CMP showed clinically relevant improvement on level of disability at discharge.

Clinical relevance: Referring patients with CMP in an earlier disease stage to interdisciplinary treatment can have a beneficial effect on the outcome on level of disability. Further research is recommended of matched-care referral policy in patients with CMP.

Keywords: chronic pain; musculoskeletal pain; patient care team; interdisciplinary treatment rehabilitation; disability

INTRODUCTION

In 2010, an estimated 11% of the population in the Western World suffered from Chronic Musculoskeletal Pain (CMP)(1, 2). CMP is defined as chronic primary musculoskeletal pain (e.g., nonspecific low-back pain) and chronic secondary musculoskeletal pain(3). Secondary CMP is defined as a persistent or recurrent pain experience lasting longer than three months that arises as a result of a disease process directly affecting bone(s), joint(s), muscle(s), or related soft tissue(s) limited to nociceptive pain(1, 4) or as a result of central sensitisation of the nervous system(5). Gender(6, 7), age(6-8), lower educational level(6, 9), fear-avoidance (10-13), depression(14-17) and chronic fatigue(18-20) are associated with CMP. Besides pain experience, CMP can lead to limitations in activities in daily living (ADL) as well as restrictions in other domains of the international classification of functioning, disability and health (ICF) such as participation(2, 21, 22). Eventually CMP may cause loss of quality of life (QoL)(21).

To decrease the level of disability in patients with CMP, patients with CMP can follow different types of treatment programs. For example, pharmacological interventions, mono-disciplinary interventions and interdisciplinary treatment(23). Interdisciplinary treatment with multi-component treatment programs focus on a behavioural modifying approach and can consist of cognitive behavioural therapy (CBT), including Acceptance and Commitment Therapy (ACT) and Relaxation Therapy (mindfulness), Graded Activity (GA), pain neuroscience education, and education in lifestyle and coping strategies(23, 24). These programs are more effective because psychological factors influence behavioural change(25). Interdisciplinary treatment consisting of CBT, strength- and endurance training, and pain neuroscience education showed to be more effective in increasing the QoL for the long-term, than mono-disciplinary- and pharma logical treatment in patients with fibromyalgia syndrome and non-specific chronic low back pain(26). Also, interdisciplinary treatment showed a positive long-term effect on the level of disability and pain experience in patients with CMP(9, 27). Factors associated with lower effect of interdisciplinary treatment are longer duration of pain(9), higher age(28), more fatigue(28), and anxiety(28).

Despite the proven long-term benefit of interdisciplinary treatment on level of disability in patients with CMP, there is an ongoing debate between health care workers and health care insurers about the Dutch referral policy. At this moment the Dutch referral policy is based on stepped care. Patients are referred to conventional (and cheaper) first line practitioners first. Only if this treatment is unsuccessful patients are referred to an often more expensive second line. This referral policy is based on unsuccessful treatments outcomes(29). Another policy form, matched care, involves identifying patients with CMP with higher risk of disability and tailor the intervention. The main assumption is that the patient with CMP receives adequate treatment earlier in the healthcare process which is saving time, money, and fail-experiences of the patients(29). Furthermore, long-term decrease of level of disability will increase participation and decrease use of healthcare. Because time and psychological factors are related with the effectivity of interdisciplinary treatment in patients with CMP it is meaningful to gather more evidence to support or falsify the existing evidence.

There is also a further point to be considered. Until now outcome measures, e.g. level of disability measured with Pain Disability Index (PDI), of interdisciplinary treatment are usually presented with mean change score, 95% confidence interval, and effect sizes(9, 30) not knowing what proportion of patients with CMP have a meaningful response to interdisciplinary treatment. A meaningful response is the minimal clinical important change (MCIC) patients must have on level of disability to benefit from interdisciplinary treatment. To calculate the proportion of patients who achieve a meaningful response to interdisciplinary treatment a responder analysis is used(31). A responder analysis is in addition to mean change score a more accurate outcome measures to assess whether interdisciplinary treatment is meaningful(32). Therefore, the aim of this study is to measure the long-term outcome of interdisciplinary treatment on level of disability in patients with CMP. Secondary aims are to calculate the proportion of patients who have a meaningful response to interdisciplinary treatment and to measure if having a depression, chronic fatigue and fear-avoidance are contributing factors on the change on level of disability in patients with CMP during interdisciplinary treatment.

Question

What is the long-term outcome measure of interdisciplinary treatment on level of disability in patients with chronic musculoskeletal pain assessed with the Pain Disability Index?

Secondary questions

What is the proportion of patients with CMP who benefit from interdisciplinary treatment?
Are depression, fatigue, or fear avoidance contributing factors on the change of level of disability in patients with CMP during interdisciplinary treatment?

METHODS

Study design

This study concerns a longitudinal observational study. Patient data is routinely gathered during the standardized interdisciplinary treatment program for patients with CMP provided by Centre for Integral Rehabilitation (CIR) and stored in electronic patient records. The study protocol was not reviewed and approved by the medical ethical committee since it does not fall within the scope of the act medical scientific research with humans. All data was coded according to the General data Protection Regulation (GDPR) and the translation key was guarded by the privacy officer. The study and the handling of data was conducted in accordance with the guidelines for Good Clinical Practice (GCP)(33) and STROBE guidelines for cohort studies(34).

Patients

All patients with CMP admitted at CIR for treatment between July 1st, 2017 and December 31st, 2018 were eligible for inclusion in the present study. Inclusion criteria were: age of 18 years or older and being diagnosed with CMP consisting longer than three months by a general

practitioner or medical specialist. Exclusion criterium was the inability to understand and speak the Dutch language. Participants were asked to stop all other treatment related to CMP, except medication, for the duration of a CIR interdisciplinary treatment program. All eligible patients gave written informed consent that their data can be used for research.
During an intake procedure, an interdisciplinary team of a physiatrist, coordinator, physical therapist and psychologist screened each patient individually for eligibility for an interdisciplinary treatment program. The screening was followed up by interdisciplinary consensus meeting. The physiatrist made the final decision in case of disagreement.

Setting

CIR is an independent rehabilitation centre with five locations in the Netherlands. Eligible patients who were admitted after the intake procedure received interdisciplinary treatment.

Intervention

The intervention consisted of three programs called CIR Active, CIR Active+Perspective and CIR Intensive (figure 1). All programs provided a standardized first two weeks with pain neuroscience education, education in lifestyle and coping strategies, followed by a more personalized and individual approach. All individual programs consists of elements of Cognitive Behavioural Therapy (CBT) such as Acceptance and Commitment Therapy (ACT) and Relaxation Therapy (mindfulness), Graded Activity (GA), individual therapy by a psychologist addressing restorative factors, individual therapy by a physical therapist addressing restorative factors, goal-setting and (mid-term) evaluation with coordinator and physiatrist. The goals were set together with the coordinator and the patient for shared decision making focusing on the ICF domains activity and participation. Additional Eye Movement Desensitization and Reprocessing (EMDR) treatment (maximum of four sessions) was provided if patients had signs of PTSS.

	Group Education by psychologist and physical therapist	Group Graded Activity by physical therapist	Interdisciplinary patient consultation between professionals only	Individual psychological treatment by psychologist	Individual physical treatment by physical therapist	Individual (existential) coping strategies, relaxation techniques, by psychologist and physical therapist	Individual consult with rehabilitation physician	Individual coaching with program coordinator for goal-setting and evaluation
All CIR programs	11 hours/ 5 days for 2 weeks	2 hours/ 2 days per week for 7 weeks	3 times 10 minutes in one program (more if necessary)	2 hours/ 2 days per week for 7 weeks	2 hours/ 2 days per week for 7 weeks	3 hours/ 2 days per week for 7 weeks	3 times 30 minutes in one program	1 hour per week for 9 weeks
After the first 10 weeks (CIR Active), there can be an additional CIR Perspective for the duration of 10 weeks with low intensity, or CIR Intensive for the duration of 10 weeks with higher intensity. The Intake procedure and discharge procedure is not taken into account in amount of treatment weeks.								
Additional CIR Perspective				1 hour per day for 4 days in 9 weeks	1 hour per day for 4 days in 9 weeks		1 consult at end of program	1 hour per day for 4 days 9 weeks
Additional CIR Intensive		2 hours/ 2 days per week for 9 weeks	3 times 10 minutes in one program (more if necessary)	2 hours/ 2 days per week for 9 weeks	2 hours/ 2 days per week for 9 weeks	3 hours/ 2 days per week for 9 weeks	1 consult at end of program	1 hour per 2 weeks for 9 weeks

Figure 1: Interdisciplinary treatment programs at Centre for Integral Rehabilitation and amount of treatment hours.
Three types of interdisciplinary treatment: CIR Active; CIR Active+Perspective; CIR Intensive.

Assessments

Assessments included both electronic questionnaires to be completed by the patient at home, as well as physical performance tests consisting of heart rate, blood pressure, length, weight, Body Mass Index, fat percentage, 6-Minute Walk Test and Timed Sit to Stand test conducted by the physical therapist. The electronic database is provided by Asterisque(35). Patients have access to their own electronic patients records by using their log-in name, personal identification code and verification code. The treating therapists have access to the electronic patient record conform the regulations of the GDPR.

Gathering data is part of routine clinical care at admission, discharge and follow-up at three months, six months, and 12 months. The follow-up consisted only of electronic questionnaires accessible by link sent by e-mail. Patients had the ability to use computers at the treatment facility when they were unable to complete the electronic questionnaires at home or somewhere else. Patients who did not complete the electronic questionnaires during admission and discharge were personally approached by the coordinator to complete them. Patients who did not complete the electronic questionnaires during the follow-up period at three months, six months and 12 months received a reminder by e-mail in which they were asked to complete the questionnaire.

Sociodemographic characteristics

The sociodemographic characteristics gathered at admission are: age (years), gender (male/female), living status (living alone, married/ living together, Living Apart Together (LAT), with parents, divorced, widow/ widower, other) and work status (payed employment, own business, self-employed, school/ study, unpaid job/ voluntary work, household, retired, unemployed, other).

Disease characteristics

The characteristics of CMP included locations of symptoms (back, neck, shoulder/ arm, pelvic, 2-5 regions in the body, >5 regions in the body, fibromyalgia, other).

Primary Outcome Measure

Level of disability

The Pain Disability Index (PDI) records the experienced level of disability because of pain(36, 37). The PDI is a valid rating scale for patients with chronic musculoskeletal pain(36, 37). The PDI consists of 7 items, representing subareas, in specific activities of daily living (ADL), recreation, social activities, profession, sexual activities, self-care and basic life needs. Each subarea is rated by the patient from 0 (no disability) to 10 (worst disability) resulting in a total score ranging from 0 to 70 points.

The PDI has shown a good test-retest reliability (ICC 0.76) in Dutch patients with CMP(37). Therefore, the PDI is considered a reliable questionnaire for repeated measurements and as such it was used in the current study. The standard error of measurement (SEM) is 6.5 points(37) and a minimal clinically important change (MCIC) is baseline dependent(38). The MCIC in patients with baseline PDI score ≤27 is 7 points, in patients with PDI score 28-42 is ≥15 points, and in patients with PDI score ≥43 is ≥20 points(38). Because the SEM is smaller than the MCIC, the PDI is a reliable instrument for assessing the level of disability. When normally distributed, the PDI will be presented at baseline with a mean score and standard deviation and mean score and standard error for longitudinal analysis.

Secondary Outcome Measures

Responder rate

Responder rate shows proportion patients with a minimal clinically important change (MCIC) on an outcome measure. A patient was considered a responder when the delta PDI score between admission and discharge reached or exceeded the threshold values of the PDI. The threshold value of the PDI in patients with baseline PDI score ≤27 is 7 points, in patients with PDI score 28-42 is ≥15 points, and in patients with PDI score ≥43 is ≥20 points(38) The responder rate will be presented with mean change score and 95% confidence interval.

Fatigue

The Checklist for Individual Strength[1] (CIS) records the subjective fatigue and contains four subscales, and 20 items. The subscales are [items]: subjective fatigue [8], concentration [5],

[1] Checklist Individuele Spankracht in Dutch

motivation [4] and physical activity [3]. Every item has a 7-point Likert scale which runs from 1= yes, that is true; to; 7= no, that is not true.
The CIS is a valid and accurate questionnaire(20), with a specificity of 90% and a sensitivity of 73%(39). The range of the CIS may vary from 20-140 points, the cut-off point for chronic fatigue is ≥76 points. When normally distributed, the CIS will be presented with a mean score and standard deviation.

Fear avoidance

The Tampa Scale of Kinesiophobia (TSK) records the fear avoidance of physical movement. The TSK contains of 17 items and can be scored with a 4-point Likert scale. The range of the TSK may vary from 17-68 points; the cut-off point for presence of kinesiophobia is ≥37 points. The TSK is moderately accurate(40, 41). When normally distributed, the TSK will be presented with a mean score and standard deviation.

Depression

The Beck's Depression Inventory[2] (BDI) records the presence of a depression. The BDI questionnaire contains of 21 items divided in 3 factors: affective, somatic and cognitive. Each item can be scored with a 4-point Likert scale. The range of the BDI may vary from 0-63 points. The cut-off points are: 0-13 indicates minimal depression; 14-19 indicates mild depression; 20-28 indicates moderate depression; and 29-63 indicates severe depression. BDI is a valid and reliable questionnaire(16). When normally distributed, the BDI will be presented with mean score and standard deviation.

Missing data and loss to follow-up

Missing items at admission such as location of symptoms were gathered by manually searching the referral letter looking for main reason of referral. Missing values of the location of symptoms and/or PDI scores at baseline were excluded from the dataset. We manually looked for patients who did not complete the questionnaires at follow-up. These patients were sent an e-mail as a reminder to do so. Reason for exclusion were not systematically recorded for every patient, the exclusion criteria used for this study are shown in figure 2.

Statistical methods

Descriptive statistics were used for sociodemographic- and disease characteristics. Comparison of sociodemographic- and disease characteristics and primary outcome measure between patients with completed questionnaires up to and including 12 months follow-up and patients who dropped out before 12 months were carried out by means of unpaired t-tests or the Mann–Whitney U test for continuous variables in case of non-normality.
Mean estimates for the various time points were calculated by using a linear mixed-model procedure with a heterogeneous Toeplitz covariance matrix for the repeated measures and

[2] BDI-II-NL-R in Dutch

time as fixed factor. This approach accommodates for missing observations and allows post-hoc tests for within-patient factors.
A responder analysis was used to calculate the responder rate(32).
Univariate analyses were used for each factor to determine if they had a contributing effect on the outcome assessment.
Multivariate linear regression analysis is used to come to a predictive model to forecast the primary outcome assessment post treatment. The possible contributing factors were manually entered and removed one by one in order of highest alpha. This process was repeated until a predictive model was reached. The significance level during modelling was set as 0.1, the significance for the final model was set at 0.05.
The normality assumption for the various outcome variables was checked by visual inspection of the residuals and with the Kolmogorov-Smirnov test was used. All analyses were done using SPSS Statistics for Windows, Version 25.0 (IBM Corp, Armonk, NY, USA).

RESULTS

Of the 2945 patients who are referred to CIR between July 1st, 2017 and December 31st, 2018, 628 patients were included to the study and provided admission data (figure 2). Data from 484 (77.1%) patients were available at discharge and 26 (4.1%), and 35 (5.8%) patients at three months and six months follow-up, respectively. No data was available at 12-months follow-up due to complete loss-to-follow up.

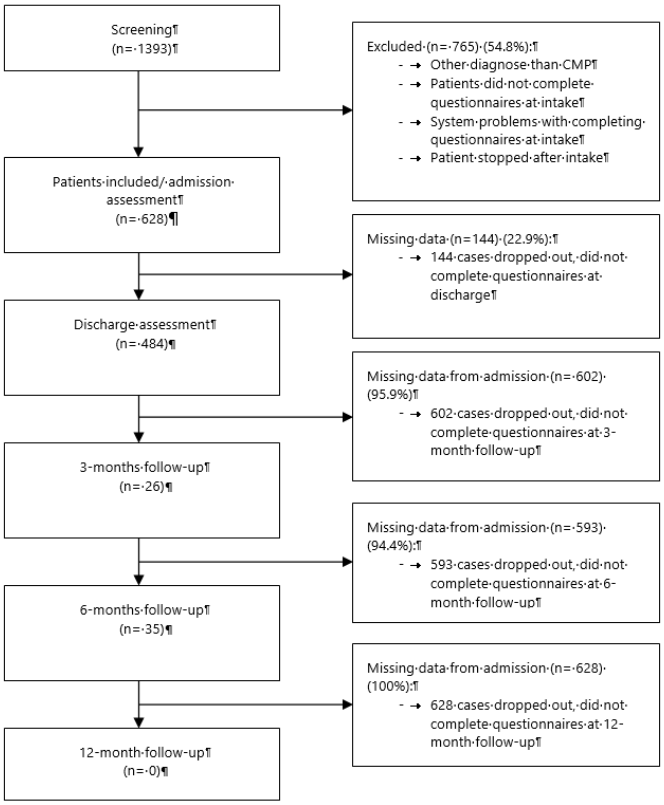

Figure2: Flow of patients with chronic musculoskeletal pain referred to an interdisciplinary treatment program

Table 1: Baseline characteristics of 628 patients with chronic musculoskeletal pain taking part in an interdisciplinary treatment program

Sociodemographic characteristics	
Number participants (female)	628 (73.2%)
Age, years: mean (SD)	44.2 (12.0)
Treatment location	
Alkmaar	143 (22.8%)
Amsterdam	186 (29.6%)
Arnhem	161 (25.6%)
Zwolle	138 (22.0%)
Living status (n=628)	
Living alone	104 (16.6%)
Married/ living together	385 (61.3%)
Living Apart Together (LAT)	34 (5.4%)
With Parents	33 (5.3%)
Divorced	27 (4.3%)
Widow/ Widower	7 (1.1%)
Other	25 (4.0%)
Not completed questionnaire	13 (2.1%)
Work status (n=628)	
Salaried employment	413 (65.8%)
Own practice	23 (3.7%)
Freelancer/ self employed	14 (2.2%)
School/ study	14 (2.2%)
Unpaid job/ voluntary work/ household	45 (7.2%)
Retired	15 (2.4%)
Unemployed	90 (14.3%)
Not completed questionnaire	14 (2.2%)
Disease characteristics	
Location of symptoms (n=628)	
Back	171 (27.2%)
Neck	33 (5.3%)
Shoulder/ arm	22 (3.5%)
Pelvic	18 (2.9%)
2-5 regions in the body	191 (30.4%)
>5 regions in the body	26 (4.1%)
Fibromyalgia	74 (11.8%)
Other	87 (13.8%)
Missing	6 (1.0%)
Pain Disability Index: mean (SD)	34.8 (13.1)
Beck's Depression Inventory: mean (SD)	19.33 (9.8)
Checklist Individual Strength: mean (SD)	96.7 (20.8)
Tampa Scale for Kinesiophobia: mean (SD)	39.7 (7.8)

SD: standard deviation

Patient characteristics

Table 1 shows patients characteristics at baseline. The populations' mean age was 44.2 years and 73.2% is female. Most of the population was married or living together (61.3%) and were salary employed (65.8%). The majority experienced chronic musculoskeletal pain at 2-5

locations (30.4%), follow up by patients who just experienced pain in the back (27.2%). 11.8% of the population was diagnosed with fibromyalgia.

Admission characteristics

The mean PDI score of the population was 34.8 points (moderate disability), the mean BDI score was 19.3 points (between light and moderate depression), the mean CIS score was 96.7 points (problematic fatigue in 85.7% of the population) and the mean TSK score was 39.7 points (kinesiophobia in 72.9% of the population). At admission patients were stratified in the different treatment programs Active, Active+Perspective and Intensive. No significant differences for PDI, BDI, CIS and TSK were found between the patient groups in these three treatment programs.

Table 2: Discharge and follow-up values[!] of level of disability assessed with the pain disability index in patients with chronic musculoskeletal pain taking part in an interdisciplinary treatment program[‡]

	Discharge (n=484) Mean (SE)	3-months follow-up (n=26) Mean (SE)	6-months follow-up (n=35) Mean (SE)
Pain Disability Index estimate	**27.7** (2.0) (p=0.001)	**13.0** (2.1) (p=0.008)	12.5 (4.3) (p=0.995)

[!]Mean estimates for the various time points were calculated using a linear mixed model analysis procedure. Time was set as a fixed effect and repeated covariance type was set at heterogenous Toeplitz.
[‡]Bold figures indicate a statistically difference, p<0.05 between admission and discharge, 3-months and 6-months follow up
SE: standard error

Level of disability

Table 2 shows a significant improvement in level of disability in patients with CMP between admission and discharge (p=0.001) and a significant improvement in level of disability in patients with CMP between admission and three months follow-up (p=0.008) when a linear mixed model analysis was performed with time a as a fixed effect and heterogenous Toeplitz repeated covariance type. There was no significant improvement in level of disability found between admission and six months follow-up (p=0.995). Because of loss to follow up it was not possible to analyze the change between admission and 12-months follow-up.

Table 3: Responder rate[!] of patients with chronic musculoskeletal pain on level of disability assessed with the pain disability index taking part in an interdisciplinary treatment program

	Admission Median (range)	Discharge Median (range)	Change in score Mean (95% CI)	Responder rate
Pain Disability Index (1-27)	20.0 (1-27) (n=175)	11.0 (0-55) (n=136)	-3.91 (-6.48--1.35) (n=136)	51.5%
Pain Disability Index (28-42)	35 (28-42) (n=274)	18.5 (0-64) (n=214)	-15.40 (-17.35--13.45) (n=214)	52.8%
Pain Disability Index (43-70)	49 (43-66) (n=179)	27 (0-67) (n=134)	-24.65 (-28.08--21.22) (n=134)	53.7%

[!]Responder rate: proportion patients with delta score between admission and discharge that reached or exceeded the threshold values of the pain disability index (PDI). The threshold value of the PDI in patients with chronic musculoskeletal pan at baseline PDI score ≤27 is 7 points, in patients with PDI score 28-42 is ≥15 points, and in patients with PDI score ≥43 is ≥20 points.
CI: confidence interval

Responder analysis

Table 3 shows that the proportion of patients with CMP achieving minimally clinical important change between admission and discharge were respectively 51.5%, 52.8% and 53.7% for the different subgroups of PDI at baseline.

Contributing factor

Fear-avoidance was found as a significantly contributing factor (beta=0.224, p=0.016) for the PDI change score in patients with CMP between admission and discharge.

DISCUSSION

The present observational study showed statistically significant improvement on level of disability in patients with CMP between admission and discharge of an interdisciplinary treatment program. The significant improvement was maintained after three months follow-up. These findings are in line with the observational study of Koele et al. (2014)(9). Although the baseline value of level of disability of the population in the present study is lower than in the population of the study of Koele et al. (2014), almost the exact same discharge value is reached(9). Also, the findings at three months follow-up are in line with the longitudinal study of Volker et al. (2017)(30). A significant improvement on level of disability was maintained after three months follow-up(30). The populations of both studies and the present study were comparable in age but differ in other sociodemographic characteristics such as percentage women, percentage of patients with paid job and location of symptoms of the patients. Other sociodemographic characteristics were not comparable because at the time they were not monitored in the database of the present study. Also, there is a minor difference in received intervention. In contrast with the present study, the interdisciplinary treatment of both Koele et al. and Volker et al. included hydrotherapy.

The responder analysis showed that respectively 51.5%, 52.8% and 53.7% of the patients with CMP clinically benefit from interdisciplinary treatment. This is useful information because it shows the proportion of patients who clinically improve with an outcome measure that has different MCIC cut-off points for different values at baseline(38). To our knowledge no other studies did a responder analysis, therefore, no comparison of the results could be made. The MCIC cut-off points of the PDI used in the present study were computed by Beemster et al. (2018)(38). A point of discussion is that Beemster et al. (2018) used the Global Perceived Effect (GPE)(38) as external validation pain anchor to calculate the different cut-off scores for the PDI, which has a different construct than the PDI(36). In absence of a golden standard as external validation for the PDI this is considered a minor limitation. The population on which MCIC cut-off points of the PDI were calculated and population of the present study were comparable.

Fear-avoidance was found as a limiting contributing factor for the outcome on level of disability between admission and discharge of an interdisciplinary treatment program. Fear-avoidance is a risk factor for CMP (10-13) and is associated with inactivity and eventually disability(42). Subsequently it affects the outcome of interdisciplinary treatment. This is contradicting the study of De Rooij et al. (2013)(28) and Lüning et al (2012)(43) who expected fear-avoidance did

not predict treatment outcome(28, 43). However, because loss to follow-up in the present study exceeds 20% there is a risk of overestimating the PDI change score(44), for that reason caution is required.

The present study had several other limitations. No comparison could be made with the long-term outcome at six months and 12 months follow-up on level of disability in patients with CMP between the present study and studies of Volker et al. (2017) and Brendbekken et al. (2016)(30, 45). No significant improvement was found at six months follow-up and no data was available at 12-months follow-up due to complete loss to follow-up. Reason for loss to follow-up is the lack of systematic checking the patient files for missing questionnaires. Patients files were checked manually, and patients were reminded by e-mail to complete the questionnaires where needed. As a result, patients were reminded too late and response was very low.

Another limitation is the set-up of the PDI questionnaire in Asterisque. When completing the PDI questionnaire patients were unable to go back to the previous question and that item was automatically scored zero. This resulted in unintended lower scores with patients who pressed "next question" too soon. Both CIS and TSK did not have this problem. In consensus meetings we agreed to exclude all patients who scored zero at admission on the CIS, TSK and PDI. An affiliated researcher manually checked the medical records of patients who did score zero at PDI but did not score zero on the CIS and TSK. These cases were finally included in the analysis. However, it is likely there were unintended lower PDI sum scores included in the analysis as well, leading to information bias. Depending if the error was made at admission, discharge or follow-up, there was an under- or overestimation of the outcome measure.

One more limitation of the current study is the missing of baseline outcome measures that can possibly act as contributing factors on the outcome of interdisciplinary treatment. Frequently used outcome measures as the Hospital Anxiety Depression Scale, Short Form Survey 36, Numeric Rating Scale, length of pain complaints and educational level(28, 46, 47) were not measured at admission of the present study, and therefore missing in the dataset.

A weakness of the present study is the observational design, there was no control group for comparison. Other factors besides interdisciplinary treatment could affect the outcome measure and were not controlled for. This could lead to overestimating the effect of interdisciplinary treatment on level of disability. Furthermore, there were selection criteria for admission. Patients with too light or too heavy diagnoses were excluded for the interdisciplinary treatment program. Also, the rehabilitation center depends on referrals from general practitioners or medical specialists. Chances are that eligible patients were missed because they were not referred or were referred too late limiting the chance of greater improvement on level of disability.

In conclusion, the outcome of interdisciplinary treatment on level of disability in patients with CMP is promising. The level of disability decreased after interdisciplinary treatment and were lasting at least at three months follow-up. The responder rate of the present study can function as comparative outcome for further research. Also, because of conflicting evidence further research of the influence of fear-avoidance on interdisciplinary treatment on level of disability is recommended. Finally, referring patients with CMP in an earlier disease stage to

interdisciplinary treatment can have a beneficial effect on the outcome on level of disability. More research is recommended to assess the effectivity of matched-care referral policy in patients with CMP.

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CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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