Opioid Use by Patients in an Orthopedics Spine Clinic

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Objective. Concerns regarding the efficacy, toxicity, tolerance, dependence, and abuse of opioids have limited their use for patients with chronic spine pain. In our previous study of rheumatology clinic patients, opioid analgesics were found to be highly effective, produced only mild side effects, and had few instances of opioid abuse. The purpose of this study was to replicate our previous study in another large cohort of patients with nonmalignant pain due to well-defined spinal diseases.

Methods. Opioid use was studied in 230 orthopedics spine clinic patients by retrospective analysis of prescriptions for 3 years and cross-sectional analysis of efficacy and toxicity by patient interviews. Opioid use and stability of the daily dose over 3 years were derived from computerized pharmacy records. Medical records, operative reports, and radiographic studies were reviewed to determine the reason for dosage escalations and to detect instances of abuse or addiction behaviors. Patients were interviewed to determine the efficacy, frequency, and types of side effects and instances of obtaining opioids from sources outside the Veterans Affairs system.

Results. Opioids were prescribed for 152 of the 230 patients, for <3 months (short-term [STO]) in 94, ≥3 months (long-term [LTO]) in 58, and none in 72 (no opioid [NTO]). Medications prescribed were codeine, oxycodone, propoxyphene, tramadol, morphine, meperidine, fentanyl, or hydroxycodone, either alone or in combination. Interviews were completed in 72 STO, 50 LTO, and 45 NTO patients. Pain severity (0–10 scale) was not different in patients with different spinal pathologies. Opioids significantly reduced the back pain severity score from 8.3 ± 1.5 to 4.5 ± 2.2 (mean ± SD). Mild side effects (most commonly, constipation and sedation) were reported by 58% of the opioid-treated patients but rarely caused them to stop taking the medication. There was no significant increase from the mean ± SD initial opioid dosage of 5.0 ± 12.2 30-mg codeine equivalents per day (30 mg oral codeine = 5 mg oral morphine) to the mean peak dosage of 7.9 ± 12.5 and the mean recent dosage of 4.3 ± 6.3, suggesting that tolerance to opioid analgesia did not appear to occur in these patients. Dosage escalations of >2 30-mg codeine equivalents occurred 19 times in 17 LTO patients and was due to worsening of the underlying painful condition, complications of spine surgery, or unrelated surgical or medical problems in all but 3 of them (5%). These 3 patients also displayed other abuse behaviors. Abuse behaviors were not more frequent in those with or without a history of abuse/addiction.

Conclusion. This study provides data on the efficacy, toxicity, tolerance, and abuse or addiction behaviors with opioid therapy in a large cohort of patients in an orthopedics spine clinic. The results provide objective data from patients with well-defined spine diagnoses to challenge the position that opioid treatment is inappropriate for chronic nonmalignant pain. This study provides clinical evidence to support and protect physicians treating patients with chronic musculoskeletal diseases, who may be reluctant to prescribe opioids because of possible sanctions from regulatory agencies. More important, it will benefit patients by permitting them to receive these effective, safe medications.

Chronic back pain is a most challenging clinical problem, costing an estimated 50–100 billion dollars per year (1) and requiring 15 million office visits per year (2) in the US. There are conflicting opinions regarding the appropriateness of opioids for the treatment of chronic back pain because of concerns about efficacy and toxi-
city and the development of tolerance, dependence, addiction, and abuse (3–6). Some physicians fear regulatory sanctions and legal penalties for prescribing long-term opioids for treatment of chronic nonmalignant pain (7,8).

This negative view of opioid treatment for chronic back pain is slowly changing (9). In 1993, Schofferman reviewed the literature and concluded that “long-term opioid treatment for nonmalignant pain is not appropriate for the large majority of patients and . . . that most patients do worse, not better” (10). More recently, his own clinical trial of opioids in 33 patients with chronic back pain demonstrated improvement in 75% of the patients, and he concluded that opioid therapy is reasonable treatment (11). Experience with long-term opioid treatment for cancer pain has demonstrated sustained analgesia without the anticipated development of tolerance, serious side effects, or addiction/abuse behaviors (12–14). Studies of opioids for nonmalignant pain have shown minimal risk of addiction or abuse behaviors in patients with burns (15), sickle cell disease (16), restless legs syndrome (17), rheumatic diseases (18,19), and neuropathic pain (20), as have surveys of hundreds of patients with diverse nonmalignant pain syndromes (3,21). In a joint statement, the American Academy of Pain Medicine and the American Pain Society acknowledged that concerns about addiction, side effects, and fear of regulation contributed to the vast undermanagement of chronic pain (22).

The purpose of this study was to evaluate the efficacy of opioid therapy and define the incidence of opioid toxicity, tolerance, and addiction/abuse behaviors in a large cohort of patients with defined spinal diseases. If fears of opioid toxicity, tolerance, addiction, and abuse/addiction are not warranted by actual occurrence, then patients with chronic spinal pain are unnecessarily being denied analgesic medications.

PATIENTS AND METHODS

Patient population. All patients examined in the Orthopedics Spine Clinic of the Minneapolis Veterans Affairs Medical Center (VAMC) between April and December 1997 (n = 230) were studied by cross-sectional analysis of their demographics, addiction history, and opioid efficacy and toxicity using patient interviews. Medication use was analyzed retrospectively for 3 years. Exclusion criteria were the absence of Minneapolis VAMC pharmacy records, patient report of obtaining opioids outside of the VA system, and patient report of being prescribed opioids for pain unrelated to the spine.

Data collection. Data were obtained from computerized pharmacy records, patient interviews, medical records, operative reports, and radiographic imaging studies. All patients who received 1 or more prescriptions for an opioid in the previous 3 years were identified. Four patients had no VAMC pharmacy record. Opioid prescription ascertainment in the pharmacy database was verified 6 months later by reexamining pharmacy records for each patient originally identified as not having received an opioid prescription. No additional opioid prescriptions were identified. The following data were collected: demographics, diagnosis, disease duration, opioid used (preparation, dosage, number of pills per day, number of days taken per week, and source of prescription), quantitative and qualitative assessment of opioid efficacy and toxicity, and history of substance abuse (alcohol or illicit drugs). Diagnoses were coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification.

The cohort was divided into 3 groups according to the opioid prescriptions identified in the pharmacy database: long-term opioid (LTO) use if prescriptions were filled for ≥3 consecutive months, short-term opioid (STO) use if prescriptions were filled for <3 consecutive months, and no opioid (NTO) use. To calculate a comparable mean daily dose for each patient, doses of opioid medications were converted to equivalents of 30 mg of codeine (C-30 equivalents; 30 mg of oral codeine is approximately equivalent to 5 mg of oral morphine). The initial, peak, and most recent daily dosages were calculated from the pharmacy records to search for evidence of opioid tolerance with long-term opioid use. Escalation of the mean daily dose of opioid was defined as an increase of ≥2 C-30 equivalents per day. The medical and surgical records were reviewed to determine whether increases in the mean daily opioid dose were attributable to increased pain severity due to disease progression, a surgical or medical complication, or were indicative of tolerance or loss of control of opioid use.

Statistical methods. Using analysis of variance and chi-square analysis (StatView 5.0.1 software; SAS Institute, Cary, NC), we compared the demographic data, diagnoses, and disease duration among the LTO, STO, and NTO groups; opioid efficacy was analyzed according to the duration of opioid use and across individual diagnoses of spinal conditions. The incidence of side effects reported was compared among the LTO, STO, and NTO groups. Post hoc comparisons of group means were made with Student’s t-tests. Because of multiple comparisons in this study, a P value of 0.0016 was selected for significance (0.05/30 = 0.0016). Fisher’s exact test was used to examine the relationship between a history of abuse/addiction and the display of abuse behaviors (StatView 5.0). Probabilities of displaying abuse behaviors in groups with and without a history of abuse/addiction were used to calculate the relative risk from having a history of abuse/addiction, and 95% confidence intervals (95% CI) were constructed through logarithmic transformation (23).

RESULTS

We identified 230 patients who were treated in the Orthopedics Spine Clinic during the study period (Figure 1). Individual medication prescriptions were extracted from the computerized pharmacy records.
Prescriptions for opioids in the previous 3 years were found for 152 patients (66% of the study cohort); 94 patients filled opioid prescriptions for ≥3 consecutive months, 58 patients filled opioid prescriptions for ≥3 consecutive months. Seventy-four patients did not have prescriptions for opioids. Data on opioid efficacy, toxicity, and tolerance were excluded from 4 patients who did not have a VAMC pharmacy record, from 7 patients who obtained opioids outside the VA system because the prescriptions could not be verified, and from 28 patients who were prescribed opioids for nonspinal pain problems before they were evaluated in the spine clinic (2 LTO and 26 STO patients).

We interviewed 169 (73%) patients in the cohort. Interview data were incomplete in 5 patients (3%; 1 LTO, 1 STO, and 3 NTO) because of cognitive or hearing impairments that limited interview responses. There were no significant differences in age, sex, or disease duration among the 3 groups (Table 1).

The diagnoses made in the spine clinic are presented in Table 2. Intervertebral disc disease with and without myelopathy and spinal stenosis were the most common causes of spinal pain in the Spine Clinic cohort (65% of the patients).

Opioid analgesics prescribed during the 3-year study period are shown in Table 3. Codeine was the most frequently prescribed opioid, and it was almost always prescribed as acetaminophen with 30 mg of codeine.

### Efficacy of opioids for spinal pain

Opioids reduced the severity of spinal pain from a mean ± SD score of 8.3 ± 1.5 to 4.5 ± 2.2 (on a 0–10 scale), a change that is both statistically significant (P < 0.0001) and clinically important (24). Subgroup analyses of patients based on spinal diagnosis and treatment group did not demonstrate any significant differences in pain severity among patients with different spinal disease diagnoses (Figure 2A). Reduction of pain severity was significant across all diagnoses (P < 0.001).

### Table 1. Characteristics of the study patients, by opioid prescription group*

<table>
<thead>
<tr>
<th></th>
<th>Total cohort (n = 230)</th>
<th>Short-term (≤3 months) opioid prescriptions (n = 94)</th>
<th>Long-term (≥3 months) opioid prescriptions (n = 58)</th>
<th>No opioid prescriptions (controls) (n = 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD years</td>
<td>59 ± 14</td>
<td>59 ± 14</td>
<td>59 ± 14</td>
<td>60 ± 15</td>
</tr>
<tr>
<td>% male</td>
<td>92.2</td>
<td>95.7</td>
<td>94.8</td>
<td>91.2</td>
</tr>
<tr>
<td>Duration of spine disease, mean ± SD years</td>
<td>13 ± 13.8</td>
<td>18.6 ± 15.9</td>
<td>16 ± 16.6</td>
<td>10.8 ± 14</td>
</tr>
</tbody>
</table>

*There were no significant differences in these characteristics among the 3 treatment groups (P = 0.77).
To determine whether opioid responsiveness decreased with longer duration of opioid treatment (i.e., opioid tolerance), we compared the decrease in pain severity in the group treated for 3 months as well as in the group treated for 3 months (Figures 2B and C).

The pain severity decreased from 8.6 ± 1.3 to 5.0 ± 2.5 (P < 0.0001) in those treated for 3 months and from 8.0 ± 1.6 to 3.9 ± 1.9 (P < 0.0001) in those treated for ≥3 months. Therefore, we did not find evidence for loss of opioid efficacy with longer duration of opioid treatment. In the subgroup analyses, the reduction in pain severity across all diagnoses was not less in those treated with long-term opioids (Figures 2B and C).

### Table 2. Diagnoses in patients of the Orthopedics Spine Clinic cohort*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (%) of study cohort (n = 230)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervertebral disc disease</td>
<td></td>
</tr>
<tr>
<td>Without myelopathy</td>
<td>55 (24)</td>
</tr>
<tr>
<td>With myelopathy</td>
<td>38 (17)</td>
</tr>
<tr>
<td>Spinal stenosis</td>
<td>55 (24)</td>
</tr>
<tr>
<td>Persistent low back pain after surgery</td>
<td>21 (9)</td>
</tr>
<tr>
<td>Spondylolisthesis</td>
<td>22 (10)</td>
</tr>
<tr>
<td>Lumbar spondylolisthesis</td>
<td></td>
</tr>
<tr>
<td>Without myelopathy</td>
<td>15 (7)</td>
</tr>
<tr>
<td>With myelopathy</td>
<td>7 (3)</td>
</tr>
<tr>
<td>Osteoporotic vertebral compression fracture</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Nonspecific low back pain disease</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Discitis</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Scoliosis and kyphoscoliosis</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Nonspecific cause of pain</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

* Persistent low back pain after surgery represents low back pain that was unrelieved by spinal surgery or was recurrent, with loosening or failure of the fixation device. Nonspecific low back pain disease represents chronic low back pain with normal findings on radiographs. Nonspecific cause of pain represents vascular insufficiency causing limb pain. There were no significant differences among the 3 treatment groups (data not shown).

### Table 3. Opioid analgesics prescribed during the 3-year study period*

<table>
<thead>
<tr>
<th>Medications</th>
<th>All opioid prescriptions (n = 236)</th>
<th>Short-term (≤3 months) opioid prescriptions (n = 134)</th>
<th>Long-term (≥3 months) opioid prescriptions (n = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>120 (79)</td>
<td>76 (81)</td>
<td>44 (76)</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>48 (32)</td>
<td>26 (28)</td>
<td>22 (38)</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>30 (18)</td>
<td>20 (21)</td>
<td>10 (17)</td>
</tr>
<tr>
<td>Tramadol</td>
<td>18 (12)</td>
<td>7 (7)</td>
<td>11 (19)</td>
</tr>
<tr>
<td>Morphine</td>
<td>9 (6)</td>
<td>2 (2)</td>
<td>7 (12)</td>
</tr>
<tr>
<td>Meperidine</td>
<td>6 (4)</td>
<td>3 (3)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>4 (3)</td>
<td>0</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>1 (1)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

* The total number of prescriptions for each medication exceeds the number of patients in the study cohort because 6 patients taking short-term opioids and 10 taking long-term opioids were prescribed >1 opioid at a time, and some patients had >1 short-term or long-term course of opioid therapy during the 3-year study period. Most patients (91%) were prescribed only 1 opioid at a time. In the long-term opioid group, 13 patients (23%) took opioids for 1–3 years and 43 patients (77%) took opioids for 3–12 months. Thirty milligrams of oral codeine is approximately equivalent to 5 mg of oral morphine. Numbers in parentheses are the percentage of patients prescribed the drug.
During the interview, 28 of the 45 NTO patients reported taking prescription or over-the-counter nonsteroidal antiinflammatory drugs (NSAIDs; ibuprofen, salicylate, piroxicam, naproxen, clinoril) or acetaminophen for pain and said these nonopioid analgesics reduced pain severity from 7.7/10 to 4.9/10 (P = 0.0001).

The mean SD reduction of pain severity was 52/19% with LTO compared with 37/30% reduction with the nonopioid analgesics (P = 0.036).

Analysis of the distribution of changes in pain severity scores (Figure 3) revealed that more LTO patients (69%) than STO patients (45%) experienced at least a 50% reduction in pain severity (χ² = 23.9, P = 0.0006). As with the quantitative decrease in pain severity, the percentage of patients reporting “a lot” of relief with longer duration of opioid treatment (54% of LTO patients) was greater, not less, than the percentage of those treated with opioids for <3 months (40% of STO patients). This finding further supports the lack of tolerance to opioid analgesia in this study cohort.

Medication side effects. Medication side effects were common in all 3 treatment groups (58%), occurring in 59% of STO patients, 73% of LTO patients, and 37% of those taking nonopioid analgesics. Constipation (49%) and sedation (31%) were the most common opioid side effects and usually did not cause the patient to stop the opioid because the symptoms were mild and transient or were easily managed. Two LTO patients had poorly managed constipation while taking codeine and were switched to oxycodone without further problems. Other side effects, such as dizziness, sedation, nausea, itching, and headache, affected <15% of the opioid-treated patients. None of the LTO patients stopped opioids because of side effects. Three STO patients (4%) stopped codeine because of confusion and sedation, dyspepsia, and constipation. In the NTO group, dyspepsia and bruising were the most common side effects from NSAIDs and acetaminophen, and 1 patient reported stopping ibuprofen because of gastrointestinal bleeding.

Opioid tolerance and abuse. Escalation of the daily dose of opioid was considered possible evidence for the development of tolerance to opioids with long-term treatment. All prescriptions in the pharmacy records were converted to 30-mg codeine equivalents (for reference, 30 mg of oral codeine is equivalent to 5 mg of oral morphine), and the mean initial, peak, and most recent or end daily dose were calculated using published dose equivalents (25).

There were small, nonsignificant changes in the

![Figure 3](cumulative_distribution_of_change_in_pain_severity_scores.png)

**Figure 3.** Cumulative distribution of change in pain severity scores. The cumulative change in pain severity scores with short-term (STO; <3 months) and long-term (LTO; ≥3 months) opioid treatment was calculated. Data points are the percentages of patients reporting at least the amount of pain relief depicted on the x-axis (e.g., 50% pain relief or better was reported by 45% of the STO group and by 69% of the LTO group).

![Figure 4](efficacy_of_opioid_therapy.png)

**Figure 4.** Efficacy of opioid therapy, as determined by qualitative assessment of pain relief. Patients were asked, “Did the pain medication help your pain?” Choices of response were “not at all,” “a little,” “some,” or “a lot.” Significantly more patients in the long-term opioid (LTO; ≥3 months) group reported “a lot” of pain relief as compared with patients in the group not taking opioids (NTO) (P = 0.0006). STO = short-term opioid (<3 months) group.
The mean ± SD initial opioid dosage was 5.0 ± 12.2 C-30 equivalents per day, the mean peak dosage was 7.9 ± 12.5 (P = 0.18), and the mean recent or end dosage was 4.3 ± 6.3 (P = 0.696). The lack of significant increase in the mean daily dose of opioid over time is further evidence against the development of opioid tolerance in this cohort.

There were 19 escalations of the average daily dose of opioid over time. The mean ± SD initial opioid dosage was 5.0 ± 12.2 C-30 equivalents per day, the mean peak dosage was 7.9 ± 12.5 (P = 0.18), and the mean recent or end dosage was 4.3 ± 6.3 (P = 0.696). The lack of significant increase in the mean daily dose of opioid over time is further evidence against the development of opioid tolerance in this cohort.

There were 19 escalations of the average daily dose of opioid during the 3-year study period (Figure 5). Sixteen dosage escalations were related to worsening of the underlying disorder, complications of spinal surgery, or development of an unrelated painful problem. In 3 patients, there was no medical explanation for the increased need for opioids, and these likely represented tolerance and/or abuse.

Opioid dependence and symptoms of opioid withdrawal were not assessed directly in this study; however, 33% of LTO patients reported that they did not take the opioid on a daily basis, which suggests that physical dependence to opioids had not developed. Some patients reported that they did not take pain medications every day because they were afraid of becoming addicted to them. To examine the relationship between a history of substance abuse and the development of addiction and/or abuse behaviors during treatment with opioids, we compared the occurrence of abuse behaviors in those with and without a history of substance abuse. During the structured interview, patients were asked about their history of addiction to alcohol and street drugs, participation in a substance abuse treatment program, medical and legal complications of substance abuse, and current alcohol use.

Self-reported history of abuse and/or addiction was common, occurring in 44% of the total cohort (45%, 43%, and 46% of the STO, LTO, and NTO treatment groups, respectively). The frequency of abuse behaviors during opioid treatment was only 5%, and the probability of the observed frequency of abuse behaviors in those with a history of abuse/addiction was not significantly different from that in those without a history of substance abuse. Therefore, the data from this study did not support the hypothesis that abuse behaviors would be more frequent in individuals with a history of abuse/addiction.

DISCUSSION
The results from this study add to the growing base of evidence supporting the appropriateness of
opioids for treating chronic musculoskeletal pain in general and pain due to spine disorders in particular. Opioids were very effective in reducing the severity of spine pain and in producing pain relief. Opioid efficacy was greater in the LTO group than in the STO group, indicating that opioid efficacy was sustained from 3 months up to 3 years in this study. These results are similar to those in our previous study of opioid use in patients with well-defined rheumatic diseases (18). In that study, rheumatic disease pain severity decreased from 8.2 to 3.6 in the STO patients and from 8.3 to 3.6 in the LTO patients. These data should reduce physician skepticism regarding the long-term efficacy and safety of opioids and lessen the concern about causing iatrogenic tolerance, dependence, and abuse or addiction (5,26).

There are no prospective randomized controlled trials that compare long-term treatment with acetaminophen, NSAIDs, and opioids against each other or against a placebo in patients with chronic back pain (27). Previous reports of opioid effectiveness in patients with chronic nonmalignant pain included patients with heterogeneous diagnoses (28–30). There are only a few prospective trials of long-term (≥3 months) opioid treatment of chronic nonmalignant pain for 16 weeks to 32 months that demonstrate a reduction in pain severity and disability related to pain (6,11,19,20,31,32). One study with negative results was reported from a multidisciplinary pain clinic (33). A randomized double-blind, active-placebo–controlled, crossover study compared sustained-release morphine and benztropine in 46 patients with noncancer pain that was resistant to treatment with codeine, tricyclic antidepressants, and NSAIDs. Minimal analgesic effects were observed with 6 weeks of morphine treatment at dosages of up to 120 mg/day. The authors commented that the patients had elevated depression scores, and they theorized that an analgesic response may not occur “if there is a major affective component to the pain or if learned pain behavior is the main problem” (33).

Tolerance refers to the diminution of a drug effect due to exposure to the drug (9) and can be demonstrated in a variety of animal experiments using repeated injections of opioids and using brief noxious stimuli to produce acute pain (34). In humans, the street addict’s need for dosage escalation is a well-recognized phenomenon that raises legitimate concerns about tolerance with long-term opioid use. The mechanisms that cause opioid tolerance have not been explained (35). Colpaert et al demonstrated that coadministration of persistent noxious stimuli to rat hind paws significantly attenuated the development of tolerance to fentanyl (36) and found that rats with adjuvant arthritis self-administered oral fentanyl in doses that paralleled the severity of the arthritis and did not develop opioid tolerance (37).

We sought evidence for the development of tolerance in this study; however, there was no loss of pain relief with a longer duration of opioid treatment, and there was no significant increase in the mean daily dose of opioid over time. Opioid dosage escalations were associated with progression of the underlying painful process, a surgical complication, or development of a new painful medical problem in all but 3 patients. These 3 patients probably had developed opioid tolerance, and their abuse behaviors were difficult to manage. These observations support the concept that a need for increased doses of analgesics has a differential diagnosis that requires a complete evaluation to identify before it is attributed to tolerance: progression of underlying pathology, failure or complication of surgical treatment, appearance of a new or different painful problem, a change in drug metabolism, increased psychological distress, or impaired cognition (delirium). The data from this study add to the accumulating clinical experience that problems of tolerance and abuse that have been anticipated based on results of animal experiments and evaluations of pain-free drug addicts are not common in patients with cancer pain (12,38) and chronic nonmalignant pain (3,18–20,28,29,39–45). These observations also support Colpaert’s theory that chronic nociceptive stimuli can modulate or prevent the development of opioid tolerance (35).

Concerns about the safety of therapy are important for patients who need long-term analgesics. Portenoy (3) emphasized that there are no major organ or irreversible toxicities due to long-term opioid use. The side effects reported in our study are similar to those in previous reports (46); however, sedation and dizziness were less frequent than in studies of shorter duration. A prospective, comprehensive, multidimensional assessment (pain, mood, cognitive function) of 19 patients treated with long-acting opioids and 10 patients treated with short-acting opioids failed to demonstrate a clinically significant decline in cognitive abilities, but noted improvement in sustained attention and psychomotor speed (5). The ability to drive a motor vehicle while taking opioids was normal (47), and the risk of injurious motor vehicle accidents was not increased in persons over the age of 65 years who were taking oral opioids (48). Nevertheless, patients should be advised not to drive a car if they experience sedation and should be
Physicians, patients, and families fear the development of an addiction disorder as a result of treatment with opioids; however, addiction behaviors have not been adequately studied in patients who take opioids because of chronic pain (3). A study of opioid use in patients of 2 primary care clinics reported that a history of substance abuse disorder and younger age were significant independent predictors of abuse behaviors (49). There are important differences between this study and our study. In the study by Reid et al (49), a single report of lost or stolen medications, 2 requests for early refills, or obtaining opioids from other sources were designated as abuse behaviors. Patients were not examined to determine whether these behaviors represented inadequate pain relief rather than “opioid abuse.” In the clinical setting with patients who have progressive, painful diseases, behaviors that are not extreme or outright illegal may be difficult to assess. Inadequately treated pain induces drug-seeking behaviors, which are often misinterpreted as evidence of drug addiction (3). Findings from our previous study of 290 opioid-treated rheumatology patients (18) and from the current study of 152 opioid-treated spine clinic patients are similar to those from the studies by Haythornwaite et al (5) and Moulin et al (33), in which opioid therapy for nonmalignant pain was not commonly associated with abuse and addiction.

What remains at issue is whether patients with a history of substance abuse disorder are at greater risk of developing abuse and/or addiction when prescribed long-term opioids for painful conditions (3,50–52). A substance abuse disorder history was reported in 54% of chronic pain patients and 52% of nonpain patients in a family practice clinic (52), which is similar to our spine clinic cohort (44%) and our rheumatology clinic cohort (33%) (18). In our 2 studies, a history of substance abuse/addiction did not predict which patients would display abuse/addiction behaviors when treated with long-term opioids. Therefore, all patients started on long-term opioid therapy should be advised of the small, but important, risk of opioid addiction as well as how they will be carefully managed to prevent abuse behaviors (53).

This study has noteworthy strengths and weaknesses that merit comment. The major strengths are the inclusion of all patients attending the Orthopedics Spine Clinic, the high interview response rates, and the use of the computerized VAMC pharmacy database to monitor medication use and to verify medication dosages and interview data. Observational studies have inherent limitations because there is an unavoidable risk of selection bias, and unrecognized confounding factors may have distorted the results (54,55). Nevertheless, observational studies such as this one may be more representative of treatments that are tailored to the individual patient, as is done in clinical practice (56). Patient report of pain severity is always subjective, and clinicians must evaluate the patient’s self-report of response to treatment (57). Patient reports of pain severity might have been subject to recall bias, because patients may overestimate or underestimate the severity of their pain. However, it is unlikely that they overestimated the first pain level and underestimated the second pain level in a consistent manner, so the calculated change in pain severity was probably not unduly influenced. The high rate of side effects reported may be an overestimate, since such reports might have been confounded by side effects from other medications taken for comorbid conditions. No patients reported stopping the opioid medication because of side effects, and there was no major organ toxicity.

The generalizability of these results is limited because the patients were predominantly male, attended a subspecialty clinic, and had more severe and or more complex spine disease than do patients in primary care clinics with a higher proportion of younger females. Because of the small number of patients with nonspecific low back pain in this study, the results may not be generalizable to clinic populations with a high proportion of such patients. However, there are no data to suggest that women are more vulnerable to opioid addiction, and it is unlikely that major organ toxicity would be more common in women than in older men.

In the last 10 years, there has been an increasing acceptance of opioids for the treatment of noncancer pain (58). In an environment influenced by the metaphor of the “war on drugs,” patients with progressive disease and increasing pain are vulnerable to inadequate treatment and/or suspicious evaluations by health care providers. However, laws are changing. States are enacting intractable pain legislation that permits physicians to prescribe controlled substances for intractable pain and prohibits medical boards from disciplining physicians for long-term prescribing of a controlled substance for intractable pain alone (this does not apply to addicts) (59).

In summary, this study demonstrated that opioid treatment of patients with well-defined chronic pain of the spine was very effective, with mild toxicity. Opioid dosages were stable for prolonged periods of time.
Dosage escalations were typically related to an identifiable worsening of the painful condition, a surgical complication, or an unrelated pain process and did not appear to be due to the development of tolerance. Abuse behaviors in this cohort study were observed in 3 patients and were not predicted by a history of abuse/addiction. Doubts or concerns about opioid efficacy, toxicity, tolerance, and abuse or addiction should not be used to justify the withholding of opioids from patients who have pain related to defined spinal diseases.

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We are indebted to Dr. Ishani Jhanjee, Amy DeLong, and Carrie Mahowald for their valuable assistance, and to the patients whose participation made this study possible. We thank Dr. Paul J. Bilka, whose observations and insight prompted and guided this study, and the late Dr. Edward McElfresh, whose cooperation and support made this study possible.

**REFERENCES**