Analgesic reduction during an interdisciplinary pain management programme: treatment effects and processes of change

British Journal of Pain
2018, Vol 12(2) 72–86
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DOI: 10.1177/2049463717734016
journals.sagepub.com/home/bjp

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Abstract

Long-term use of opioid medication is associated with a host of negative effects on health and quality of life. Guidelines state that people with chronic pain taking high doses of opioids without benefit should be supported to discontinue them. Little research has investigated psychological processes associated with analgesic use and tapering. This study investigated (1) analgesic use pre- and post-participation in an interdisciplinary pain management programme and its relationship to functioning and (2) psychological processes associated with analgesic use. Opioid use was associated with poorer functioning at baseline. Participating in an interdisciplinary pain management programme was associated with reductions in opioid dose and number of classes of analgesics used. Reductions in analgesic use were associated with improvements in functioning. Psychological inflexibility was associated with using higher doses of opioid medication and with using a greater number of classes of analgesics. Psychological flexibility appears relevant in explaining analgesic use. Future research could focus on targeting this process to improve tapering outcomes.

Keywords

Chronic pain, opioid, opiate, pain management programme, analgesic reduction, analgesic taper, medication reduction, medication taper

Introduction

Chronic pain is common, affecting about one out of five people in the United Kingdom.¹ A proportion of people with chronic pain derive limited benefit from medical treatments aiming to reduce pain, and treatments aiming specifically to improve functioning and quality of life (such as exercise and cognitive behavioural therapy (CBT)) are recommended.² Current National Institute for Health and Care Excellence (NICE) guidelines² state opioids should not be offered for chronic low back pain, for example, especially not in the long term. The Royal College of Anaesthetists and British Pain Society (BPS) identify a risk of harm associated with sustained doses above the equivalent of 120mg total oral morphine equivalent dose (TOME) per 24 hours³ (TOME is also termed daily morphine equivalent dose (MED) and morphine milligrams equivalent (MME)). If a patient

with chronic pain is taking high doses of opioids and is not experiencing benefits, it is typically recommended that the opioids should be discontinued.³

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There has been a sizeable increase in the use of opioids for chronic pain in the United Kingdom⁴⁻⁶ and other countries, such as the United States.⁷ Zin et al.'s⁶ large UK cross-sectional study between 2000 and 2010 showed the majority (87.8%, $n=2,347,282$) of strong opioid prescriptions were for non-cancer pain. Continuation rates of opioid prescribing for chronic pain are high; over half of people prescribed 90 days of opioid therapy, excluding cancer pain/palliative care, over a 6-month period remain on opioids 5 years later.^{8,9} This is concerning given the mounting evidence that opioids are associated with a host of negative health outcomes when taken for long periods of time for chronic pain. Long-term opioid use for chronic pain has been associated with hyperalgesia.^{10,11} Higher doses are associated with poorer outcomes.¹²⁻¹⁵ These include increased risk of fractures,¹⁶ myocardial infarction,¹⁷ androgen deficiency/hypogonadism,¹⁸ abuse,^{12,13,19,20} addiction,^{21,22} overdose²³ and narcotic bowel syndrome.²⁴ Unsurprisingly, there is an associated economic cost. In Hong et al.'s²⁵ retrospective cohort study of UK data, estimates of the 12-month costs associated with the treatment of chronic low back pain were at least double those of the matched controls without this diagnosis, representing a cost of £1.5 to £2.8 billion nationally. Most of the cost was associated with general practitioner (GP) consultation time, but 19% was accounted for by analgesics alone.²⁵ The NHS spend on opioids in the community in England in 2016 was £292 million.²⁶ Opioids for chronic pain are also associated with taking additional medications to prevent or minimise side effects, more frequent healthcare visits and increased and more costly lengths of stay in hospital.^{3,25} There are of course also significant indirect costs associated with impaired physical, psychological, social and work functioning.³

There are available interventions specifically to help people with chronic pain taper opioids.²⁷⁻³⁰ However, evidence for these is unclear so far and a significant proportion of patients do not complete them successfully; drop-out rates of between 34% and 100% are reported.²⁷ Several factors may interfere with successful tapering in people with chronic pain who are taking opioids. These include mental health problems, poor or avoidant coping styles and factors associated with risk of substance use.^{9,14,31-34} Frank et al.'s³⁵ qualitative study identified barriers to tapering including fear of opioid withdrawal and pessimism about the availability of alternatives to opioids. McCracken et al.'s³⁶ survey of 220 patients with chronic pain showed over 80% endorsed the statement 'without medication my pain would be unbearable'. Of course, prescriber factors are relevant too.⁵ McCracken et al.³⁷ found over 55% of GPs surveyed felt they had no alternatives than prescribing opioids for chronic pain.

Interdisciplinary pain management programmes (PMPs) based on cognitive behavioural principles are 'the treatment of choice for people with persistent pain which adversely affects their quality of life'³⁸ (p. 8) and there is good evidence for their efficacy.^{39,40} Such programmes usually include input from a nurse specialising in chronic pain, and sometimes information sessions from a consultant in pain medicine. Over the last 20 years, several (mostly uncontrolled) studies have indicated that participation on a PMP is associated with reduced healthcare consumption, including analgesic use.⁴¹⁻⁴⁵ However, a recent meta-analysis⁴⁶ of randomised controlled trials of psychological interventions for chronic pain did not find a significant effect for analgesic reduction (although it did find a significant reduction in other types of healthcare use). The authors urge cautious interpretation of this negative finding due to concerns about data quality and trial methodology and call for more study of this important outcome domain.⁴⁶ Few studies have specifically examined which factors are associated with successful and unsuccessful opioid reduction and the specific processes that determine success. Of the seven RCTs identified by Pike⁴⁶ that included changes in analgesic use as an outcome measure, only one⁴¹ investigated the association between demographic variables and treatment gains (it did not find any significant associations) and none specifically investigated psychological factors as mediators of change.

Current developments in PMPs include the psychological flexibility (PF)⁴⁷ model (the model underlying Acceptance and Commitment Therapy (ACT)^{48,49}). PF can be defined as openness to experiencing pain and unwanted feelings, present-moment awareness and values-oriented behaviour.⁴⁷ Psychological *in*-flexibility, on the other hand, is the opposite with respect to these qualities. It is reflected in behaviour that is guided by the urge to avoid unpleasant sensations, thoughts and emotions. The PF model is highly relevant to opioid reduction from a theoretical perspective and, because it clearly specifies relevant processes and mechanisms of change, the model offers a promising avenue for further refinement of treatment methods designed to help patients taper their analgesics.

Long-term opioid use for chronic pain can be conceptualised as an understandable attempt to avoid pain and, when continued use is proving ineffective and is associated with interference in health and functioning, as a behaviour pattern that is a reflection of psychological inflexibility. Prospective data suggest that greater PF, including the component of openness to experiencing pain, is associated with less analgesic medication use.⁵⁰ Participation on a PMP based on the PF model has been associated with reductions in analgesic use.⁵¹ Outside of chronic pain, this treatment approach has been used

successfully to promote behavioural change in smoking cessation and alcohol and substance use.^{52–58}

In summary, long-term opioid use for chronic pain continues to be a significant and costly problem in the United Kingdom and elsewhere. There is little research on processes that may be relevant to facilitating tapering of analgesics, including opioids, in chronic pain. Methods based on the PF model that have been demonstrated to be effective in chronic pain are considered likely to facilitate opioid reduction by precisely targeting the same relevant underlying processes and appear well designed to target the complexities that make tapering a challenge. Preliminary evidence in chronic pain and evidence from related fields support this.

The aim of this study is to investigate clinical outcomes and therapeutic processes of change in relation changes in analgesic use in the context of an interdisciplinary PMP based on ACT. More specifically, we aim to examine (1) differences on health-related variables between people who do and people who do not take opioid medication for chronic pain, (2) analgesic use pre- and post-treatment and its relationship to functioning and (3) psychological processes associated with analgesic use at baseline and with changes in analgesic use.

Method

Participants

Participants were recruited from 452 people with chronic pain referred to a speciality pain service in central London. All had been assessed by a psychologist and physiotherapist and deemed suitable to attend a 4-week, residential, interdisciplinary, group-based PMP between August 2014 and April 2016. Approximately 55% of patients assessed by the service are offered a PMP, preparation for a programme (with the majority going on to begin a programme) or individual sessions within the service. The assessment included recording current medications to establish whether medicines were being taken as prescribed and that patients were able to self-administer them. When necessary, clinical nurse specialists provided advice to the assessing psychologist and physiotherapist (such as calculating approximate TOME dose/24 hours). Inclusion criteria to attend the PMP included pain duration of more than 6 months, presence of significant disability or distress from pain, and no plan for surgical or medical treatments that might impact the patient's participation on the PMP. Exclusion criteria included the use of injectable analgesia, use of oral liquid opioids (as quantity taken had previously been found to be difficult to assess accurately) and use of high doses of opioids (above 300 mg approximate TOME/24 hours). If appropriate, patients who either met these exclusion criteria or whose

Table 1. Demographic characteristics of the sample.

	<i>n</i> (%) or mean (<i>SD</i>)
Age (years)	Mean = 46.3 (12.5)
Years education	Mean = 13.5 (4.2)
Gender	
Male	128 (29.4)
Female	307 (70.6)
Ethnicity	
White	334 (76.8)
Black	45 (10.3)
Asian	21 (4.8)
Mixed	19 (4.4)
Latin/Hispanic	12 (2.8)
Other	1 (0.2)
Missing	3 (0.7)
Living status	
With a partner and child(ren)	123 (28.3)
Alone	108 (24.8)
With partner	101 (23.2)
With child(ren)	60 (13.8)
With other relatives	35 (8)
With friend(s)/flatmate(s)	8 (1.8)
Employment status	
Unemployed	234 (53.8)
Employed	117 (26.9)
Retired	49 (11.3)
Homemaker	25 (5.7)
Student	7 (1.6)
Carer	1 (0.2)
Missing	2 (0.5)

SD: standard deviation.

medication use was associated with side effects (e.g. drowsiness) that were likely to affect their ability to engage with the programme were offered the opportunity to work with a clinical nurse specialist prior to attending the programme. This might include, for example, transferring from liquid morphine to tablet form, or reducing their TOME/24 hours dose prior to attending.

Participants ranged in age from 18 to 87 years old (mean = 46.3 years, *SD* = 12.47), and the majority of participants defined their ethnicity as White (76.8%) and were unemployed because of pain (53.8%). In total, 28.3% lived with their partner and child/children. The mean number of years of education was 13.49 (*SD* = 4.18) (see Table 1 for further details). In total, 178 (40.9%) participants reported their primary pain as lower back, and the median pain duration was 104 months (range: 4–703 months). The mean number of analgesic classes taken was 3.8 (*SD* = 1.6), and the mean approximate TOME/24 hours dose was 65 mg (*SD* = 97.7; median = 25 mg, interquartile range = 94.5 mg). In all, 297 (68.3%) of the sample were taking opioid medication (see Table 2 for further details).

Table 2. Pain characteristics and medications used.

	<i>n</i> (%) or median/ mean (range/ <i>SD</i>)
Pain duration (months)	Median = 104 (4–703) ^a
Pain location	
Lower back	178 (40.9)
Generalised	156 (35.9)
Lower limbs	43 (9.9)
Upper shoulder or upper limbs	18 (4.1)
Neck region	10 (2.3)
Head, face or mouth	9 (2.1)
Abdominal region	8 (1.8)
Pelvic region	6 (1.4)
Chest region	3 (0.7)
Anal or genital region	2 (0.5)
Missing	2 (0.5)
Medication	
Total classes of medication	Mean = 3.8 (1.6)
Approximate total oral morphine equivalent dose per 24 hours (mg)	Mean = 64.6 (97.7) Median = 25 Interquartile range = 94.5
Immediate-release opioids	248 (57)
Modified-release opioids	143 (32.9)
Anticonvulsants	193 (44.4)
Tricyclic anti-depressants	133 (30.6)
Non-steroidal anti-inflammatories	206 (47.4)
Paracetamol	259 (59.5)
Selective serotonin reuptake inhibitors/serotonin noradrenalin reuptake inhibitors	147 (33.8)
Hypnotics	38 (8.7)
Anxiolytics/muscle relaxants	81 (18.6)

SD: standard deviation.

^aPain duration showed a large dispersion and is thus reported in terms of the median and range.

Procedure

Appropriate ethics and research and developmental committee approval was obtained prior to the study (North East Research Ethics Committee – South Central, REC reference 12/SC/0451). Written consent was given by the patients for their data to be used for research. Of the 452 patients commencing treatment during the time frame of the study, a total of 435 patients consented to have their information used for research purposes.

As part of standard clinical procedure, participants completed a set of self-report questionnaires including demographic questions (Table 1) and questions about their pain and medication use (Table 2), plus treatment-relevant process and outcome measures (further detailed below). These were completed on the first and

last day of treatment, taking the majority of participants between 20 and 60 minutes to complete. The questionnaires were checked at the time of completion to ensure minimal missing data. Physical performance measures were also obtained at these time points.

On the first day and penultimate day of treatment, every participant met with the clinical nurse specialist individually. In this consultation, detailed lists of all the participants' current medications were recorded, including over-the-counter and herbal/alternative medications. The participants were asked specific questions about their analgesics, including dose, route, length of use, efficacy and presence of side effects. In most cases, participants' recollections of their medications were checked against the most recent medicines information from a GP summary, hospital discharge letter or community NHS care record. Occasionally, it was deemed appropriate to check against available packaging information, where the participant's full name, date and dose were clearly documented.

Outcome measures

Medication use. Local guidelines (see Appendix 1) were used to calculate approximate total oral morphine equivalent doses in 24 hours, recording separately an approximate oral immediate-release dose, modified-release dose and TOME. The local guidelines used to calculate these doses are in line with the approximate guides provided by the British National Formulary (BNF) and the resource Opioids Aware³ produced by the Faculty of Pain Medicine. The remaining analgesics were categorised by class, as per local guidelines in line with the BNF classification of medications. The categories are anticonvulsant; tricyclic anti-depressants; non-steroidal anti-inflammatories, paracetamol, selective serotonin reuptake inhibitors/serotonin noradrenalin reuptake inhibitors; hypnotics; anxiolytics/muscle relaxants; and other.

Pain intensity. Participants rated their pain intensity on average over the last week on a standard numeric rating scale from 0 (no pain) to 10 (extremely intense pain).

Pain interference. The Brief Pain Inventory – Interference Scale (BPI-IS)⁵⁹ is a seven-item self-report measure of pain interference with seven domains of daily activity that include general activity, mood, walking ability, normal work, relations with others, sleep and enjoyment of life. Participants report how much pain interfered with functioning over the past week on a scale of 0 (does not interfere) to 10 (completely interferes). Higher scores indicate greater interference of pain. The BPI-IS has been well validated among patients with chronic pain.⁶⁰

Functioning. The Work and Social Adjustment Scale (WSAS)⁶¹ is a five-item self-report measure assessing specific domains of functional impairment. Patients report how much their current condition impairs their ability to work, manage household activities, engage in social leisure activities, private leisure activities, and relationships with others on a scale of 0 (no impairment) to 8 (severe impairment). Higher total scores indicate greater functional impairment. The WSAS has been validated and is widely used in research in chronic health conditions.⁶¹

Depression. The Patient Health Questionnaire (PHQ-9)⁶² is a measure of depression based on standard *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; DSM-IV) criteria. It includes nine items, measuring symptom frequency over the last 2 weeks on a scale of 0 (not at all) to 3 (nearly every day). Higher total scores indicate greater symptom severity. The PHQ-9 has been well validated among patients with chronic health conditions.⁶² Emotional functioning is a core outcome domain recommended by consensus guidelines.⁶³

Insomnia. The seven-item Insomnia Severity Index (ISI)⁶⁴ is a screening measure of insomnia severity. Considering the last 2 weeks, participants are asked to rate the severity of difficulties falling asleep, staying asleep, sleep quality and its impact on daily functioning, as well as their concerns on a scale of 0 (not at all) to 4 (extremely). The summed items produce a total score, with more severe sleep problems indicated by higher scores. Total scores are categorised as not clinically significant (0–7), sub threshold (8–14), moderate insomnia (15–21) and severe insomnia (22–28).⁶⁵ The ISI has been validated and shows good internal consistency in clinical samples⁶⁴ and in this sample (Cronbach's $\alpha = 0.86$).

Physical performance measures

Participants were invited to complete three performance-based measures of physical functioning: 5-minute walk, 1 minute sit-to-stand and 1-minute stair climb.⁶⁶ The three measures have been validated among patients with chronic health conditions^{66,67} and have been used in outcome studies of interdisciplinary treatment programmes for chronic pain.^{52,68–71} For the sake of brevity, only the 5-minute walk is reported on in this study. The 5-minute walk is a timed test of the number of metres a participant walks within 5 minutes up and down an empty 20-m-long corridor, with distance markers placed along the floor. Assessors were trained in standardised test administration and to give neutral responses with no encouragement or advice during testing. Participants were asked to perform the walk test without walking aids, such as crutches or sticks, if they

were willing to do so. They were given permission to use the walls for support or to sit down as needed. Any stops against the wall or chair were recorded. Patients were informed of the time elapsed on each lap or at each minute if laps were very slow. This was not qualitative feedback but was intended to reflect real-life situations where patients may be likely to refer to time to determine their capacity to carry out activities.

Treatment-relevant process measures

The following measures capture different facets of the PF model.

Acceptance. General psychological acceptance was measured using the seven-item measure, the Acceptance and Action Questionnaire (AAQ-II).⁷² This concept encompasses a willingness to experience difficult feelings and emotions, particularly when doing so enables one to pursue meaningful activities. Items are rated on a 7-point scale from 1 (never true) to 7 (always true). In this study, higher scores reflect lower acceptance. Previous research has shown good internal consistency, temporal stability and construct validity of the AAQ-II, including among patients with chronic pain.^{72,73} The AAQ showed excellent internal consistency in this sample (Cronbach's $\alpha = 0.9$).

Pain acceptance. Acceptance of chronic pain was measured using the eight-item Chronic Pain Acceptance Questionnaire (CPAQ-8).^{74,75} This reflects degrees of engaging in normal daily activities with pain and refraining from ineffective avoidance or control strategies. Items are rated on a scale of 0 (never true) to 6 (always true) and higher total scores indicate greater acceptance of pain. The CPAQ-8 has been validated and shown to have good reliability in people with chronic pain.⁷⁴ The CPAQ-8 showed acceptable internal consistency in this sample (Cronbach's $\alpha = 0.7$).

Cognitive fusion. Cognitive fusion, the failure to experience distinctions between the content of thoughts and direct experience, was measured using the self-report seven-item measure, the Cognitive Fusion Questionnaire (CFQ-7).⁷⁶ Cognitive defusion in contrast, is similar to mindfulness processes in which participants see their thoughts as transient events which may or may not reflect reality, with the aim of reducing their impact. Participants are asked to rate how true a list of statements are for them using a scale of 1 (never true) to 7 (always true). When summed, higher total scores indicate greater cognitive fusion. The CFQ-7 has previously been validated among people with chronic pain⁷⁷ and demonstrated excellent internal consistency in this sample (Cronbach's $\alpha = 0.95$).

Decentering. A total of 12 items of the Experiences Questionnaire (EQ)^{78,79} were used to assess decentering. This reflects one's ability to observe thoughts and feelings as temporary, objective events in the mind and not necessarily true reflections of oneself or one's circumstances. Each statement is rated on a scale of 1 (never) to 5 (always). Higher total scores suggest greater decentering. The EQ has been validated among people with chronic pain.⁷⁹ The decentering scale showed good internal consistency in this sample (Cronbach's $\alpha = 0.9$).

Committed action. The Committed Action Questionnaire (CAQ-8)^{80,81} was used to measure persistence in flexible goal-oriented behaviour. The measure consists of eight items and asks participants to rate how true a list of statements are for them, using a scale of 0 (never true) to 6 (always true). The item pool consists of four positively and four negatively phrased items. Negatively phrased items are reverse scored before the total score is calculated, with higher scores indicating greater committed action. The reliability and validity of the CAQ is supported by previous research in a chronic pain population^{80,81} and this good internal consistency was evident in this sample (Cronbach's $\alpha = 0.8$).

Patient impression of change

In addition, at the end of treatment, patients were asked to rate their impression of change overall and in the specific areas of physical and social functioning, work-related activities (including household work), mood and pain using a scale of 1 (very much improved) to 7 (very much worse).⁸² Patient impression of change is recommended as an outcome measure by consensus guidelines.⁶³ The factor structure and performance of this instrument has been examined in people with chronic pain upon completion of an interdisciplinary PMP, supporting its use.⁸² The following question was also included for the purposes of this study and it is the sole one of the questions analysed here: 'Compared to the start of treatment, on average, has your pain medication use: decreased, stayed the same, increased'.

Description of treatment

The PMP was delivered in a residential, interdisciplinary rehabilitation context by a team of psychologists, physiotherapists, occupational therapists, nurses and physicians. Treatment was provided in groups over four full days per week for 4 weeks. An ACT^{48,49} approach was used. This approach seeks to develop processes and skills relating to PF:⁴⁷ openness to experiencing pain and unwanted feelings, present-moment awareness and values-oriented behaviour.

Pain reduction was not an explicit focus of treatment. Consistent with BPS guidelines, treatment included (1) education sessions about medication to facilitate an informed choice about whether to reduce it; (2) individualised medication review, rationalisation and reduction under the guidance of the clinical nurse specialist; (3) the application of PF for overall improvement of daily functioning and to the goal of medication reduction (e.g. making choices that are based on awareness and values, not habits and thoughts); and (4) liaison with the patient's GP and other agencies as appropriate. The PMP operates on an assumption of trust and negotiation of any medication reduction in a supportive environment. Individual reduction plans are developed in liaison with the patient, frequency of individual reviews are agreed and if required a written plan is provided. The clinical nurse specialist ensures that the multidisciplinary team are aware of the reduction plans at team meetings and the patients are monitored by the whole team, ensuring that the reduction process has minimal impact on patients' engagement in the programme and to highlight when additional individual reviews are required. The clinical nurse specialist explains to the patient that they are in control of the reduction rate, with the aim to minimise the risk of withdrawal symptoms. Occasionally, patients are unable to tolerate the reduction process while attending the programme. In these cases, the clinical nurse specialist liaises with the GP and the individual support is provided following the programme.

Statistical analyses

Data analyses were conducted using SPSS version 22. Normality was assessed through examination of skewness and kurtosis values (between -2 and $+2$), and inspection of histograms and normal q-q plots. Independent-samples *t*-tests and chi-square tests were computed to compare participants who provided data at post-treatment with those who did not. For the pre- to post-treatment analyses, all of the paired differences were considered to be normally distributed except for TOME. Log natural transformation was used to address non-normality. Independent-samples *t*-tests were used to compare people who did and people who did not take opioid medication on the study outcome and process variables. Means and standard deviations were computed for pre- and post-treatment scores and paired sample *t*-tests were then computed to determine the statistical significance of changes from pre- to post-treatment. The Bonferroni correction was used to adjust for multiple comparisons ($p < 0.004$). Within-subjects effect sizes (Cohen's *d*) were computed as the difference between pre- and post-treatment means divided by the pooled standard deviation.

Effect sizes were interpreted, according to Cohen's⁸³ guidelines, as small (>0.20), medium (>0.50) or large (>0.80). Participants making clinically significant changes in their analgesic use were defined as those whose raw change scores were greater than one half of a pooled standard deviation from their baseline score. A systematic review has shown that, across a number of chronic conditions, one half of a standard deviation reliably discriminates people who achieve a minimally important difference following treatment.⁸⁴

Pearson correlations were computed to examine the associations between the number of classes of medication at pre-treatment and demographic, pain, outcome and process variables, as well as changes in these variables (using standardised change scores). Scatter plots for all variable pairs from the correlation analyses were examined for linearity. None of the variable pairs were considered to have significant non-linear associations. Independent-samples *t*-tests were performed to examine differences in medication use between genders, and there were no significant differences on either medication variable.

A series of hierarchical multiple linear regression were computed, first using pre-treatment scores and then residualised change scores, to examine the shared and unique contributions of the medication variables to measures of functioning. Pain intensity was controlled for in the first step of each analysis, followed by the medication variables in the final step of the regression equation. Only medication variables that were significantly correlated with the functioning variables in zero-order correlations were entered, simultaneously, into the equations as potential independent variables.

Pairwise deletion was used to address missing values on study variables.

Results

Preliminary analyses

In total, 35 people (8%) did not provide post-treatment data because they dropped out of treatment. A further 61 (14%) did not provide post-treatment data but did not drop-out of treatment (e.g. they may have missed the session in which post-treatment measures were taken). Participants who provided data at post-treatment were compared with those who did not in terms of age, years of education, duration of pain, pain intensity during the last week, TOME and number of classes of medication, as well as all other outcomes and all process variables. Those providing data at post-treatment had completed significantly more years of education $t(428) = 3.690, p < 0.001$. No significant differences were found on any of the other variables, including gender (chi-square test >0.05).

Compared to those not taking opioid medication at pre-treatment, those taking opioid medication scored higher for depression ($t(373) = 2.881, p < 0.01$), pain-related interference ($t(375) = 2.787, p < 0.01$) and sleep problems ($t(374) = 3.403, p < 0.01$). They walked less far ($t(374) = -2.635, p < 0.01$) and scored lower on pain acceptance ($t(372) = -2.446, p < 0.05$). The groups did not significantly differ on the other variables, including on average pain intensity over the last week.

Treatment effects

Mean values and standard deviations for all outcome and process measures at pre- and post-treatment are presented in Table 3. Paired-samples *t*-tests and effect sizes were calculated to analyse the difference between pre- and post-treatment data for all measures (see Table 3). Statistically significant reductions were observed for all treatment outcomes and process measures including the variables of primary interest: log-TOME $t(363) = 9.391, p < 0.004$; total number of classes of medication $t(362) = 11.619, p < 0.004$. Immediate-release opioids, non-steroidal anti-inflammatories and paracetamol were the three classes of medication most frequently dropped during treatment, both in terms of raw numbers and when analysed by proportion of participants taking them at pre- and post-treatment.

Large effect sizes were observed for depression and pain interference. Medium effect sizes were observed for average pain intensity, functioning (as measured by the WSAS), walking, pain acceptance and committed action. Small effect sizes were observed for TOME, number of classes of medication, insomnia, acceptance and decentering. The average effect size was 0.55 and ranged from 0.17 for cognitive fusion to 1.11 for pain interference.

Clinical significance of treatment changes and patient impression of change

The number of patients experiencing clinically significant reductions or increases in medication use is presented in Table 4. In total, 12.4% made a clinically significant reduction in their TOME dose and 34.5% made a clinically significant reduction in the number of classes of medication they used.

At the start of treatment, 71 people (16.3%) were taking doses of 120mg/24hours TOME or greater, compared to 42 (9.7%) at the end of treatment. This was a significant reduction (McNemar Test $p < 0.001$). Of those taking doses of 120mg/24hours TOME or greater at the start of treatment, 52.3% made a clinically significant reduction in TOME and 47.7% made

Table 3. Means (standard deviations) at pre- and post-treatment, *t*-tests and effect sizes (*n*=435).

	Pre-treatment, mean (SD)	Post-treatment, mean (SD)	<i>t</i> -tests	Cohen's <i>d</i>
Log-TOME/24 hours	1.27 (0.83)	1.05 (0.85)	<i>t</i> (363)=9.391**	0.26
TOME/24 hours	64.58 (97.71)	44.04 (67.61)	<i>t</i> (363)=6.969**	0.24
Classes of medication	3.82 (1.64)	3.20 (1.75)	<i>t</i> (362)=11.619**	0.37
Average pain intensity	7.77 (1.59)	6.65 (1.68)	<i>t</i> (374)=12.718**	0.68
PHQ-9	17.33 (5.69)	11.99 (5.77)	<i>t</i> (365)=18.323**	0.93
BPI-IS	7.79 (1.44)	5.87 (1.99)	<i>t</i> (368)=18.855**	1.11
WSAS	32.35 (6.06)	27.75 (8.24)	<i>t</i> (368)=11.925**	0.64
ISI	20.08 (5.63)	17.65 (6.59)	<i>t</i> (369)=8.373**	0.40
5-minute walk	180.99 (108.96)	236.22 (108.31)	<i>t</i> (307)=-12.910**	-0.51
AAQ	31.94 (10.82)	28.89 (9.86)	<i>t</i> (369)=6.869**	0.29
CFQ	30.22 (11.50)	28.39 (10.54)	<i>t</i> (366)=3.864**	0.17
EQ	35.13 (8.38)	39.13 (7.98)	<i>t</i> (357)=-8.601**	-0.49
CPAQ	17.34 (7.25)	23.19 (7.64)	<i>t</i> (366)=-14.094**	-0.79
CAQ	26.02 (8.45)	27.51 (7.37)	<i>t</i> (368)=-3.717**	-0.57

SD: standard deviation; TOME: total oral morphine equivalent; PHQ: Patient Health Questionnaire; BPI-IS: Brief Pain Inventory-Interference Scale; WSAS: Work and Social Adjustment Scale; ISI: Insomnia Severity Index; AAQ: Acceptance and Action Questionnaire; CFQ: Cognitive Fusion Questionnaire; EQ: Experiences Questionnaire; CPAQ: Chronic Pain Acceptance Questionnaire; CAQ: Committed Action Questionnaire.

***p*<0.004 (Bonferroni adjustment).

Table 4. Clinical significance^a of changes in medication use pre- to post-treatment (*n*=435).

	<i>N</i> (%)			
	Significantly worse	No significant change	Significantly improved ^b	Missing
TOME/24 hours	3 (0.7)	307 (70.6)	54 (12.4)	71 (16.3)
Classes of medication	11 (2.5)	202 (46.4)	150 (34.5)	72 (16.6)

TOME: total oral morphine equivalent.

^aSee section 'Statistical analyses' for definition of clinical significance used here.

^bAmong those taking 120mg/24 hours or greater TOME at baseline, 52.3% made a clinically significant reduction in TOME and 47.7% made a clinically significant reduction in number of classes of medication used. None made clinically significant increases.

a clinically significant reduction in number of classes of medication used.

The following were the participants' responses to the question 'Compared to the start of treatment, on average, has your pain medication use ...': reduced (41.6%), stayed the same (36.8%), increased (8%) and missing (13.6%).

Pre-treatment correlations between demographic factors and outcome variables, and medication use

At pre-treatment, there were no significant correlations between medication use and age, education, pain duration or average pain intensity. Number of classes of medication and log-TOME were significantly correlated with the following measures of functioning, in the expected directions: PHQ-9, BPI-IS, 5-minute walk and ISI (see Table 5). In addition, log-TOME was significantly correlated with the WSAS.

Pre-treatment correlations between process variables and medication use

Number of classes of medication was significantly correlated with all measures of PF (as measured by the AAQ, CFQ, EQ, CPAQ and CAQ), in the expected directions. Log-TOME was significantly correlated with acceptance of pain (as measured by the CPAQ) only (see Table 5).

Correlations between demographic factors and changes in outcome variables, and changes in medication use

Demographic and pain variables did not correlate with changes in medication use. Changes in numbers of classes of medications were significantly correlated with changes in PHQ-9, BPI-IS, WSAS and ISI in the expected direction. Changes in TOME were correlated

Table 5. Correlations between medication variables and outcome and process variables at pre-treatment.

	Pearson correlation coefficient (n)	
	Log-TOME/24 hours	Classes of medication
PHQ-9	0.130* [375]	0.223** [374]
BPI-IS	0.141** [377]	0.112* [376]
WSAS	0.123* [375]	0.094 [374]
5-minute walk	-0.186** [326]	-0.161** [325]
ISI	0.134** [376]	0.155** [375]
AAQ	0.053 [376]	0.211** [375]
CFQ	-0.028 [373]	0.162** [372]
EQ	-0.038 [364]	-0.151** [363]
CPAQ	-0.161** [374]	-0.184** [373]
CAQ	-0.076 [371]	-0.178** [370]

TOME: total oral morphine equivalent; PHQ: Patient Health Questionnaire; BPI-IS: Brief Pain Inventory-Interference Scale; WSAS: Work and Social Adjustment Scale; ISI: Insomnia Severity Index; AAQ: Acceptance and Action Questionnaire; CFQ: Cognitive Fusion Questionnaire; EQ: Experiences Questionnaire; CPAQ: Chronic Pain Acceptance Questionnaire; CAQ: Committed Action Questionnaire.

* $p < 0.05$; ** $p < 0.01$.

with changes in BPI-IS, WSAS and ISI in the expected direction (see Table 6).

Correlations between changes in process variables and changes in medication use

Changes in number of classes of medication were correlated with changes in PF as measured by the AAQ and CFQ, in the expected direction. Changes in TOME did not correlate with changes in process variables (see Table 6).

Regression analyses

Five multiple regression analyses using a hierarchical entry method were carried out to assess the contribution of TOME and medication classes to measures of patient functioning at baseline, after the contribution average pain intensity during the last week had been taken into account (see Table 7). The dependent variables in the analyses were PHQ-9, BPI-IS, WSAS, 5-minute walk and ISI. Only those variables that correlated significantly with the medication variables were used. Multicollinearity was not a concern (variance inflation factor (VIF) < 10 and tolerance statistic > 0.1). The proportion of variance explained by the two medication variables together was significant for the PHQ-9, BPI-IS, WSAS, 5-minute walk and ISI, over and above average pain

Table 6. Correlations between changes in medication variables and changes in outcome and process variables (standardised change scores).

	Correlation coefficient (n)	
	Δ TOME/24 hours (Pearson)	Δ Classes of medication (Pearson)
Δ PHQ-9	0.092 [339]	0.144** [338]
Δ BPI-IS	0.141** [344]	0.187** [344]
Δ WSAS	0.117* [343]	0.180** [342]
Δ 5-minute walk	-0.110 [299]	-0.042 [299]
Δ ISI	0.148** [344]	0.164** [343]
Δ AAQ	-0.029 [343]	0.120* [342]
Δ CFQ	-0.032 [340]	0.156** [339]
Δ EQ	-0.064 [332]	-0.092 [331]
Δ CPAQ	-0.077 [341]	-0.102 [340]
Δ CAQ	0.051 [342]	0.019 [341]

TOME: total oral morphine equivalent; PHQ: Patient Health Questionnaire; BPI-IS: Brief Pain Inventory-Interference Scale; WSAS: Work and Social Adjustment Scale; ISI: Insomnia Severity Index; AAQ: Acceptance and Action Questionnaire; CFQ: Cognitive Fusion Questionnaire; EQ: Experiences Questionnaire; CPAQ: Chronic Pain Acceptance Questionnaire; CAQ: Committed Action Questionnaire.

* $p < 0.05$; ** $p < 0.01$.

intensity. The proportion of variance explained by the two medication variables was small (1.2–4.6%). Number of medication classes uniquely predicted PHQ-9 and log-TOME/24 hours uniquely predicted the WSAS and 5-minute walk.

Regressions were carried out with changes in the standard clinical outcomes as the dependent variables, and changes in TOME and medication classes as the predictors (as well as changes in pain intensity) (see Table 8). Multicollinearity was not a concern (VIF < 10 and tolerance statistic > 0.1). The proportion of variance explained by changes in the medication variables was significant for changes in the PHQ-9, BPI-IS, WSAS and ISI, over and above changes in average pain intensity. The proportion of variance explained by changes in the two medication variables was small (1.5–3.0%). Changes in number of medication classes uniquely predicted changes in all four outcome variables. Changes in TOME/24 hours did not uniquely predict changes in any outcome variables.

Finally, independent t -tests were carried out to determine if opioid use at baseline was associated with the magnitude of the change scores on measures of functioning (PHQ-9, BPI-IS, WSAS, 5-minute walk and ISI). However, the differences in changes on these measures between those using opioids or not, or those using above 120 mg or below 120 mg, were not significant.

Table 7. Regression analyses of functioning in relation to pain intensity and medication use at pre-treatment.

Model	Predictors	Coefficients – standardised beta	ΔR^2	F change
<i>PHQ-9</i>				
1	Pain intensity	0.294**	0.095	$F(1,371)=38.816^{**}$
2	Log-TOME/24 hours	0.004	0.046	$F(2,369)=9.876^{**}$
	Classes of medication	0.213**		
<i>BPI-IS</i>				
1	Pain intensity	0.462**	0.221	$F(1,373)=105.99^{**}$
2	Log-TOME/24 hours	0.092	0.014	$F(2,371)=3.456^*$
	Classes of medication	0.042		
<i>WSAS</i>				
1	Pain intensity	0.290**	0.089	$F(1,372)=36.196^{**}$
2	Log-TOME/24 hours	0.109*	0.012	$F(1,371)=4.854^*$
<i>5-minute walk</i>				
1	Pain intensity	-0.271**	0.076	$F(1,322)=26.648^{**}$
2	Log-TOME / 24 hours	-0.138*	0.036	$F(2,320)=6.441^{**}$
	Classes of medication	-0.075		
<i>ISI</i>				
1	Pain intensity	0.346**	0.128	$F(1,372)=54.749^{**}$
2	Log-TOME/24 hours	0.049	0.020	$F(2,370)=4.422^*$
	Classes of medication	0.111		

TOME: total oral morphine equivalent; PHQ: Patient Health Questionnaire; BPI-IS: Brief Pain Inventory–Interference Scale; WSAS: Work and Social Adjustment Scale; ISI: Insomnia Severity Index.

* $p<0.05$; ** $p<0.01$.

Table 8. Regression analyses of changes in functioning in relation to changes in pain intensity and changes in medication use (standardised change scores).

Model	Predictors	Coefficients – standardised beta	ΔR^2	F change
Δ PHQ-9				
1	Δ Pain intensity	0.351**	0.133	$F(1,335)=51.191^{**}$
2	Δ Classes of medication	0.123*	0.015	$F(1,334)=5.846^*$
Δ BPI-IS				
1	Δ Pain intensity	0.472**	0.237	$F(1,340)=105.609^{**}$
2	Δ TOME/24 hours	0.076	0.022	$F(2,338)=5.080^{**}$
	Δ Classes of medication	0.106*		
Δ WSAS				
1	Δ Pain intensity	0.342**	0.127	$F(1,339)=49.473^{**}$
2	Δ TOME/24 hours	0.062	0.026	$F(2,337)=5.182^{**}$
	Δ Classes of medication	0.130*		
Δ ISI				
1	Δ Pain intensity	0.302**	0.101	$F(1,339)=37.909^{**}$
2	Δ TOME/24 hours	0.103	0.030	$F(2,337)=5.831^{**}$
	Δ Classes of medication	0.110*		

TOME: total oral morphine equivalent; PHQ: Patient Health Questionnaire; BPI-IS: Brief Pain Inventory–Interference Scale; WSAS: Work and Social Adjustment Scale; ISI: Insomnia Severity Index.

* $p<0.05$; ** $p<0.01$.

Discussion

The purpose of this study was to investigate analgesic use among participants attending an interdisciplinary PMP. Specifically, it aimed to investigate general correlates of

opioid use, changes in analgesic use during treatment and its relationship to functioning, and PF processes associated with medication use and changes in medication use.

In summary, at baseline, people taking opioids showed higher rates of depression and poorer

functioning than those not taking opioids. Number of classes of analgesics used and opioid dose correlated with depression, sleep problems, interference in functioning and walking. Higher opioid doses and using more classes of medication were correlated with poorer functioning. The two medication variables explained a significant proportion of variance in functioning (as measured by the PHQ-9, BPI-IS, WSAS, 5-minute walk and ISI). Participation on an interdisciplinary PMP was associated with reductions in number of classes of analgesics used and TOME dose. Changes in number of analgesic classes used predicted changes in functioning pre-post treatment. Higher PF was associated with using fewer analgesic classes and lower TOME dose at baseline, and pre-post treatment changes in some measures of PF correlated with changes in number of classes of medication.

The higher rates of depression and interference and poorer functioning in the group using opioids compared to those not using opioids is consistent with a large body of evidence showing long-term opioid use for chronic pain is associated with poorer health and functioning.¹⁰⁻²³ Of course, it is not possible to infer causation from these results, but they are further evidence of the psychosocial needs of this group of patients. These results indicate people using opioids are likely to require support as they taper their analgesics.

Participation on an interdisciplinary PMP is associated with reductions in analgesic use, and this is correlated with improved functioning on key clinical outcomes, consistent with existing evidence.⁴¹⁻⁴⁵ The improvements are independent of pain reduction. These results indicate that number of classes of medication used and TOME are both appropriate targets for treatment; if we can help patients to make reductions to these, functioning may improve. Nevertheless, the effect sizes for medication reduction are small and a sizeable proportion (46% or 71% according to how it is measured) do not make clinically significant reductions to their analgesics. This confirms that we need to continue to refine our treatment methods to help more people make more meaningful reductions.

The results provide further evidence that PF is associated with analgesic use.^{50,51} Higher PF as measured by the AAQ, CFQ, EQ, CPAQ and CAQ is associated with using a smaller number of analgesic classes at baseline. This is consistent with the PF model in which medication use is conceptualised as pain avoidance behaviour. The relationship of PF with TOME dose was weaker, although TOME was correlated with the CPAQ. The weaker relationship is not surprising given that TOME is highly variable (as evidenced by the large standard deviation in this sample). How a particular dose affects a person is idiosyncratic and may depend on variables not captured in these data (such

as length of time an individual has been taking opioid medication and variations in individual sensitivity to side effects). Pre-post treatment changes in number of medication classes were correlated with the AAQ and CFQ. These results are preliminary and larger studies will be needed to investigate this further.

The limitations of this study include the time frame; some patients require longer than 4 weeks to make significant changes to their medication. The lack of follow-up means that those who make changes over longer periods would not be represented here and also that it is not possible to ascertain whether the significant reductions in medication use identified at post-treatment were sustained. For example, in a study of outcomes following interdisciplinary pain rehabilitation with weaning, 22% of participants followed up at 12 months reported resuming opioids post-programme.⁸⁵ It is also possible that level of education influences medication changes; in this study, those providing data at post-treatment had completed significantly more years of education than those who dropped out of treatment. As Song and Foell⁸⁶ showed, opioid use tends to follow a fluctuating course and some people discontinue spontaneously so we cannot confirm that the changes were a result of participating in treatment. The sample size of this study was not sufficient to carry out sub-group analyses. For example, future research could specifically investigate people taking doses above 120mg TOME. Preliminary analysis here indicates more people in this group make clinically significant reductions to their analgesic use. Other limitations concern how medication use was measured in this study. As Pike et al.⁴⁶ note, prescription data and patient self-report may differ as self-report is more likely to capture variation in adherence to prescribed use. This study triangulated patient self-report and prescription data in recognition of this as an attempt to obtain the most accurate information possible. However, this method does not capture other relevant healthcare use, such as GP visits or pain procedures in secondary care. A related limitation is that no information was analysed about prescriber variables, which are of course just as relevant to analgesic use as patient variables.³⁷ Finally, it should be acknowledged that the sample in this study refers to a highly selected population, given that participants had been referred to, assessed as suitable for and were willing to engage in an intensive PMP. This means that the generalisability of the findings is unclear and remains to be demonstrated.

In conclusion, this study provides further evidence that opioid use is a marker for greater difficulties in people with chronic pain and that reductions in medication use may contribute to improvements in key clinical outcomes, including depression, pain interference and work and social functioning. Together with the results of previous studies, there is converging evidence

that PF is significantly negatively associated with analgesic use in chronic pain. Future, larger studies could investigate this preliminary finding further and follow up whether changes made during a PMP are sustained over time. This study confirms that we need to continue to refine our methods to better help those who do not successfully reduce their medication use despite intensive interdisciplinary input. The PF model offers an avenue for treatment development. By better targeting key processes of the PF model, we may improve outcomes. It is also important to note that not all patients are referred to, access or successfully complete an interdisciplinary PMP. Helpful developments might include other treatment formats that are accessible to a wider range of patients.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

This report represents independent research funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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Appendix 1

Guidelines used to calculate total oral morphine equivalent doses

Pain management approximate opioid equivalent doses of morphine.

Medication name	Typical adult dose	Approximate equivalent oral dose of morphine
Oral tablets (mg)		
Codeine	30	2.5
Dihydrocodeine	30	3
Tramadol	50	10 ^a
Tapentadol	50	20
Morphine	10	10
Oxycodone	5	10
Sublingual tablets		
Buprenorphine	200 µg	10 mg
Fentanyl	200 µg	No direct conversion available
Transdermal patches		
Approximate equivalent oral dose of morphine (in 24 hours)		
Buprenorphine (7-day patches)	5 µg/h	12 mg
	10 µg/h	24 mg
	20 µg/h	48 mg
Buprenorphine (4-day patches)	35 µg/h	84 mg
	52.5 µg/h	126 mg
	70 µg/h	168 mg
Fentanyl (3-day/72-hour patches)	12 µg/h	45 mg
	25 µg/h	90 mg
	50 µg/h	180 mg
	75 µg/h	270 mg
	100 µg/h	360 mg

^a1/5–1/10 potency (5–10 mg), clinically approximated in local practice as 10 mg.

Please note:

- We acknowledge that there is variance in the conversion charts used by different clinical sites, including pain management services. Furthermore, it is widely acknowledged that conversion charts are an approximate guide, as comprehensive data are lacking and there is significant inter-individual variation.
- These figures were locally agreed on to ensure consistency when calculating total daily oral morphine equivalent doses by means of inclusion/exclusion criteria for treatment pathways.
- If using these figures for opioid rotation, please ensure that a 30% reduction in total daily dose is considered.