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Problems and concerns of patients receiving chronic opioid therapy for chronic non-cancer pain

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Abstract

The value of chronic opioid therapy (COT) for chronic non-cancer pain (CNCP) patients is determined by a balance of poorly understood benefits and harms. Traditionally, this balance has been framed as the potential for improved pain control versus risks of iatrogenic addiction, drug diversion, and aberrant drug-related behaviors. These potential harms are typically defined from the providers' perspective. This paper seeks to clarify difficulties with the long-term use of opioids for CNCP from the patients' perspective. We used the Prescribed Opioids Difficulties Scale (PODS) to assess current problems and concerns attributed to opioid use by 1144 adults receiving COT. Subjects were grouped into low (56.9%), medium (25.6%) and high (17.5%) PODS scorers. Among patients with high PODS scores, 64% were clinically depressed and 78% experienced high levels of pain-related interference with activities, compared to 28% depressed and 60% with high interference with activities among those with low PODS scores. High levels of opioid-related problems and concerns were not explained by differences in pain intensity or persistence. Patients with medium to high PODS scores were often concerned about their ability to control their use of opioid medications, but prior substance abuse diagnoses and receiving excess days supply of opioids were much less common in these patients than depression and pain-related interference with activities. These results suggest two types of potential harm from COT attributed by CNCP patients to opioids: psychosocial problems that are distinct from poor pain control and opioid control concerns that are distinct from opioid misuse or addiction.

Keywords

Depression; Addiction; Substance abuse; Activity interference; Aberrant behaviors; Misuse; Difficulties; PODS; Patient centered

1. Introduction

Long-term use of opioids for chronic non-cancer pain (CNCP) has increased dramatically in the past two decades [5,17]. The overall value of chronic opioid therapy (COT) for patients with CNCP is determined by a complex balance of benefits and harms that is not well understood. This balance has been framed in guidelines as the potential for sustained pain relief for patients suffering from CNCP versus the potential of iatrogenic or recurrent addiction, or drug diversion for non-medical use [1,15]. A recent consensus panel recommended that this pain relief be evaluated in at least two of four core outcome domains: (1) Pain intensity, (2) physical functioning, (3) emotional functioning, and (4) participant ratings of overall improvement [9]. The potential harms of COT have recently been broadened beyond addiction and diversion to include aberrant drug-related behaviors, which encompass various forms of abuse and misuse of prescription opioids (e.g., forging prescriptions, going to multiple doctors to obtain opioids) as well as behaviors potentially indicative of poor pain control and “pseudo-addiction” (e.g., raising opioid dose on one’s own, patient concerns that opioid use might lead to addiction) [7,13,19].

Beyond opioid misuse and abuse, there is a broader spectrum of psychosocial difficulties potentially associated with COT that may be of concern to patients, e.g., disturbances of mood and cognition or reduced activity levels. Because these kinds of psychosocial difficulties may be caused by chronic pain or by opioid medications used to treat chronic pain, it is difficult to establish causation for such difficulties. However, an important first step is to understand the perspectives of patients receiving COT regarding the kinds of difficulties they attribute to opioid use. Research to date on the potential harms of COT has largely focused on harms perceived by clinicians such as aberrant behaviors and abuse. However, patients may perceive difficulties with COT that differ from the concerns of their clinicians. Furthermore, patients’ experiences with COT are central to the ongoing debate about the benefits and risks of chronic opioid therapy for CNCP.

This study assessed psychosocial difficulties that patients attribute to their use of prescribed opioid medications using the Prescribed Opioid Difficulties Scale in a telephone survey of patients using COT for CNCP. We report on two types of patient-reported difficulties, psychosocial problems and opioid control concerns derived by exploratory and confirmatory factor analyses [3]. This paper has four objectives: (1) to estimate the percent of COT users who report elevated levels of problems and concerns related to opioid use, (2) to compare the frequency of specific difficulties attributed to opioid use among patients with low, medium and high levels of opioid-attributed difficulties, (3) to assess how strongly these difficulties are associated with unrelieved pain, and (4) to assess the extent to which patients who report significant opioid difficulties also have independently documented evidence of significant psychosocial dysfunction and opioid abuse or misuse.

2. Methods

This paper reports findings from a survey of adults age 21–80 years who were current long-term users of prescribed opioid medications for chronic non-cancer pain. This survey was conducted under the auspices of CONSORT – Consortium to Study Opioid Risks and Trends [19]. The health plan included in this analysis, Group Health Cooperative (GHC), provides comprehensive care on a pre-paid basis to about 500,000 persons in Washington State who are demographically representative of the general population.

2.1. Inclusion/exclusion

To be eligible for the survey, a Group Health enrollee must have filled at least 10 opioid prescriptions and/or received at least 120 days supply in a 1-year period prior to the sample

selection date, with at least 90 days between the first and last opioid dispensing in that year. The use of opioids was ascertained from Group Health's electronic pharmacy database, where members report obtaining over 90% of their prescription medications. These criteria for long-term opioid use have been shown to predict a high probability of sustained opioid use 1 year later [19]. Additional eligibility criteria were continuous enrollment in GHC for at least 1 year prior to sampling and enrollment at a Western Washington Group Health clinic. Patients who had received a cancer diagnosis in the Western Washington cancer registry (except for non-melanoma skin cancer) or who had two or more cancer diagnoses in the automated visit records in the year prior to sampling were excluded.

2.2. Sampling

Since the majority of long-term opioid users receive less than 20 mg. MED per day in this population [19], survey respondents receiving higher dosage levels were oversampled to provide greater precision in the analyses of patient sub-groups using opioids at higher dosage levels. Patients were sampled for the survey within three dosage strata (1–49 mg, 50–99 mg, and 100+ mg, morphine equivalent dose). Equal numbers of patients were randomly selected from each stratum. Observations were then weighted within dosage strata by the inverse of the probability of selection so that survey estimates are representative of the population of long-term opioid users from which the sample was selected. Means, variances, proportions and other estimates reported in this paper were obtained using estimation methods for a stratified random sample. Patient interviews began in June 2008 and ended in November 2008.

2.3. Telephone survey procedures

Potentially eligible patients were mailed a letter explaining the study, with a two dollar bill included. Survey interviewers working for Group Health's Survey Research Center then called potential participants. The interviewers, highly experienced in research interview techniques, conducted the interviews using a Computer- Assisted Telephone Interview. Patients were asked to participate in a 25–30-min telephone interview and to allow the study to access their electronic health care data from the time they enrolled in Group Health until 3 years after the date of the interview. Patients who completed the interview were mailed a \$20 reimbursement for their time. Only interviewees who reported having used opioid medications in the 2 weeks prior to the interview were included in the analyses reported in this paper. This excluded only a small number of respondents not currently using opioid medications. The study procedures, including oral informed consent, were reviewed and approved by the GHC Institutional Review Board.

2.4. Assessment of prescribed opioid difficulties

Patient problems and concerns attributed to opioid use were measured using the Prescribed Opioid Difficulties Scale (PODS). The development and psychometric properties of the PODS including items and scoring rules are described in a companion scale development paper [3] and provided in Appendix A to this paper. The PODS has one sub-scale measuring psychosocial problems attributed to opioids and a second sub-scale measuring opioid control concerns. A typical item in the Problems sub-scale is "In the past 2 weeks, opioid medicines have caused me to lose interest in my usual activities," rated from strongly disagree to strongly agree. A typical item in the Concerns sub-scale is "In the past 2 weeks, I have been preoccupied or thought constantly about use of opioid pain medicines," rated from strongly disagree to strongly agree. An additional PODS item, not included in the PODS scoring, asks patients to rate how helpful they have found opiate pain medicines in controlling their pain over the past month.

The PODS focuses on recent problems and concerns related to opioid use from the patient's perspective (in the past 2 weeks for common problems, in the past month or year for less common problems). It asks potentially sensitive questions using a 'strongly disagree' to 'strongly agree' scale, permitting patients to report that a particular problem or concern does or does not apply to their situation. While PODS does ask whether the patient perceives opioid-related family and work problems, or concerns among family members and co-workers about the patient's opioid use, it does not ask questions about aberrant drug-use behaviors (e.g., obtaining early refills or doctor-shopping). The scale was designed to permit a researcher or clinician to assess the problems and concerns that patients themselves attribute to using chronic opioid therapy.

Since the two sub-scales are correlated 0.52, and the combined scale is highly reliable (Cronbach's $\alpha = 0.82$), this paper uses the combined scale to group patients as having low, intermediate and high PODS scores based on the recommended cutpoints of 0–7 (low), 8–15 (intermediate) and 16+ (high). The rationale for the PODS score cutpoints is discussed in more detail in the scale development paper [3]. Briefly, a cutpoint of 8 was selected as a medium score level because this required endorsing at least two difficulties and 16 was selected as a high score because this required endorsement of at least four difficulties. Rates of endorsement of individual scale items (answering 'agree' or 'strongly agree') are displayed according to the three overall score groups in order to provide a descriptive profile of how specific problems and concerns differ among patient groups who attribute low, medium and high levels of difficulties to their use of opioids.

2.5. Relation to validated clinical measures

2.5.1. Pain intensity and interference with activities—Pain intensity was measured using 0–10 pain intensity rating scales (average pain in the prior 3 months, worst pain in the prior 3 months, and pain right now) from the Graded Chronic Pain Scale [18]. This scale has been validated and widely used in studies of chronic pain prevalence and severity [12,16]. Three 0–10 ratings of the extent to which pain interfered with activities (work, school, housework) in the past 3 months from the Graded Chronic Pain Scale were also used, as was a question about the number of days in the past 3 months the respondent was kept from usual activities due to pain. The three 0–10 interference ratings were averaged, and a mean of 5 or greater was defined as high interference. A Pain Impact Scale [18] consisting of 11 yes–no items concerning effects of pain in the last 2 weeks (e.g., staying in bed more, avoiding jobs around the house, doing fewer social activities) was also included. We report the percent of patients who endorsed 8 or more of the 11 items included in this scale, reflecting a high level of interference with activities due to pain.

2.5.2. Depression—The severity of depressive symptoms was measured with the 8-item version of the Patient Health Questionnaire, a validated and widely used self-report measure of depressive symptoms [8,11]. Based on recommended cutpoints for the PHQ-8 [11], persons with a score of 10 or greater were classified as having clinically significant depressive illness.

2.5.3. Indicators of substance abuse problems—Two objective indicators of potential substance abuse problems were developed from health plan electronic medical records data to determine whether patient control concerns were associated with these indicators. The percent of survey respondents who had received a drug abuse diagnosis from a Group Health provider in the prior 3 years was estimated. The percent of patients who either received more than 216 days supply of long-acting opioids in the prior 180 days (i.e., 120% or greater excess days supply), or more than 216 days supply of short-acting opioids

in the prior 180 days, was determined. Since some patients use both short- and long-acting opioids, this provided a conservative estimate of patients receiving excess days supply.

2.6. Statistical analysis

All analyses reported in this paper were weighted to adjust for differences in sample selection probabilities by average daily opioid dose over the past year as revealed in electronic pharmacy data. They were weighted back to be representative of the COT recipients at Group Health that were the source of the study sample. First, we report bivariate Spearman correlations between the total PODS and the problems and Concerns sub-scales with the independently validated scales. In order to contrast the extent of differences on PODS items for patients with low, medium and high scores on the Prescribed Opioid Difficulties Scale, we report the percent endorsing ('agree' or 'strongly agree') for each of the PODS items for patients in each of these three scoring groups. We then examined differences in pain status, indicators of psychosocial dysfunction and opioid control concerns across the three PODS groups (low, medium and high). We compared the percent with high average pain intensity (a pain rating of 5+) for each of the three PODS groups, and the percent who reported that opioid medications were very or extremely helpful in relieving their pain. We then compared the extent of high levels of psychosocial dysfunction across the three PODS groups including the percent with: (a) clinically significant depression (a PHQ-8 score of 10+); (b) average pain interference ratings of 5+, and (c) endorsement of 8 or more of the 11 items on the Pain Impact Scale. We also compared the percent of persons in each of the three PODS groups who had indicators of potential drug misuse (the percent with a drug abuse diagnosis in the prior 3 years and/or receiving substantial excess in days supply of opioids in the prior 180 days) across the three PODS levels.

In order to assess whether any differences in the above external indicators of psychosocial problems and substance abuse might be explained by patient differences in pain intensity, pain duration or other patient characteristics, we carried out logistic regression analyses adjusted for age, sex, level of education, average pain intensity, and number of days with pain in the prior 6 months. To determine whether the Problems and Concerns sub-scales differed in their relationship to independently validated measures, we examined the logistic regression results for the two sub-scales separately. We report adjusted odds ratios for each of the independently validated measures that indicate whether patients with intermediate and high Problems and Concerns sub-scale scores differ significantly on other measures of psychosocial problems and potential substance abuse indicators from patients with low scores. Because we carried out multiple (5) statistical tests, we used a Bonferonni correction to control the Type I error; resulting in a 0.01 the threshold for statistical significance at the 0.05 level.

3. Results

3.1. Sample characteristics

Of 2054 eligible subjects contacted about study participation, 1191 (58%) gave informed consent (including access to their medical records data) and completed the interview. We report on 1144 subjects who reported the use of opioid medications in the prior 2 weeks (96% of those interviewed). Response rates differed by age, with 66% of persons age 65 or older agreeing to participate compared to 56% of persons age 21–64 ($t = -2.62, p < 0.01$). Females (59%) were more likely to agree to participate than males (55%) ($\chi^2 = 4.08, p < 0.05$). Response rates did not differ by average daily dose ($t = 1.57, p = 0.12$).

Table 1 displays the characteristics of the study sample. Participants were predominately middle age or older and female. The vast majority (83%) were Caucasian, most were married and educational attainment was high, reflecting demographic characteristics of the regional population. A quarter of the sample was unemployed. The average body mass index (BMI) was 31, indicating that obesity was common in this population (a BMI of 25 is considered overweight while a BMI of 30 is considered obese).

The pain problems most commonly rated as bothersome in the past 6 months were back pain, widespread pain and leg pain. Nearly the entire sample (98%) reported pain at multiple anatomical locations. Over the past 6 months, subjects most commonly took opioids for back and leg pain, and 60% reported taking opioids for multiple pains. On average, subjects reported being in pain 162 of the past 180 days (90% of days) and 92% of the sample reported pain on at least 90 days. Mean ratings of pain right now were 4.7/10, worst pain 8.6/10, and average pain 5.8/10. Subjects reported a mean of 36 disability days due to pain in the past 90 days.

Mean daily opioid dose, estimated from pharmacy prescription data over the year prior to the interview, was generally modest. An average daily dose per day of 0–49 mg MED was observed for 74%, while only 11% used 100 mg or more per day. The most common opioid preparation taken was hydrocodone combined with acetaminophen or aspirin (35%) followed by oxycodone (22%) and long-acting morphine (17%). Three-fourths of the sample reported taking an opioid on every day of the 2 weeks prior to the interview, generally multiple times per day. Participants reported that their pain was 6.3/10 before taking opioids and 3.5/10 two hours after taking opioids, with a median self-rated pain reduction of 40%. The vast majority of patients rated opioids as helpful in pain relief, with 56% rating opioids as very to extremely helpful.

3.2. Opioid-related problems and concerns item endorsement

Based on their responses to questions about problems and concerns related to the use of prescribed opioid medications (see the PODS scale in Appendix to this paper), study participants were grouped as having low, medium or high levels of opioid-related difficulties. The percent of long-term opioid users falling in these three groups was 57% (low, a total score of less than 8), 25% (medium, a total score of 8–15) and 18% (high, a total score of 16+).

Fig. 1a displays the percent of subjects endorsing ('agree' or 'strongly agree') on each of the Problems sub-scale items for subjects overall and those with low, medium or high overall PODS scores. Among the 18% of patients with high scores on the PODS, more than half attributed the following problems to opioid use in the past 2 weeks: trouble concentrating or remembering; feeling slowed down, sluggish, or sedated; interference with work, family or social responsibilities; difficulty thinking clearly; being sleepy or less alert when driving or doing something requiring alertness (in the past year); and having bothersome side effects (in the past month). Among the 25% of long-term opioid users with medium scores, these problems were substantially less common, with only problems of sluggishness, alertness, and bothersome side effects being reported by more than 20% of the patients. These problems were uncommon among persons with low-scale scores.

Fig. 1b displays the percent of subjects positive on Concerns sub-scale items for subjects overall and those with low, medium or high overall PODS scores. More than 40% of the study participants with high PODS scores reported that: they needed a higher dose to get the same effect; they were worried that they might be dependent on or addicted to opiate pain medicines; they wanted to stop using or cut down on the use of opiate pain medicines; and their family or friends thought they might be dependent or addicted to opiate pain medicines.

Among study participants with medium PODS scores, more than 30% reported the same concerns about the use of prescribed opioids for three of the four items, but these patients were much less likely to report that their family or friends thought that they might be addicted. Among the 57% with a low overall scale score, concerns about control of prescribed opioids were uncommon.

The PODS were not significantly correlated with average pain intensity over the previous 3 months: Spearman $r = 0.034$, $p = 0.25$ with PODS total score; $r = 0.005$, $p = 0.86$ with PODS concerns, $r = 0.050$, $p = 0.09$ with PODS problems. The PODS were significantly but weakly correlated with pain interference with daily activities: Spearman $r = 0.144$, $p < 0.001$ with PODS total score; $r = 0.094$, $p = 0.002$ with PODS concerns; $r = 0.148$, $p < 0.0001$ with PODS problems. The PODS were more strongly correlated with depression symptoms on the PHQ: Spearman $r = 0.317$, $p < 0.0001$ with PODS total score; $r = 0.221$, $p < 0.0001$; PODS concerns, $r = 0.314$, $p = 0.0001$ PODS problems.

Fig. 2 displays the percent positive on the selected external measures of psychosocial problems, contrasting patients with low, medium and high scores on the PODS Scale. Overall, 38% of those surveyed scored 10 or more on the PHQ depression scale, indicating at least moderate depressive symptoms. In the group with a low PODS score, 28% scored in the clinically depressed range, compared to 40% in the medium group and 64% in the high group. Overall, 67% of those surveyed rated their level of pain-related interference (average of daily, work-related, and social/recreational activities) as 5 or greater on a 0–10 scale (where 10 is unable to carry out any activities due to pain). Similarly, 49% percent of those surveyed had high Pain Impact Scores ($\geq 8/11$ items positive). The percent with pain-related activity limitations increased with PODS score for both these measures (Fig. 2).

Fig. 3 displays the percent positive on other selected measures of substance abuse problems. Overall, 9% percent of those surveyed had received a diagnosis of drug abuse/dependence in their medical records in the prior 3 years. Overall, 10% percent of those surveyed were classified as having received excess days supply of prescribed opioids in the 180 days prior to the survey based on health plan pharmacy data. In contrast to depression and pain-related interference with activities, indicators of potential substance abuse and misuse were much less common among patients receiving chronic opioid therapy for CNCP.

One possible interpretation of the above-mentioned results is that patients who report more problems related to the use of opioid medications may have less adequate pain control. However, Fig. 4 shows that the endorsement of average pain intensity ratings ≥ 5 among patients with low, medium and high scores on the PODS do not differ greatly (72–86%). Overall, 76% percent of those surveyed reported average pain intensity of 5/10 or more. Given these results, it is striking that 56% percent of those surveyed reported that opioids were very or extremely helpful in relieving their pain (see Fig. 4). In the low PODS group, 59% reported that opioids were very helpful compared to 55% in the medium group and 50% in the high group.

We sought to determine whether the differences in depression, pain-related interference with activities and potential drug misuse seen in the groups with low, medium and high rates of opioid problems and concerns were explained by patient differences in average pain intensity, pain persistence or demographic variables. Table 2 displays adjusted odds ratios for various adverse outcomes for those with medium and high Problems sub-scale scores controlling for age, gender, education, average pain intensity and number of days in pain in the prior 6 months. Neither the odds of having received a diagnosis of drug dependence or abuse nor the odds of having received excess days supply of opioids was elevated in either the medium or high Problems sub-scale score groups. On the other hand the odds of clinical

depression and significant pain impact were increased in both the medium and high Problems subscale score groups after adjusting for pain status and demographic variables. Elevated risk of activity interference was observed in the group attributing high levels of problems to opioid use, but not in the medium group.

Table 3 displays adjusted odds ratios for various adverse outcomes for those scoring in the midrange and high level for the Concerns sub-scale controlling for age, gender, education, average pain and number of days in pain. Both the midrange and high scoring groups had moderately increased odds of having previously received a diagnosis of drug abuse or dependence in the medical record. The odds of reporting significant depression was moderately increased in the midrange and markedly increased in the high level Concerns groups. Activity interference was moderately elevated in the midrange but not in the high level Concerns group.

4. Discussion

In this survey of patients receiving chronic opioid therapy, patients often reported significant difficulties that they attributed to opioid therapy. Almost one in five patients reported high levels of psychosocial problems and opioid control concerns, while an additional one-quarter attributed intermediate levels of problems and concerns to opioid use. A large majority of patients reporting elevated levels of problems and concerns attributed to opioids experienced high levels of depressive symptoms and pain-related interference with activities. These patient-centered problems and concerns have received little consideration in prior discussions of the risks of COT. By describing patients' own sense of the difficulties they experience with COT, PODS adds an important element to our understanding of the complexities of this increasingly common treatment modality.

Though patients reporting higher levels of opioid-related problems and concerns had higher average pain levels, their high rates of clinical depression and pain-related interference could not be explained by differences in pain intensity or pain persistence. Although patients with medium to high PODS scores were often worried about their ability to control the use of opioid medications, actual poor control of opioids, as evidenced by prior substance abuse diagnoses and receiving excess days supply of opioids was observed much less frequently among these patients than depression and pain-related interference with activities. This suggests that patients' concerns about opioid control may be distinct from, and more common than, traditional substance abuse. Based on these findings, we may need to reframe our understanding of potential harms associated with chronic opioid therapy to include psychosocial problems and opioid control concerns. These appear to be distinct from poor pain control and opioid misuse or addiction. These difficulties are neither classical side effects of opioids (such as constipation and myoclonus), nor are they a loss of opioid efficacy (sometimes called 'analgesic failure') [2]. Rather, they are important components of the experience of COT that has implications for patients' overall quality of life.

The possible harms of chronic opioid therapy have commonly been framed in terms of the risks of addiction [1,14,17]. This has been expanded in recent years into the concept of aberrant drug-related behaviors [14]. Our data suggest that an even broader set of potential psychosocial harms of chronic opioid use need to be considered. In this study, objective indicators of substance abuse or aberrant use (receiving a substance abuse diagnosis or evidence of receiving excess days supply) were observed in a modest sub-set of patients. These objective indicators of substance misuse were not strongly associated with the patient-reported level of opioid problems and concerns. This is true despite the fact that over half of the patients with high levels of problems and concerns about opioid use reported that they needed a higher dose to get pain relief, that they were worried about being dependent, and

that they wanted to stop or cut down their opioid use. Over half of subjects in the medium PODS groups also reported that they wanted to stop or cut down their opioid use. It is important to note that these groups endorsed at much lower rates the PODS items describing the core signs of addiction: preoccupation with use, inability to control use, opioid-related problems with family and friends. These findings suggest that patients receiving COT have significant concerns about controlling their opioid use, but do not necessarily manifest the classic high risk drug-use behaviors typical of illicit drug addiction. This is consistent with a previous survey of patients receiving COT that showed a lack of correspondence between DSM IV opioid abuse and dependence and other indicators of addiction or problematic use [4]. Drug dependence criteria may need to be revised when applied to patients using COT to adequately capture the problems and concerns that these patients report. In contrast to the less common occurrence of substance use problems, clinical depression and pain-related activity limitations were quite common among patients using COT, especially among patients reporting high levels of problems and concerns related to the use of opioid medications.

The recently released APS/AAPM guidelines for COT discuss “opioid-related adverse effects” including constipation, nausea and vomiting, sedation, hypogonadism, pruritis and myoclonus [6]. In addition to these physical adverse effects, the data reported here raise the possibility that opioids might be associated with adverse psychosocial effects in some patients. A recent review of COT states: “An extensive clinical experience indicates that long-term opioid therapy is able to help selected patients have a better quality of life, less use of healthcare, and improved productivity. The medical community is no longer debating the reality of these outcomes, but rather, is now focused on the more fruitful debate about patient selection and the benefits and burdens of these drugs in varied subpopulations [19].” Our study suggests that further research and closer monitoring of patients to assess the balance of positive vs. negative psychosocial outcomes of COT are indeed necessary.

The PODS described in this paper could be used in this effort to elicit the perspective of patients regarding psychosocial effects of their opioid medications. The recent APS guideline on aberrant drug-related behaviors accompanying COT states, “Proper patient selection could mitigate potential risks and enhance potential benefits associated with the prescription of opioids for CNCP”. Recent clinical guidelines emphasize the value of risk stratification when contemplating a therapeutic trial of opioids, focusing on “...assessment of risk for aberrant drug-related behaviors consistent with abuse, addiction or diversion [6].” If potential harms of COT are more broad-based than abuse, addiction and diversion, it will be necessary to evaluate patients for a broader range of potential adverse psychosocial effects, particularly for clinical depression and behavioral deactivation.

This study has important limitations. Our response rate of 58% is typical of telephone surveys of persons receiving chronic opioid therapy. Younger, middle-aged and male patients were slightly underrepresented in our sample. These are generally considered higher risk patients for COT, so we may be providing an underestimation of rates of difficulties. We present data from a cross-sectional observational survey. We do not know how these patients would be doing without opioid therapy. The observation that many patients attribute relevant psychosocial problems to their use of opioids (e.g., sluggishness, trouble concentrating) does not prove that opioids caused depression or reduced activity levels. However, in the absence of randomized trials assessing the long-term consequences of opioid use for psychosocial function, these data suggest efforts should be taken to monitor opioid problems and concerns among patients using chronic opioid therapy, as is already recommended by expert guidelines [6].

Furthermore, these data do not explain discrepancies between patient-reported pain and interference levels and reports of helpfulness of opioid therapy. Average pain intensity was rated 5+ (on a 0–10 scale) by three of four patients, and pain-related interference with activities was rated as 5+ (on a 0–10 scale) by two of three patients. On the other hand, over half of the patients described opioids as very to extremely helpful in pain relief. While patients reporting more difficulties related to opioid use were less likely to rate opioids as very or extremely helpful, half of those reporting high levels of difficulties related to their use of opioids still rated opioids as very to extremely helpful. This apparent contradiction between perceived difficulties and perceived benefits of chronic opioid use cannot be adequately explained with data from this cross-sectional study. We do not understand in general why some patients perceive net benefits of chronic opioid therapy while others do not. Follow-up studies of participants in opioid randomized trials have found that most subjects discontinue open label opioid treatment 7–24 months after trial completion [10]. Given the high levels of pain and pain-related interference with life activities among patients reporting that opioids are very to extremely helpful, it is possible that pain levels were even higher prior to initiation of COT. Further longitudinal research with patients receiving COT is needed to clarify these findings.

The PODS might serve as a clinically useful tool to assess potential harms in patients receiving COT by eliciting the patients' perspective. Prescribers who focus on pain relief and aberrant behaviors in their refill decisions may be missing other important problems and concerns of patients receiving COT. Even if opioids are not causing psychosocial problems, it is important that the prescriber understand concerns being attributed to opioids by their patients. These problems and concerns represent an important component of the overall set of risks and benefits associated with chronic opioid therapy that should be considered in refill decisions.

In summary, our study suggests that the range of possible harms from COT may be broader and of a different nature than has been described in treatment guidelines. The Problems and Concerns sub-scales of the Prescribed Opioid Difficulties Scale describe dimensions of difficulties attributed to opioids that are not the same as inadequate pain control, classic opioid side effects, addiction, or aberrant drug-use behaviors. Further research is needed to understand whether these problems and concerns are caused by COT or if they arise as part of prolonged experience with CNCP itself.

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References

1. The use of opioids for the treatment of chronic pain. A consensus statement from the American academy of pain medicine and the American pain society. *Clin J Pain*. 1997; 13:6–8. [PubMed: 9084947]
2. Ballantyne JC, Shin NS. Efficacy of opioids for chronic pain: a review of the evidence. *Clin J Pain*. 2008; 24:469–78. [PubMed: 18574357]
3. Banta-Green, C.; VonKorff, M.; Merrill, J.; Doyle, S.; Saunders, K.; Sullivan, M. Developing a scale to measure problems and concerns of patients receiving chronic opioid therapy for chronic non-cancer pain. 2009. Under Review
4. Banta-Green CJ, Merrill JO, Doyle SR, Boudreau DM, Calsyn DA. Measurement of opioid problems among chronic pain patients in a general medical population. *Drug Alcohol Depend*. 2009; 104:43–9. [PubMed: 19473787]

5. Caudill-Slosberg MA, Schwartz LM, Woloshin S. Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs. 2000. *Pain*. 2004; 109:514–9. [PubMed: 15157714]
6. Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foley KM, Fudin J, Gilson AM, Kelter A, Mauskop A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009; 10:113–30. [PubMed: 19187889]
7. Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK. Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American pain society and American academy of pain medicine clinical practice guideline. *J Pain*. 2009; 10:131–46. [PubMed: 19187890]
8. Dobscha SK, Corson K, Perrin NA, Hanson GC, Leibowitz RQ, Doak MN, Dickinson KC, Sullivan MD, Gerrity MS. Collaborative care for chronic pain in primary care: a cluster randomized trial. *JAMA*. 2009; 301:1242–52. [PubMed: 19318652]
9. Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, Haythornthwaite JA, Jensen MP, Kerns RD, Ader DN, Brandenburg N, Burke LB, Cella D, Chandler J, Cowan P, Dimitrova R, Dionne R, Hertz S, Jadad AR, Katz NP, Kehlet H, Kramer LD, Manning DC, McCormick C, McDermott MP, McQuay HJ, Patel S, Porter L, Quessy S, Rappaport BA, Rauschkolb C, Revicki DA, Rothman M, Schmader KE, Stacey BR, Stauffer JW, von Stein T, White RE, Witter J, Zavisic S. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: impact recommendations. *J Pain*. 2008; 9:105–21. [PubMed: 18055266]
10. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. *Pain*. 2004; 112:372–80. [PubMed: 15561393]
11. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The phq-8 as a measure of current depression in the general population. *J Affect Disord*. 2009; 114:163–73. [PubMed: 18752852]
12. Lungenhausen M, Lange S, Maier C, Schaub C, Trampisch HJ, Endres HG. Randomised controlled comparison of the health survey short form (sf-12) and the graded chronic pain scale (gcps) in telephone interviews versus self-administered questionnaires. Are the results equivalent? *BMC Med Res Methodol*. 2007; 7:50. [PubMed: 18034900]
13. Passik SD, Kirsh KL, Donaghy KB, Portenoy RK. Pain and aberrant drug-related behaviors in medically ill patients with and without histories of substance abuse. *Clin J Pain*. 2006; 22:173–81. [PubMed: 16428952]
14. Portenoy RK. Appropriate use of opioids for persistent non-cancer pain. *Lancet*. 2004; 364:739–40. [PubMed: 15337386]
15. Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: report of 38 cases. *Pain*. 1986; 25:171–86. [PubMed: 2873550]
16. Schmidt CO, Raspe H, Pflingsten M, Hasenbring M, Basler HD, Eich W, Kohlmann T. Back pain in the german adult population: prevalence, severity, and sociodemographic correlates in a multiregional survey. *Spine (Phila, PA, 1976)*. 2007; 32:2005–11. [PubMed: 17700449]
17. Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC. Trends in use of opioids for non-cancer pain conditions 2000–2005 in commercial and medicaid insurance plans: the group study. *Pain*. 2008; 138:440–9. [PubMed: 18547726]
18. Von Korff M, Ormel J, Keefe FJ, Dworkin SF. Grading the severity of chronic pain. *Pain*. 1992; 50:133–49. [PubMed: 1408309]
19. Von Korff M, Saunders K, Thomas Ray G, Boudreau D, Campbell C, Merrill J, Sullivan MD, Rutter CM, Silverberg MJ, Banta-Green C, Weisner C. De facto long-term opioid therapy for noncancer pain. *Clin J Pain*. 2008; 24:521–7. [PubMed: 18574361]

Appendix A

Problems scale items

*1. [In the past 2 weeks] Opiate medicines have caused me to lose interest in my usual activities.

Strongly Disagree(0) Disagree(1) Neutral(2) Agree(3) Strongly Agree(4)

*2. [In the past 2 weeks] Opiate medicines have caused me to have trouble concentrating or remembering.

Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*3. [In the past 2 weeks] Opiate medicines have caused me to feel slowed down, sluggish or sedated.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*4. [In the past 2 weeks] Opiate pain medications have caused me to feel depressed, down, or anxious.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
5. [In the past 2 weeks] How often have side effects of opiate medicine interfered with your work, family or social responsibilities?				
Never(0)	Rarely(1)	Sometimes(2)	Often(3)	Always or Almost Every Day(4)
6. [In the past 2 weeks] How often did opiate medicine make it hard for you to think clearly?				
Never(0)	Rarely(1)	Sometimes(2)	Often(3)	Always or Almost Every Day(4)
7. In the past year, about how many times did opiate medicines make you sleepy or less alert when you were driving, operating machinery or doing something else where you needed to be alert?				
Never(0)	Once or Twice(2)	Three or More Times(4)		
8. Considering the side effects of opiate medicines you experienced in the past month, how bothersome were these side effects?				
Not at All Bothersome(0)	A Little Bothersome(1)	Moderately Bothersome(2)	Very Bothersome(3)	Extremely Bothersome(4)
*Items marked with an asterisk are scored with Agree/Strongly Agree assigned a 4 and all other responses assigned a 0 for the recoded version of the scale.				
<i>Concerns scale items</i>				
*9. [In the past 2 weeks] I have been preoccupied with or thought constantly about use of opiate pain medicines.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*10. In the past year, I have felt that I could not control how much or how often I used opiate medicine.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*11. [In the past year] I have needed to use a higher dose of opiate pain medicine to get the same effect.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*12. [In the past year] I have worried that I might be dependent on or addicted to opiate pain medicines.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*13. [In the past year] I have wanted to stop using opiate pain medicines or to cut down on the amount of opiate medicines that I use.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*14. In the past year, opiate medicines have caused me to have problems with family, friends or co-workers.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
*15. [In the past year] Family or friends have thought that I may be dependent on or addicted to opiate pain medicines.				
Strongly Disagree(0)	Disagree(1)	Neutral(2)	Agree(3)	Strongly Agree(4)
<i>Asked but not scored</i>				
16. Over the past month, how helpful have you found opiate pain medicines in relieving your pain.				
Not at all helpful	A little helpful	Moderately helpful	Very helpful	Extremely helpful
*Items marked with an asterisk are scored with Agree/Strongly Agree assigned a 4 and all other responses assigned a 0 for the recoded version of the instrument.				

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi: 10.1016/j.pain.2010.02.037.

Fig. 1a.

Fig. 1b.

Fig. 1.

Fig. 1a. Profile of problems attributed by patients to opioid use by total Prescribed Opioid Difficulties Scale score group (low, medium, and high).

Fig. 1b. Profile of concerns about opioid control by total Prescribed Opioid Difficulties Scale score group (low, medium, and high).

Fig. 2.
Percent of patients with clinical depression, high pain interference and high pain impact by level of Prescribed Opioid Difficulties.

Fig. 3.
Percent of patients with substance abuse diagnosis (in the prior 3 years) and with excess opioid days supply (in past 6 months) by the level of Prescribed Opioid Difficulties.

Fig. 4.

Percent of patients rating their average pain over the prior 3 months as 5 or greater (0–10 scale) and rating opioid medications as very or extremely helpful for relieving pain by the level of Prescribed Opioid Difficulties.

Table 1Sample characteristics ($N = 1144$).

Variable	N (unweighted) % (weighted)
<i>Demographics</i>	
Age (mean (SE))	55.7 (0.53)
21–44	$N = 194$; 14.5%
45–64	$N = 719$; 64.1%
65+	$N = 231$; 21.4%
Gender (% F)	$N = 700$; 63.1%
Race	
African American	$N = 57$; 5.3%
Caucasian	$N = 942$; 83.4%
Asian	$N = 6$; 0.4%
Other	$N = 118$; 11.0%
Marital status	
Married/living as married	$N = 762$; 66.4%
Never married	$N = 130$; 11.7%
Widowed	$N = 80$; 6.7%
Separated/divorced	$N = 171$; 15.2%
Education	
12+ years	$N = 1070$; 94.1%
Employment	
Full-time or part-time work	$N = 439$; 45.0%
Homemaker	$N = 30$; 2.8%
Retired	$N = 290$; 27.6%
Unemployed	$N = 380$; 25.5%
Student	$N = 30$; 2.5%
BMI (mean (SE))	31.3 (0.38)
<i>Pain</i>	
Pain problems (most bothersome in last 6 months)	
Back pain	$N = 332$; 28.9%
Widespread/multiple	$N = 285$; 20.0%
Leg	$N = 220$; 24.5%
2+ pains in last 6 months	$N = 1121$; 98.3%
Top 5 pains for which took opioids in last 3 months	
Back	$N = 686$; 55.2%
Leg	$N = 499$; 44.5%
Neck	$N = 224$; 15.8%
Shoulder	$N = 200$; 15.1%
Hip	$N = 183$; 15.8%
Took opioids for multiple pains in last 3 months	$N = 730$; 60.3%
Days in pain past 6 months (mean (SE))	162.9 (2.0)

Variable	N (unweighted) % (weighted)
90 + days of pain in last 6 months	N = 1049; 91.9%
Pain intensity (0–10) (mean (SE))	
Now	4.7 (0.12)
Worst	8.6 (0.07)
Average	5.8 (0.09)
Disability days in past 3 months (mean (SE))	36.5 (1.7)
<i>Opioids</i>	
Average daily dose in year before interview	
0–49 mg MED/day	N = 387; 74.2%
50–99 mg MED/day	N = 385; 15.0%
100 + mg MED/day	N = 372; 10.8%
Top five opioids taken in past 3 months (based on days supply)	N = 231; 34.9%
Hydrocodone combination	N = 193;
Oxycodone	21.64%
Long-acting morphine	N = 283; 16.7%
Long-acting oxycodone	N = 184; 8.5%
Codeine combination	N = 35; 5.2%
Took opioids every day in past 2 weeks	N = 1001; 76.8%
Opioid times per day in past 2 weeks	
1	N = 137; 22.8%
2	N = 355; 35.0%
3	N = 384; 24.2%
4	N = 163; 10.8%
5+	N = 90; 7.1%
Usual pain level before opioid dose (0–10) (mean (SE))	6.3 (0.10)
Usual pain after opioid dose (0–10) (mean (SE))	3.5 (0.09)
Median percent change in pain 2 h after opioid use	–40%
Helpfulness of opioids in pain relief	
Not at all	N = 10; 7.0%
A little	N = 77; 8.8%
Moderate	N = 357; 34.3%
Very	N = 440; 39.3%
Extremely	N = 259; 17.1%

Table 2

Adjusted odds ratios for external measures by Problems sub-scale scores relative to persons with a low sub-scale score.

Variable	Mid (8–15) OR (95% CI)	High (16+) OR (95% CI)	Significance * (<i>p</i> -values <0.01 are significant)
External measures drug abuse or misuse			
Previous diagnosis of drug dependence/abuse	1.08 (0.55–2.13)	1.45 (0.62–3.42)	<i>p</i> = 0.15
Excess days supply	0.74 (0.31–1.81)	1.75 (0.69–4.46)	<i>p</i> = 0.62
Functioning			
Clinical depression ^a	1.73 (1.02–2.91)	7.68 (3.43–17.18)	<i>p</i> < 0.001
High pain impact ^b	2.07 (1.17–3.68)	4.70 (2.13–10.35)	<i>p</i> < 0.001
High pain interference ^c	1.25 (0.67–2.35)	3.01 (1.15–7.87)	<i>p</i> = 0.002

Weighted results, confidence intervals adjusted for stratified sampling.

Controlling for age, gender, education, average pain, pain days.

Reference group score (0–7).

^aPHQ score ≥10.

^bSIP pain impact score ≥8.

^cPain interference score ≥ 5.

* Significance based on logistic regression using continuous Problems scale scores.

Table 3

Adjusted odds ratios for external measures by Concerns sub-scale scores relative to persons with a low sub-scale score.

Variable	Mid (8–15) OR (95% CI)	High (16+) OR (95% CI)	Significance * (<i>p</i> -values <0.01 are significant)
External measures drug abuse or misuse			
Previous diagnosis of drug dependence/abuse	2.25 (1.30–3.90)	2.75 (1.27–5.95)	<i>p</i> = 0.0005
Excess days supply	1.09 (0.58–2.03)	2.16 (0.81–5.78)	<i>p</i> = 0.36
Functioning			
Clinical depression ^a	1.85 (1.18–2.90)	6.54 (2.97–14.43)	<i>p</i> < 0.0001
High pain impact ^b	1.39 (0.88–2.20)	2.83 (1.31–6.11)	<i>p</i> < 0.0001
High pain interference ^c	2.25 (1.37–3.72)	1.65 (0.70–3.90)	<i>p</i> = 0.006

Weighted results, confidence intervals adjusted for stratified sampling.

Controlling for age, gender, education, average pain, pain days.

Reference group score (0–7).

^aClinical depression = score ≥10 on PHQ-9.

^bHigh pain impact = endorsing at least half of pain impact items on Sickness Impact. Profile scale.

^cHigh pain interference = reporting at least 5/10 on pain interference scale.

* Significance based on logistic regression using continuous Concerns scale scores.