TREATMENT IMPROVEMENT PROTOCOL (TIP) SERIES

Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders:

A Review of the Literature—Updates*

TIP 54

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Treatment Improvement Protocol (TIP) 54,

Managing Chronic Pain in People With or in Recovery From Substance Use Disorders

Updated Findings From the Literature

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Introduction

The following updates are intended to keep current the literature review component of Treatment Improvement Protocol (TIP) 54, *Managing Chronic Pain in People With or in Recovery From Substance Use Disorders*, published in 2012. Literature searches are performed every 6 months; reviews are written every 6 to 12 months, depending on whether the search results produce relevant articles. The same search methodology used in developing the literature review for TIP 54 is used for the updates.

October 1, 2011, Through May 31, 2012

The original review of the literature for this Treatment Improvement Protocol (TIP) noted that there is scant research to guide treatment for chronic noncancer pain in patients with or in recovery from substance use disorders. This continues to be true. For the period of time covered by this update, no articles met the criteria for inclusion. Please check back in December 2012 for the next update.

June 1, 2012, Through November 30, 2012

Three articles met the selection criteria for this literature review update for TIP 54, *Managing Chronic Pain in People With or in Recovery From Substance Use Disorders*. Several articles not meeting selection criteria (e.g., review articles, association position papers) that may be helpful to the reader are listed under "Other Articles of Interest."

Pain Relief

In a longitudinal cohort study of office-based buprenorphine treatment, Fox et al. (2012) found that pain was common among the 82 individuals seeking buprenorphine treatment for opioid dependence. The data were collected through interviews and medical record extraction. Study duration was 6 months. To the authors' knowledge, the study was the first to consider the relationship between pain and treatment outcomes in office-based buprenorphine treatment.

The pain variables were "baseline pain" and "persistent pain." The participants rated their pain for the preceding week on a scale of 0 through 10 (0=no pain, 10=intense pain). Those reporting pain scores ≥ 5 at the initial interview were considered to have baseline pain. Those reporting pain scores ≥ 5 at all followup visits were considered to have persistent pain. Among the 82 participants, 60 percent had baseline pain and 38 percent had persistent pain.

Fifty-six percent of participants remained in buprenorphine treatment at 6 months. Participants with either type of pain (versus those without pain) were more likely to have HIV infection, history of injection drug use, depressive symptoms, and baseline substance abuse of alcohol, sedatives, and opioid analgesics in addition to their substance of choice. For those with baseline pain, mean pain score decreased from 7.3 to 6.0 during the 6-month followup period.

The researchers found no association between either type of pain and buprenorphine treatment outcomes (treatment retention and self-reported opioid use). The authors wrote that this lack of an association between pain and treatment outcomes contradicts the findings of some previous studies. They conjectured that for patients with co-occurring opioid dependence and pain, the treatment modality may be important: buprenorphine or methadone may reduce the negative impact of pain on treatment outcomes, and buprenorphine may provide some pain relief.

Limitations of the study include the small sample size and that opioid use could not be checked with urine drug testing. In addition, the study site served a hard-to-reach population, which limits the generalizability of the results.

Raisch et al. (2012) analyzed a subset of data from a study that compared buprenorphine oral tablet with buprenorphine oral liquid formulation. The goal of the substudy was to evaluate whether treatment of opioid dependence with buprenorphine was associated with changes in health-related quality of life (HRQOL). Taking into account relevance to TIP 54, only results from the "bodily pain" domain of the HRQOL are presented here.

Ninety-six participants enrolled in the study. Participants were administered buprenorphine daily for 16 weeks. In addition, they received psychosocial counseling and weekly group therapy.

HRQOL assessments were completed at baseline and 4, 8, 12, and 16 weeks after baseline. At the 16-week assessment, 44 participants remained in the study.

Participants' bodily pain scores were lower at every followup assessment point than they were at baseline. The decreases were significant at the week 8 and week 12 evaluations and in the intention to treat (last observation) analysis.

Model Development

Rice et al. (2012) attempted to identify and analyze patient characteristics and behavior associated with diagnosed opioid abuse to build a model that identifies patients at risk for prescription opioid abuse, dependence, and misuse.

The researchers used medical and drug information from an administrative claims database (stripped of identities) of privately insured members. Patients ages 12 to 64 years, with at least one prescription opioid claim (n=821,916) were selected. Patients were divided into two groups: those diagnosed with opioid abuse (n=6,380) and those without a diagnosis for opioid abuse (n=815,536).

A logistic regression model was developed to estimate the association between an opioid abuse diagnosis and patient characteristics. These characteristics included demographics, prescription drug use and filling behavior, co-occurring disorders, medical resource use, and family member characteristics.

The following were identified as key characteristics associated with opioid abuse:

- Male gender
- Prior opioid prescriptions
- At least one diagnosis of nonopioid drug abuse
- At least one prior prescription of buprenorphine or methadone
- History of mental illness
- History of hepatitis
- Family member diagnosed with opioid abuse or a mental illness

The authors concluded that it is possible to make predictive models using medical and drug claims data. This model could help payers identify patients who may be at increased risk for opioid abuse. These models are unique in that they include medical information that is not available in prescription drug monitoring programs.

Other Articles of Interest

The following are not original research studies. They are review articles or position statements, and much of the information presented is covered in TIP 54. They may be of interest to the reader, however.

1. Gibson, C. A. (2012). Review of posttraumatic stress disorder and chronic pain: The path to integrated care. *Journal of Rehabilitation Research and Development, 49*(6), 753–776.

2. Krashin, D., Murinova, N., & Ballantyne, J. (2012). Management of pain with comorbid substance abuse. *Current Psychiatry Reports, 14*(5), 462–468.

3. Magnani, B., & Kwong, T. (2012). Urine drug testing for pain management. *Clinics in Laboratory Medicine, 32*(3), 379–390.

4. Oliver, J., Coggins, C., Compton, P., Hagan, S., Matteliano, D., Stanton, M., et al. (2012). American society for pain management nursing position statement: Pain management in patients with substance use disorders. *Pain Management Nursing: Official Journal of the American Society of Pain Management Nurses, 13*(3), 169–183.

5. Reisfield, G. M. & Friedman, C. K. (2012). Methadone in the chronic pain patient with a substance use disorder. *Journal of Pain and Palliative Care Pharmacotherapy, 26*(4), 368–370.

6. Sehgal, N., Manchikanti, L., & Smith, H. S. (2012). Prescription opioid abuse in chronic pain: A review of opioid abuse predictors and strategies to curb opioid abuse. *Pain Physician, 15*(3 Suppl), ES67–ES92.

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Raisch, D. W., Campbell, H. M., Garnand, D. A., Jones, M. A., Sather, M. R., Naik, R., & Ling, W. (2012). Health-related quality of life changes associated with buprenorphine treatment for opioid dependence. *Quality of Life Research, 21*(7), 1177–1183.

Rice, J. B., White, A. G., Birnbaum, H. G., Schiller, M., Brown, D. A., & Roland, C. L. (2012). A model to identify patients at risk for prescription opioid abuse, dependence, and misuse. *Pain Medicine, 13*(9), 1162–1173.

December 1, 2012, Through May 31, 2013

Seven articles met the selection criteria for the Treatment Improvement Protocol (TIP) 54 literature review update for this period.

Chronic Pain Entering Substance Abuse Treatment

Barry et al. (2013) assessed the need for chronic pain (CP) treatment among a group of individuals seeking substance abuse treatment. They surveyed 244 people entering office-based treatment with buprenorphine–naloxone combination medication for opioid dependence. Thirty-six percent (n=88) of respondents reported having CP, defined as pain lasting at least 3 months; another 36 percent (n=87) reported having some pain (SP), defined as pain being felt in the past week and not meeting the definition of CP.

People experiencing CP were older than the SP survey respondents. No difference in gender was found between the two groups. The CP group reported pain that was more frequent, greater, more intense, and of longer duration. Back and leg were the most frequently mentioned pain sites for both the CP and the SP groups. The most commonly cited cause of pain for the CP group was "accident"; this was followed by "nerve damage" and "don't know." SP group members reported "other," "accident," and "don't know" as the most common causes of their pain.

Members of both groups abused or misused substances to ease their pain. That is, people in both groups reported that during the past week they took more than their prescribed opioid medication, took someone else's prescription opioid medication, or used heroin, other illicit drugs, or alcohol to relieve their pain.

This article supports the information in the TIP that states that people with substance use disorders (SUDs) have high rates of pain and that people entering SUD treatment should be assessed for pain.

Nonmedical Use of Opioids

Bohnert et al. (2013) studied the nonmedical use of prescription opioids in a group of adults entering a large SUD residential treatment program. This study concentrated on the differences between nonmedical use of prescription opioids for self-treatment of pain and other motivations for opioid use. The researchers compared those who engaged in nonmedical use of prescription opioids for reasons other than pain relief with those who used these types of substances for pain relief only.

The study was a cross-sectional self-report survey. Participants were asked to report whether they had used opioids during the past 30 days for pain or for reasons other than pain relief (e.g., help sleep, improve mood, relieve stress, cope with positive and negative emotions and experiences). A total of 351 individuals completed the survey. The vast majority were not entering treatment for opioid medication abuse but were seeking treatment for dependence on other substances. These substances and the corresponding percentages were 30.2 percent for alcohol, 19.4 percent for heroin, 16.0 percent for cocaine, 9.7 percent for marijuana, 4.0 percent for opioids other than heroin, and 20.8 percent stated other or the data were missing. Of the

sample, 238 (68%) reported past-month nonmedical use of opioid medications. Exhibit 1 presents the percentages of participants who used nonmedical opioid medications for pain relief only and those who used such medications for other reasons.

Exhibit 1 Distribution of Past-Month Nonmedical Prescription Opioid (PO) Use, by Motives for Use

Motive	Number (*N*=238)	Percentage
Heavy PO use, pain relief use only	9	4
Heavy PO use, other reasons for use	69	29
No heavy PO use, pain relief use only	72	30
No heavy PO use, other reasons for use	88	37

Use not related to pain was more common (66%) than use for pain relief only (34%). Those who used for non-pain-related reasons were more likely to report heavy use than those who used for pain relief only (43% versus 11%). They were also more likely to have a history of overdose, heroin use, and barbiturate and other sedative use. In addition, participants whose prescription opioid use was nonpain related had more depressive symptoms and worse mental health in general. They also expected more pleasure/social enhancement and greater reductions in pain and negative experiences to result from the opioid use than did the pain-relief-only group. Participants who reported use for reasons other than pain relief were more likely to be female, White, and younger.

Because this survey was done in a residential treatment center, it may not be generalizable to other settings such as outpatient treatment centers. However, given both the level of pain among people entering SUD treatment and the use of prescription opioids for non-pain-related reasons, it may be advisable to assess for the presence of pain (frequency, severity, and condition) and for the reasons (in addition to pain) for the nonmedical use of prescription opioids. This information may help with SUD treatment planning and in making treatment more individualized.

The authors concluded, “The findings of the present study indicate those who use prescription opioids for pain relief only may have less severe substance use and mental health concerns than those who use for reasons other than pain relief, but additional treatment (beyond that traditionally incorporated in addictions settings) focused on pain may be helpful for individuals who are using opioids beyond their prescribed dose in order to treat their pain” (Bohnert et al., 2013, p. 1781).

Dhingra et al. (2013) performed a study to identify the prevalence and correlates of pain among a group of patients in methadone maintenance treatment (MMT) programs. They used secondary data from a hepatitis care coordination trial. The study was a randomized controlled trial of 489 patients (31.8% women; 36.0% non-Hispanic White, 30.3% Hispanic, 29.4% non-Hispanic Black).

They found clinically significant pain in almost half the patients and found that the pain was associated with medical and mental disorders. The pain was often treated with other opioids and was not associated with measures of drug use.

Many patients had additional disorders or issues: 60.1 percent had hepatitis C, 10.6 percent had HIV, 46.8 percent had symptoms of moderate or severe depression, and approximately half of the study sample had another co-occurring medical condition. These factors may complicate both pain and SUD treatment.

Findings included:

- 237 patients (48.5%) had clinically significant pain (>5 on a scale of 1 to 10).
- 76 (15.5%) had nonclinically significant pain (≤5 on a scale of 1 to 10).
- 176 (36.0%) had no pain.

Of those with clinically significant pain, 46.7 percent had pain classified as greater than 7, which in this study was considered severe pain. Unexpectedly, the authors found that neither hepatitis C nor HIV was associated with pain.

Pain treatments included prescribed opioids (38.8%), prescribed nonopioids (48.9%), and self-management approaches (60.8%) including prayer (33.8%), vitamins (29.5%), and distraction (12.7%). Pain was associated with higher methadone dose, prescribed opioid therapy, and more severe depressive symptoms; it was not associated with positive urine drug test results or self-reported substance use. The authors stated that the association of pain and higher methadone dose was a unique finding and postulated that patients with more severe addictive disorders have more severe pain or that practitioners in MMT may try to treat pain as well as addiction with once-daily methadone dosing, which is not effective for pain control.

Urine Drug Monitoring

Clancy, O'Connell, and Couto (2013) conducted an online survey to determine how urine drug monitoring (UDM) is used in clinical practice when treating chronic pain. Survey invitation letters were sent to 1,014 randomly selected clinicians who used UDM in their practices; 93 responded. The two most common specialties reported were pain management (35%) and family practice (27%). Ninety-two percent of participants reported prescribing chronic opioid therapy (COT) for more than 10 patients per week.

In answer to the question "when to test and how often," 76 percent (n=72) responded that they require all new patients to have UDM performed when beginning treatment. The most commonly cited patient characteristics influencing the frequency of UDM were aberrant behaviors and a history of substance abuse. Less common were history of mental illness, family history of substance abuse, and patient demographics. Forty-one percent of the clinicians reported testing patients four times per year, 25 percent reported testing two times per year, and 13 percent reported testing six times per year. Frequency of UDM for the remaining 21 percent ranged from more than once per month to less than once a year.

When asked which substances are important to detect, participants were asked to answer whether testing for the substance was "imperative," "helpful," or of "little value." Cocaine, methamphetamine, heroin, amphetamines, phencyclidine, marijuana, and ecstasy were rated as imperative to test for by at least 60 percent of respondents. They also tested for the majority of

opioids (e.g., oxycodone, morphine, methadone, hydrocodone) and some prescription medications that can be abused (e.g., benzodiazepines, barbiturates).

Many different types of answers were received to the question of what practitioners do if a patient who is receiving COT has an unexpected urine test result (i.e., positive for illicit drugs or negative for the prescribed medication). With a positive urine test result for an illicit drug, the most commonly reported actions were to discharge the patient, discuss the result with the patient, discontinue COT, or review the pain treatment agreement with the patient. However, practitioners had a different reaction to positive urine test results for marijuana versus other illicit drugs. In comparison with other illicit drugs, practitioners tended to be more lenient when UDM results were positive for marijuana. If a patient tested positive for opioid use, many practitioners stated they would review the pain treatment agreement with the patient, discuss the result with the patient, or place the patient on probation with possible termination of COT. If the test result was negative for a prescribed opioid, the reactions were similar to those above: discuss the result with the patient, review the pain treatment agreement with the patient, or place the patient on probation with possible termination of COT.

The authors concluded that this survey found a general consensus among respondents regarding which patients to monitor, the frequency of UDM, and the substances most important to detect. There was, however, a wide range of answers for the actions taken regarding test results.

Buprenorphine

Neumann et al. (2013) ran a small preliminary study and concluded that both buprenorphine/naloxone (BUP/NLX) and methadone treatment for 6 months reduced nonmalignant chronic pain (NMCP) in participants with co-occurring dependence on prescription opioids used to treat pain. Fifty-four participants were randomized to two groups. One group received BUP/NLX, and the other group received methadone. The medications were supposed to treat both the opioid dependence and the NMCP. All participants were asked to refrain from taking any opioid medications, illicit drugs, or alcohol. Approximately one-quarter of participants changed medications because they thought the medications were either not controlling their pain or not controlling their cravings for opioids.

All participants had some form of spinal disorder causing the NMCP. The majority of participants had been treated for a mental illness (n=28, 51.9%) and had a family history of substance abuse (n=31, 57.4%).

Participants were followed monthly for 6 months. Pain was rated on a scale of 1 to 10. Thirteen participants in each group completed the study. Both treatments produced analgesia. No statistical differences were found between those who dropped out of the study and those who completed it. No differences were found between the BUP/NLX group and the methadone group as far as treatment retention or pain relief. No participants in the methadone group reported using opioids, compared with five participants in the BUP/NLX group; this difference was statistically significant. In addition, family members noticed an improvement in terms of personality, mood, energy, motivation, coping with pain, and functioning; however, improvement in functioning was not statistically significant between the two groups.

The study had several limitations. It was limited to 54 participants and had a dropout rate of more than half (26 people completed the study). It used a convenience sample of people seeking treatment for opioid dependence who had NMCP. It was not a randomized, double-blind, placebo-based trial.

Pade, Cardon, Hoffman, and Geppert (2012) performed a retrospective chart review to ascertain the results of a quality improvement project in primary care. The project used BUP/NLX to treat co-occurring chronic noncancer pain (CNCP) and opioid dependence in a primary care setting. The study was performed in the Co-occurring Disorders Clinic for veterans, which was established to treat co-occurring chronic pain and substance use problems. The authors considered this approach to be an innovative clinical model that suggests that both CNCP and opioid dependence can be successfully treated at the same time and in a primary care setting.

Data from the charts were collected for 143 patients who had both CNCP and opioid dependence; 71 percent also had psychiatric diagnoses, the most common being major depressive disorder (49%) and posttraumatic stress disorder (30%). Many also had an SUD in addition to opioid dependence, the most common being alcohol abuse or dependence (n=59, 42%). Most patients reported more than one pain complaint: 56 percent had only musculoskeletal complaints, 39 percent had mixed nociceptive and neuropathic pain, 55 percent had low back pain, 9 percent had chronic headaches, and 4 percent had fibromyalgia. Most patients were male (93%).

All patients were inducted onto BUP/NLX treatment. Instead of a single daily dose for addiction treatment, patients received two or three BUP/NLX maintenance doses daily to treat both the CNCP and the opioid dependence. (At the clinic, BUP/NLX therapy is discontinued for patients who use opioids without clinic consent, have more than two urine toxicology screens positive for illicit drugs, miss more than two visits, or request early refills more than twice. These patients are referred for more intensive SUD treatment.)

Of the 143 patients who began taking BUP/NLX, 93 (65%) continued on BUP/NLX; 60 of the 93 (65%) continued taking it longer than 6 months. Of the 50 patients no longer prescribed BUP/NLX in the study, 7 were no longer taking any opioids, and those who continued to require opioid agonists to manage their chronic pain condition were using lower doses than prescribed before receiving the BUP/NLX.

The authors had hypothesized that treating CNCP with BUP/NLX would be inadequate. However, average pain scores did not increase; conversely, pain scores showed a modest, yet statistically significant, improvement for patients taking BUP/NLX.

Review Articles of Interest

The following are not original research studies. They are review articles or position statements, and much of the information presented is covered in TIP 54. They may be of interest to the reader, however.

1. Eyler, E. C. (2013). Chronic and acute pain and pain management for patients in methadone maintenance treatment. *American Journal on Addictions, 22*(1), 75–83.

2. Haroutiunian, S., McNicol, E. D., & Lipman, A. G. (2012). Methadone for chronic non-cancer pain in adults. *Cochrane Database of Systematic Reviews.* doi:10.1002/14651858.CD008025.pub2.

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