Global reprints distributed only by Postgraduate Medicine USA. No part of Postgraduate Medicine may be reproduced or transmitted in any form without written permission from the publisher. All permission requests to reproduce or adapt published material must be directed to the journal office in Berwyn, PA, no other persons or offices are authorized to act on our behalf. Requests should include a statement describing how material will be used, the complete article citation, a copy of the figure or table of interest as it appeared in the journal, and a copy of the "new" (adapted) material if appropriate CLINICAL FEATURES

Pain Management in Primary Care: Strategies to Mitigate Opioid Misuse, Abuse, and Diversion

Bill H. McCarberg, MD¹

¹Founder, Chronic Pain Management Program, Kaiser Permanente, San Diego, CA; Adjunct Assistant Clinical Professor, University of California, San Diego, CA Abstract: Pain is among the most common reasons patients seek medical attention, and the care of patients with pain is a significant problem in the United States. Acute pain (mild-tomoderate intensity) represents one of the most frequent complaints encountered by primary care physicians (PCPs) and accounts for nearly half of patient visits. However, the overall quality of pain management remains unacceptable for millions of US patients with acute or chronic pain, and underrecognition and undertreatment of pain are of particular concern in primary care. Primary care physicians face dual challenges from the emerging epidemics of undertreated pain and prescription opioid abuse. Negative impacts of untreated pain on patient activities of daily living and public health expenditures, combined with the success of opioid analgesics in treating pain provide a strong rationale for PCPs to learn best practices for pain management. These clinicians must address the challenge of maintaining therapeutic access for patients with a legitimate medical need for opioids, while simultaneously minimizing the risk of abuse and addiction. Safe and effective pain management requires clinical skill and knowledge of the principles of opioid treatment as well as the effective assessment of risks associated with opioid abuse, addiction, and diversion. Easily implementable patient selection and screening, with selective use of safeguards, can mitigate potential risks of opioids in the busy primary practice setting. Primary care physicians can become advocates for proper pain management and ensure that all patients with pain are treated appropriately.

Keywords: nonmedical use; pain medication; prescription opioids; primary care; risk management

Introduction

Pain is among the most common reasons that patients seek medical attention; moreover, the care of patients with pain is a significant problem in the United States. More than one-fourth of all adults aged ≥ 20 years report experiencing pain that continues for > 24 hours.^{1,2} This includes an estimated 25 million individuals with acute pain and 50 million individuals enduring chronic pain.³ This often-overlooked health care concern affects more individuals than diabetes, coronary heart disease/stroke, and cancer combined.^{1,2} Most patients with pain present in the primary care setting, establishing pain as an important clinical concern for these physicians.^{1,4}

Acute pain of mild-to-moderate intensity represents one of the most frequent complaints encountered by primary care physicians (PCPs) and accounts for approximately 40% of patient visits.⁵⁻⁷ Although many of these cases are short term and only require brief pharmacologic treatment, pain can become consistent and intractable.^{3,8} Chronic pain is highly prevalent among the adult population; a recent survey of 27 035 adults in the United States revealed a national prevalence of 31% for pain occurring on a regular basis for ≥ 6 months.⁹ Similarly, a Massachusetts survey

Correspondence: Bill H. McCarberg, MD, 732 N. Broadway, Escondido, CA 92025 Tel: 760-839-7008 E-mail: bill.h.mccarberg@kp.org

found that 24% of its general population experiences pain lasting \geq 3 months.¹⁰ Primary care physicians are often the first clinicians to evaluate patients with chronic pain, and approximately 20% of these patients report experiencing pain lasting for > 6 months.^{1,4,6,7,11} Beyond diagnosis, PCPs play an important role in the treatment of patients with pain. The majority (60%) of respondents in the Massachusetts survey relied predominantly on their PCP for pain care, and minorities (76%) and the elderly (67%) were the most dependent on their PCP.¹⁰

Pain arises from a variety of sources, making appropriate pain management a central goal of medical care.¹² The prompt, effective treatment of acute pain is critical to patient relief.^{1,8} Pain negatively impacts activities of daily living, as well as emotional and mental health, productivity, and the use of health care resources.^{11,13,14} In addition to the consequences of acute pain itself, unmanaged acute pain may contribute to the development of a chronic pain condition that persists long after the initial injury or illness resolves.^{1,8,15} Clinicians should realize that acute pain requires appropriate treatment to help prevent chronic pain.1 Routine treatment of moderate-to-severe pain includes prescription opioids as part of a comprehensive pain-management plan.^{11,16} However, the increasing use of prescription opioids coincides with the increasing aberrant use, abuse, and diversion of these medications.^{17,18} Thus, PCPs may hesitate to initiate opioid therapies or may prescribe these agents at suboptimal levels, resulting in the undertreatment of pain.^{17,19,20} Despite potential clinician discomfort with opioid therapy, a large number of patients with pain treated in the primary care setting receive opioid prescriptions.²¹

Primary care physicians should become advocates for proper pain management and ensure that all patients with pain are treated appropriately.²² A recent position paper from the American Academy of Pain Medicine (AAPM) determined the overall quality of pain management remains unacceptable for millions of US patients with acute or persistent pain.³ Underrecognition and undertreatment of pain are a particular concern in primary care.^{4,6} These clinicians face dual challenges from the emerging epidemics of undertreated pain and prescription opioid abuse.¹⁷ The objective of this review is to update PCPs on effective pain management, while providing practical strategies to mitigate the risks of abuse, misuse, and diversion of opioid analgesics.

Clinical Concerns

Patients who present with pain test the PCP's ability to balance 2 potentially divergent clinical concerns. Optimal

patient care requires adequate pain management, yet these clinicians must consider the risks of potential aberrant drugrelated behaviors and prescription opioid abuse. Each of these concerns presents potential risks to the patient and society.

Risk of Undertreating Pain

Patients depend on pain medication to manage their pain and enable them to engage in normal activities; unfortunately, pain remains undertreated despite the availability of effective treatment options.^{20,23,24} Among 1204 adults in a 2005 California survey, 63% had spoken to their physician about pain, yet only 31% had achieved complete relief and 21% indicated little or no pain relief.¹⁷ This undertreatment of pain is representative of practices across the United States. In a survey commissioned by the Massachusetts Pain Initiative, although most patients reported that their chronic pain was diagnosed, few achieved relief and many rated their pain intensity as a \geq 7 on a 10-point scale.¹⁰ Nearly one-third of these patients resorted to emergency room visits for their pain, indicating that it was not being managed effectively. Undertreatment of pain in the primary care setting results from a variety of factors, including inadequate knowledge regarding pain management, fear of regulatory or liability consequences. and the lack of accountability to provide appropriate pain relief.⁸ In addition, patients can contribute to inadequate pain-management treatment because of fears of addiction and adverse effects of therapy.^{20,25}

Undertreatment of pain is an important health care concern in the United States, and several patient-advocacy groups and professional organizations actively focus on improving pain management.^{11,13} Suboptimal pain treatment escalates medical problems and negatively impacts economic, social, health, and quality-of-life outcomes.^{11,13,24} For example, inadequately managed acute pain can become chronic pain, leading to long-term disability, clinical complications, and subsequent utilization of health care resources.^{1,15} Many musculoskeletal effects of pain, such as atrophy, contractures, and changes in posture, can generate further pain.³ Pain is one of the most frequent causes of disability, resulting in lost productivity of working Americans estimated to cost employers > \$61 billion annually.²⁶

Conversely, effective treatment of both acute and chronic pain improves patient outcomes.²⁷ For example, physical therapy can improve function and rehabilitation; however, adequate pain management is necessary for physical therapy participation.¹² Therefore, timely and effective management of acute pain is a central component of primary care.⁸ Similarly, chronic pain requires assessment and treatment according to best practices to provide comfort, reduce burdens on society, improve patient quality of life, and ensure equitable care for all patients.^{1,14} Effectively managed chronic pain not only reduces suffering, it also may reduce the public burden of disability due to chronic pain by improving function and allowing patients to return to productive work.¹⁴

Several classes of medication are available to manage pain and they are most often applied in a progressive approach (Figure 1).^{12,28} Originally devised to address pain in patients with cancer, the World Health Organization analgesic ladder describes a stepwise use of analgesics, including opioids, based on pain intensity.^{12,28} A growing consensus that opioid therapy is appropriate for a wide range of patients with pain is emerging, and this therapy represents a legitimate medical need in many cases.^{23,29,30} The 2009 clinical guidelines recently published by the American Pain Society (APS) and the AAPM comprehensively review the best available evidence for the safe and effective use of opioids in patients with chronic noncancer pain.^{23,29} This expert panel concluded these medications can be an effective therapy for carefully selected and monitored patients. Patients suitable for opioid therapy include those with moderate-to-severe pain and pain with an adverse impact on function or quality of life, as well patients in whom the potential therapeutic benefits outweigh potential harm.23

Based on the growing consensus on the benefits of pain management, opioid prescribing by US PCPs has increased over the past decade.^{30,31} The recently published Trends and Risks of Opioid Use for Pain (TROUP) study analyzed opioid use in both national commercially insured and state-based publicly insured patients over the 6-year period from 2000 to 2005.^{30,32} The TROUP study reported significant increases in opioid use across reimbursement models and pain site, a trend reported for the previous 2 decades. Of particular note, the TROUP study documented the growing long-term use of opioids among patients with noncancer pain.³² Clinical practice treatment decisions must balance the benefits of improved pain management through the increased use of opioids with the risks associated with opioid therapy.

Risk of Aberrant Drug-Related Behaviors and Abuse

Drug abuse is a significant issue in society, and the recently released 2009 National Survey on Drug Use and Health (NSDUH), prepared by the Substance Abuse and Mental Health Services Administration of the US Department of Health and Human Services, reported that 21.8 million individuals (~ 8.7% of the total population) aged \geq 12 years used illicit drugs in the month prior to the survey, including 5.3 million individuals who had used pain relievers in a nonmedical manner.³³ The nonmedical use of prescription pain medications is a growing concern and rivals that of most other illicit drugs. In 2009, 2.2 million persons aged \geq 12 years began the illicit use of marijuana.³³

Select populations are at a higher risk for misuse of prescription opioids. Positive trends exist between poverty or unemployment rate and prescription opioid misuse, and

Figure 1. World Health Organization Analgesic Ladder.²⁸ Medications across analgesic categories can be applied in a stepwise fashion based on the intensity of a patient's pain.^{12,28}



teenagers are particularly vulnerable.^{34,35} The problem of pain medications being used as a "gateway drug" (ie, a habitforming substance whose use may lead to the abuse of drugs that are more addictive or more dangerous) in this population is resurfacing.36 Teenagers may view prescription drugs as relatively safe, and these agents are easily accessible.³⁷ In 2009, among those aged ≥ 12 years who used illicit drugs, 17.1% cited pain medication as the first illicit drug used.³³ Prescription drug abuse in teenagers is growing at a faster rate than that in older patients.35,38 The current rate of nonmedical use of prescription drugs, including pain medications, is approximately 3.3% among individuals aged 12 to 17 years and 6.3% among those aged 18 to 25 years.³³ The 2009 Partnership Attitude Tracking Study reported that 4.7 million teenagers in grades 7 through 12 have abused prescription drugs at some point in their lives.³⁵ This number is less than use of marijuana by teenagers, but substantially more prevalent than use of other drugs (Figure 2). Another notable population with an accelerating rate of illicit drug use is older patients. Between 2002 and 2009, the rate of illicit drug use increased from 2.7% to 6.2% among adults aged 50 to 59 years.³³ This trend follows the aging of the baby boom group, who have demonstrated a higher rate of illicit drug use than other populations.

The aberrant use of prescription drugs negatively affects the US health care system. Abuse of prescription drugs is implicated in at least 23% of drug-related emergency room admissions.³⁵ Further, the need for treatment of pain reliever abuse has grown (Figure 3), with an increasing number of individuals seeking treatment for addiction to prescription pain medications.³³

Because PCPs prescribe a large number of opioids, there is a great potential for diversion of these drugs. Concurrent with efforts to raise awareness of the legitimate need for opioid



Figure 2. The number of teenagers who have ever abused specific drugs (in millions).³⁸ The prevalence of prescription drug abuse is second only to that of marijuana.

Reproduced with permission from The Partnership at Drugfree.org's 2008 Partnership Attitude Tracking Survey, sponsored by MetLife Foundation. **Abbreviations:** LSD, *d*-lysergic acid diethylamide; GHB, γ-hydroxybutyric acid. **Figure 3.** Most recent treatment for pain reliever abuse among individuals aged ≥ 12 years: 2002–2009.³⁴ The need for treatment of pain reliever abuse has grown, with an increasing number of individuals seeking treatment for addiction to prescription



*Difference between this estimate and the 2009 estimate is statistically significant at the 0.05 level.

analgesics to effectively manage pain, these medications have become among the most prescribed agents in the United States.^{17,39} Approximately 3.8 million patients received outpatient prescriptions for an extended-release/long-acting opioid in 2009, a significant increase over time compared with 2.7 million patients who received these prescriptions in 2002.²¹ Approximately 44% of opioid prescriptions in 2009 were written by primary care (27%) and internal medicine (17%) physicians.²¹ These prescriptions are at risk for drug diversion, which is the unlawful channeling of prescription drugs to the illicit marketplace.

Abused prescription drugs come from several sources, including "doctor shopping," leftover supplies following an illness or injury, and theft.⁴⁰ More than half (60.3%) of those who abuse prescription pain medications are given or steal the drugs from a friend or relative, and 80.0% cite that the friend or relative was prescribed the drugs from only 1 physician.³³ Recent data from Utah showed that 72% of patients who were prescribed an opioid had leftover medication, and 71% of those with leftover medication kept it.⁴¹ In this study, the majority (97%) that reported using a prescription opioid that had not been prescribed for them obtained the drug from a friend or relative. In most cases (55.3%), the medication was given to them, whereas others took it without the knowledge or permission of the owner.33 Similarly, the current NSDUH reported that among those aged ≥ 12 years who used pain relievers in a nonmedical fashion, 55.3% obtained the drugs for free from friends or relatives, and 17.6% indicated that the drugs they most recently used had been prescribed by 1 physician.³³ Another 9.9% bought the drugs from a friend or relative, and 5.0% took them from a friend or relative without

asking. Only 4.8% obtained pain relievers from a drug dealer

or other stranger, and 0.4% bought them on the Internet. Inadequate support and training of PCPs and internists on aberrant drug-related behavior may contribute to the risk of pain medications misuse.¹ The National Center on Addiction and Substance Abuse at Columbia University reported that only 19% of physicians surveyed had received training in prescription drug diversion in medical school and that clinicians were poorly trained in recognizing substance abuse and addiction.³⁵ Approximately half of these physicians routinely screen for previous abuse before prescribing opioid therapy. Primary care physicians should become adept in assessing for these risks and integrate this screening into their clinical

Practical Considerations in a Busy Primary Care Practice

practices.

Primary care physicians often work in practices that allow little time with each patient and have limited options for specialist referrals.^{1,42} Today's clinicians face the practical challenge of optimizing pain management while minimizing the risk of abuse.¹⁷ However, the recommended processes and safeguards on prescription of opioids can be onerous and daunting for PCPs. Although experts widely recommend that urine drug testing be done in primary care,^{11,23} interpretation of this testing is challenging and requires an in-depth understanding of opioid drug metabolism, pharmacokinetics, and laboratory test limitations.^{11,23}

Pain management can be complex, and the use of opioids carries risks, such as accidental overdose and fractures (especially in the elderly),43 and potential side effects, including gastrointestinal effects (eg, nausea, vomiting, and constipation).⁴⁴ Further, the use of opioids in chronic noncancer pain remains controversial.⁴⁵ Although strong evidence supports the initial efficacy of opioids in these patients, how these agents are optimally used for the long term is unclear. Analgesic decline, opioid-induced hyperalgesia, and the full spectrum of neuroadaptations that arise with opioid use are important areas of continued investigation.45 Understanding the clinical implications of these controversies can challenge clinicians. For example, hyperalgesia can be difficult to clinically distinguish from pharmacologic tolerance.45 In addition, clinical practices to preserve long-term effectiveness, such as dose escalation or opioid rotation, further complicate pain management for PCPs.44,45

Several factors may contribute to PCPs being reluctant to prescribe opioids to their patients. The most notable obstacle to opioid prescribing is the potential for abuse or addiction,

a concern elevated among general practitioners.⁴⁶ A recent subset from a (N = 2750) Texas family physician survey found that among the 267 relevant responses, approximately half (51%) believed that prescribing long-acting opioids for chronic noncancer pain would result in patient addiction.47 Primary care physicians can also be uneasy about regulatory or liability issues and the potential censure of opioid prescribing.19,48 This Texas survey also demonstrated the concern of physicians on regulatory scrutiny; 78% indicated they were "somewhat likely" to "extremely likely" to be subjected to regulatory scrutiny when they prescribed opioids for chronic noncancer pain.⁴⁷ In addition, some PCPs may feel they have inadequate knowledge of pain management. Another recent survey of 186 PCPs in West Virginia revealed that the majority of respondents felt their formal medical training did not provide them with the skills to effectively manage pain.⁴⁸ Incorrect responses from these physicians to several opioid-use knowledge statements ranging from 21% to 67% confirmed this finding.48

All of these concerns of PCPs are valid. However, the subsequent reluctance to prescribe opioids can act as a barrier to optimal treatment for patients who may benefit from this therapy.^{19,47} Despite the practical challenges, these clinicians have a responsibility to integrate sensible approaches for effectively managing pain in patients while minimizing opioid therapy abuse and diversion.²⁴

Screening for Abuse or Addiction Risks

Many patients who receive opioids pose only a slight risk for addiction and abuse, and therefore may not need rigorous screening. Primary care physicians most commonly encounter mild or moderate pain as a result of musculoskeletal injuries, such as strains, sprains, minor fractures, or low back injuries.⁵ These patients require only short-term pain-management treatment.⁵ Approximately 11.5% of patients exposed to chronic opioid analgesic therapy reported aberrant drugrelated behaviors.⁴⁹ However, these behaviors are significantly less frequent among those with no previous or current history of abuse or addiction. Only 0.59% of these lowerrisk patients exhibited aberrant drug-related behaviors.^{13,49} Primary care physicians can implement simple, practical methods to identify those patients at risk of abuse or aberrant drug-related behavior.

Patient selection and screening can mitigate potential risks and enhance potential benefits associated with prescribing pain medications.^{23,50} Before initiating opioid therapy, clinicians should conduct a thorough medical history, including assessment for risk of substance abuse,

misuse, or addiction as well as psychiatric factors. A strong predictor of opioid misuse is a personal history of illicit drug and alcohol abuse.⁵¹ Prescription drug abusers tend to abuse multiple substances and often have comorbid psychiatric conditions, such as anxiety, depression, or posttraumatic stress disorder.^{52,53}

Patients with chronic pain have a greater incidence of depression and anxiety than those with other medical conditions, and a history of mood disorders, psychologic problems, and psychosocial stressors may place patients at risk of opioid misuse.^{54,55} Patients with chronic pain identified as having a high psychiatric comorbidity exhibit more frequent abnormal urine toxicology screens and significantly higher scores on the Drug Misuse Index than those with fewer psychiatric disorders (P < 0.001).⁵⁴

Several tools may be used by PCPs to screen patients being considered for opioid pain-management treatment. These assess either abuse potential in patients or current alcohol and/or drug use.⁵⁶ Examples of useful tools to determine a patient's abuse potential include the Screener and Opioid Assessment for Patients in Pain (SOAPP) and the Opioid Risk Tool (ORT).⁵⁶⁻⁶⁰ The SOAPP is a tool that helps identify patients at high risk of abuse. A 5-question version of SOAPP is available and may be particularly suited to the time constraints of primary care practices.¹³ Similarly, the ORT assesses family history of substance abuse, personal history of substance abuse, age, history of sexual abuse, psychologic disease, and depression. To determine a patient's current substance abusive behaviors, the Cut down, Annoyed, Guilty, Eye opener (CAGE) Alcohol Screening instrument and the Drug Abuse Screening Test (DAST) are tools that may be used.^{13,56} The CAGE questionnaire is a quick and reliable method to identify abuse problems based on 4 questions about a patient's alcohol use, whereas the DAST focuses on 28 statements about the patient's involvement with drugs over the past year.¹³ In addition to assessing the suitability of patients for opioid therapy based on their abuse or addiction risk, these tools can provide physicians with insight into the level and frequency of monitoring a patient should receive.¹³

Clinicians may also query patients for specific behaviors predictive of substance abuse, such as oversedating themselves, feeling intoxicated, and increasing the dose on their own.⁶¹ Beyond relevance in screening, predictors of abuse are also helpful to assess patient behaviors that may indicate the emergence of aberrant drug-related activity.^{55,62} Differentiating between common behaviors of patients with chronic pain and those of patients with substance use disorders is central to assess patients for aberrant drug-related behaviors.⁶² Figure 4 summarizes key differences in behavior between these 2 conditions.^{62,63} Other specific patient behaviors are indicative of addiction.^{52,56} Table 1 provides some commonly observed behaviors associated with addiction and abuse.¹³

Once those patients at risk of abuse or aberrant drugrelated behavior have been identified, PCPs can selectively implement safeguards to minimize the risk of opioid abuse or addiction.^{13,24}

Selectively Implementing Safeguards

Universal precautions suggested to safeguard against potential aberrant drug-related behaviors may not be feasible for busy



Table 1. Selected Warning Signs of Potential Aberrant Drug-Related Behavior¹³

Likely Less Predictive of Addiction	Likely More Predictive of Addiction
Aggressive complaining	Selling prescription drugs
Drug hoarding when symptoms are milder	Prescription forgery
Requesting specific drugs	Stealing or "borrowing" drug from another person
Acquisition of drugs from other medical sources	Injecting oral formulations
Unsanctioned dose escalation once or twice	 Obtaining prescriptions from nonmedical sources
Unapproved use of the drug to treat another symptom	 Multiple episodes of prescription "loss"
Reporting psychic effects not intended by the clinician	Concurrent abuse of related illicit drugs
Occasional impairment	• Multiple dose escalations despite warnings
	Repeated episodes of impairment or dishevelment

primary care offices and not necessarily needed for all patients prescribed opioids. Practitioners who acquire clinical competency and experienced judgment may implement safeguards selectively for patients at various risk levels.¹⁹ For example, although some patients taking opioids require rigorous monitoring, patients at low risk of aberrant drug-related behavior may need monitoring only every 3 to 6 months unless their therapy or behavior changes.²⁹

Urine Drug Testing

Periodic urine testing is recommended for all patients with a high risk of aberrant drug-related behavior.^{23,29} Conversely, this may not be necessary for all patients. Periodic urine monitoring poses logistical challenges in a primary care practice and may not provide a definitive course of action. The 2009 APS/AAPM clinical guidelines provide only a weak recommendation for periodic urine drug screens or other tests to confirm adherence in patients not at high risk with no known aberrant drug-related behavior.23,29 This expert panel concluded that only low-quality evidence supported routine urine drug screens or other tests in these cases, which represent many patients seen by PCPs. In low-risk patients, they are encouraged to use their clinical judgment on urine drug screening, therefore developing plans within the context of individual patient circumstances.^{23,29} Routine urine testing for all patients with pain seen by PCPs may pose burdens on busy practices, and the yield may be too low to warrant the costs.²⁹

Opioid Agreements

In some situations, the use of an opioid agreement assists in the sometimes-difficult process of treating pain on an ongoing basis. The longer-term care given by PCPs often promotes a deeper physician-patient relationship. Within such relationships, having a patient sign an opioid agreement may facilitate consistent and positive physician-patient communications.¹⁹ Busy PCPs may find this tool particularly helpful in managing opioid use in complex patients or those with potential risks.^{19,64}

Structured Opioid Renewal Program

A recent evaluation of a structured opioid renewal program in a busy veterans' hospital demonstrated the value of nurse practitioners and clinical pharmacists who provide support to PCPs using opioids in patients with chronic noncancer pain.⁴² This outcome study followed 335 primary care patients referred to a prescription-management clinic led by a clinical pharmacist and a nurse practitioner; the program at this clinic also involved a multidisciplinary pain-management team that met regularly. After approximately 2 years, nearly half (45%, 77/171) of the patients with documented aberrant drugrelated behaviors were adherent to their opioid-treatment agreement.⁴² Further, the 164 (49%) patients who had been referred with a complex history, substance abuse, or a need for opioid rotation or titration continued to adhere to the opioid treatment agreement.42 This evaluation also revealed significant pharmacy cost savings through more effective opioid prescribing practices.42

Typical Versus Atypical Opioid Prescribing

Being mindful of whether their opioid prescriptions are typical or atypical can alert PCPs to the potential need to increase their rigor in patient monitoring or documentation.⁶⁰ Five factors have been proposed to assess whether opioid use is typical or atypical: pain type, dose, the patient's psychiatric comorbidities and substance abuse potential, amount of contact with nonmedical drug users, and age. Opioids typically pose less risk in patients with cancer or perioperative pain, patients who have no current psychiatric conditions or substance abuse, individuals with limited contact with nonmedical drug users, and those of older age. Conversely, a more controversial use of opioid therapy is for conditions such as fibromyalgia.⁶⁵

Opioid doses of ≤ 180 -mg morphine sulfate (MSO₄) equivalents administered daily can be considered to be moderate or lower.⁶⁰ Atypical opioid use is when these agents are applied in a pain syndrome where opioid use is controversial, in patients with active psychiatric disorders or substance abuse, in patients with significant contact with nonmedical drug users, and in patients of a younger age. Opioid doses exceeding 180-mg MSO₄ equivalents daily can be considered to be on the high side for patients with chronic noncancer pain.⁶⁰ Figure 5 summarizes precautions that PCPs can take when prescribing opioids to maximize pain management while minimizing risks of abuse and addiction.^{13,66}

Specialist Referrals

Chronic pain can be addressed similarly to other chronic conditions, and, if feasible, pain-management treatment should be implemented by a PCP with the skills to evaluate the pain and devise a treatment plan.¹ Most patients with pain can be successfully treated by their PCP, and only ~7% of patients with chronic pain depend primarily on a pain specialist.¹⁰ At some point, clinicians may need to consider referring a patient to a specialty clinic or pain specialist for high-risk or complex patients. For example, a patient with aberrant drug-related behavior with opioids might optimally be managed by a pain

medicine or an addiction expert.²³ Table 2 provides general guidance on patient risk characteristics and how to triage patients to treatments and caregivers best suited to address patient needs.^{64,66}

Clinicians should pursue consultation, including interdisciplinary pain management, when patients may benefit from skills or resources that they may not have.^{1,23} For example, consultation or comanagement with specialists in addiction or mental health issues may be warranted for patients at high risk of abuse.⁶⁴ Multidisciplinary care, such as specialized nurse practitioners and pharmacists at an outpatient clinic, can also support PCPs managing patients undergoing chronic opioid therapy.⁴² Similarly, pain specialists may be accessed by PCPs to implement more aggressive patient selection and monitoring, such as informed consent, opioid contracts, documented management plans, use of methadone, and periodic urine tests.²³

Pain specialist referral may be difficult for many PCPs without easy access to a pain specialist. There is a functional shortfall in pain medicine specialists available to meet the demand of patients with pain in the United States.⁶⁷ Analysis of board-certified pain specialists and census data reveals only approximately 6 pain specialists per 100 000 adult patients with chronic pain, which is reduced to 4 per 100 000 if children

Figure 5. Precautions in pain medicine for primary care physicians to maximize pain management while minimizing risks of abuse and addiction.^{13,66}



Reproduced with permission from Pain Pract.13

Patient Characteristic	Risk Level	Management Setting
 No history of substance abuse; minimal or no risk factors 	Low	Can be managed by primary care physician
ODL		 If aberrant drug-related behaviors are observed, consider raising risk category
 Past history of alcohol or illicit drug abuse; significant other risk factors 	Medium	• Comanage with addiction and/or pain specialists
Aberrant drug-related behaviors manifesting		• If aberrant drug-related behaviors are observed or persist,
in a low-risk patient		consider assigning to high-risk category
• Active substance abuse problem; history of	High	Opioids may not be appropriate; change to nonopioid
prescription opioid abuse		therapy
 Aberrant drug-related behaviors manifesting 		 Consult with or refer to specialists who manage patients
in a medium-risk patient	NDV	with comorbid pain and addictive disorders
		 Continue to manage patient's medical care including pain relief and monitor specialized care

Adapted with permission from | Pain.64

are included.⁶⁷ These specialists are also underrepresented in rural areas. Although 21% of the overall US population resides in zip codes containing pain practices, only 8% of those in rural areas have a local pain specialist.67 Recent legislation in Washington state exemplifies the challenge posed by the limited number of pain specialists in rural areas. A major hurdle to the recent requirement for referral to a pain specialist for higher doses of opioids is the lack of pain-management specialists for referral, particularly in rural areas of the state.⁶⁸ This shortage of pain specialists is exacerbated by a large number of these practices that focus on areas other than the full interdisciplinary care optimal for most complicated pain patients.⁶⁷ In settings where local access to specialists is limited, PCPs can consider patient-management alternatives, such as telemedicine or Web-based access to specialized consultation.^{23,68} Clinicians should also be aware of, and use, other available resources in their area, such as prescription-monitoring programs, to assist in identifying patients who obtain drugs from multiple sources.

Preventing Theft and Diversion

Several initiatives can be implemented in primary care settings to safeguard against theft and diversion of controlled substances. Taking the actions summarized in Figure 6 can minimize the risk of these incidents.¹³ Patients should be encouraged to discourage theft and diversion of prescription medications by locking them away and disposing of unused medications properly.

Abuse Deterrents and Surveillance

Opioids are the drug of choice for a large segment of recreational drug abusers, thus there is the need for innovative formulations to inhibit this use.⁶⁹ These formulations deter

tampering by either reducing easy access to the active opioid for abuse or diminishing or changing its effects.^{14,69} Abuseresistant formulations (ARFs) create physical barriers to stop alteration of the formulation. These products make it difficult to tamper with or extract the active opioid, or render the tampered-with product unsuitable for snorting or injecting.64 Abuse-deterrent formulations (ADFs) discourage misuse by pharmacologically modifying the formulation. These products involve a chemical modification such as the addition of another compound that decreases or prevents the opioid effect or induces an adverse effect. 64 Several types of ADFs are possible, including agonist-antagonist formulations, aversion, prodrugs, and alternative methods of administration.⁷⁰ Recreational drug users administer opioids through oral, nasal, and injectable routes, and each type of ADF or ARF will potentially impact a specific type of prescription drug abuse.^{16,70–73} Matching abuse-deterrence approaches to types of opioid abuse is a central challenge in the development of ADFs.¹⁶

Numerous ARFs and ADFs are currently in clinical development.^{64,74} These agents have the potential to reduce the public health burden of opioid abuse and should ultimately replace traditional formulations.16 Therefore, PCPs should be knowledgeable of these emerging therapies so they can be integrated into their clinical practice in a timely manner. However, these formulations are only 1 component of a comprehensive approach to opioid-risk management.^{16,70} Appropriate patient assessment, supply chain control, and prescription monitoring all play a role in minimizing the risk of opioid abuse.¹⁶ In addition, manufacturers of opioids have created systems to measure abuse of these products from various perspectives including clinicians, the criminal justice system, and susceptible patients.



rigure	or sareguards that physicians can implement to mitigate their and diversion.	
Ø	Keep all prescription blanks in a safe place where they cannot be stolen	
	Write out the actual amount prescribed in addition to giving a number to discourage alterations of the prescription order	
Ø	Use prescription blanks only for writing a prescription order and not for notes	
Ø	Never sign prescription blanks in advance	
Ø	Assist the pharmacist when he or she telephones to verify information about a prescription order	
	Contact the nearest Drug Enforcement Agency field office to obtain or furnish information on suspicious prescription activities	
Ø	Use tamper-resistant prescription pads	Y
		_

Reproduced with permission from Pain Pract.13

Conclusion

Primary care physicians are often the first to see a patient with pain, and this group represents the largest population of physicians treating these pain patients. Consequently, PCPs are in a unique position to improve pain management. Without adequate training, reluctance to prescribe pain medications in the primary care setting is understandable. However, these clinicians routinely address incurable and complex chronic conditions, such as heart disease or diabetes in elderly patients.^{1,42} Although pain management is complex and requires expertise, PCPs can develop the skills to successfully manage pain. The negative impact of undertreated pain on patient quality of life and public health expenditures, combined with growing evidence on the successful use of opioid analgesics, provide a strong rationale for PCPs to learn best practices for pain management.14 A well-informed PCP can prescribe effective treatment and coordinate multidisciplinary pain care. Thus, primary pain management can improve the lives of most patients suffering from pain and reduce the economic burdens of untreated pain on society.¹

In practice, the significant need for pain management, combined with the increasing misuse and abuse of these medications, creates increasing pressure on PCPs. They must address the challenge of maintaining therapeutic access for patients with a legitimate medical need for opioids, while simultaneously minimizing the serious public health problem of potential abuse.^{23,24} Safe and effective pain management requires clinical skills and knowledge of the principles of opioid treatment as well as the effective assessment of risks associated with opioid abuse, addiction, and diversion. Easily implementable patient selection and screening, followed by

selective application of safeguards, can mitigate potential risks and enhance potential benefits associated with prescribing pain medications in the busy primary practice setting.⁵⁰ Key steps in effective pain-management treatment that minimizes risk of abuse or addiction include^{13,24}:

- An appropriate differential diagnosis evaluating the cause of pain and the appropriateness of opioid therapy
 Psychologic assessment for comorbid conditions that may exacerbate pain, such as depression and anxiety
 Screen patients for risk of abuse or aberrant drug-related behavior
- Document informed consent, including a discussion with the patient about the risks and benefits of any course of therapy¹³
- Use a treatment agreement to reinforce expectations and obligations for both the clinician and patient¹³
- Selectively implement safeguards against aberrant drugrelated behavior in high-risk patients at elevated risk
- Referral of high-risk patients or those exhibiting aberrant drug-related behavior to pain specialists
- Periodically review and modify the treatment plan should aberrant drug-related behavior appear
- Document assessments and care plans to reduce medicolegal exposure and risk of regulatory sanctions¹³

By employing these practices, PCPs can become important advocates for their patients with pain, ensuring enhanced access to pain treatment while minimizing potential risks of aberrant drug activities or addiction.²²

Acknowledgments

Writing and editorial assistance was provided by Jonathan Kamien, PhD of Ogilvy CommonHealth Scientific Communications, Parsippany, NJ, and was supported by King Pharmaceuticals,[®] Inc.

Conclusion

Bill H. McCarberg, MD discloses conflicts of interest with Abbott, Cephalon, Eli Lilly & Co, Endo Pharmaceuticals, Forest Pharmaceuticals, King Pharmaceuticals, Ligand Pharmaceuticals, Merck & Co, Inc, Mylan, Neurogenex, Pfizer Inc, PriCara, and Purdue Pharma.

References

 The Mayday Fund Special Committee on Pain and the Practice of Medicine. A call to revolutionize chronic pain care in America: an opportunity in health care reform. http://www.maydaypainreport.org/ report.php. Accessed January 6, 2011.

© Postgraduate Medicine, Volume 123, Issue 2, March 2011, ISSN – 0032-5481, e-ISSN – 1941-9260

- **Property of**
 - American Pain Foundation. Pain facts and figures. http://www.painfoundation.org/media/resources/pain-facts-figures.html. Accessed January 6, 2011.
 - 3. Dubois MY, Gallagher RM, Lippe PM. Pain medicine position paper. *Pain Med.* 2009;10(6):972–1000.
 - Khouzam RH. Chronic pain and its management in primary care. South Med J. 2000;93(10):946–952.
 - McCarberg B. Treatment of mild-to-moderate acute pain: what can we do to improve the standard of care? *Am J Ther*. 2008;15(suppl 10): S5–S6.
 - Haanpää ML, Backonja M-M, Bennett MI, et al. Assessment of neuropathic pain in primary care. *Am J Med.* 2009;122(10 suppl):S13–S21.
 - Mäntyselkä P, Kumpusalo E, Ahonen R, et al. Pain as a reason to visit the doctor: a study in Finnish primary health care. *Pain*. 2001;89(2–3):175–180.
 - McCarberg BH, Adler JA. Updates on managing acute and chronic pain in primary care practice: optimizing pain reduction, minimizing adverse events. *JAAPA*. 2008;Suppl Pain:1–13.
 - Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH. The prevalence of chronic pain in United States adults: results of an Internet-based survey. J Pain. 2010;11(11):1230–1239.
 - Massachusetts Pain Initiative. Massachusetts Pain Initiative. Pain Survey Executive Summary. http://masspaininitiative.org/files/MassPI%20 Pain%20Survey%20-%20Executive%20Summary%20v3.pdf. Accessed January 6, 2011.
 - Trescot AM, Boswell MV, Atluri SL, et al. Opioid guidelines in the management of chronic non-cancer pain. *Pain Physician*. 2006;9(1): 1–39.
 - 12. D'Arcy Y, McCarberg B. Field guide to pain. Part 2: developing a plan of care. *Nurse Pract.* 2005;30(10):60–62.
 - McCarberg B, Stanos S. Key patient assessment tools and treatment strategies for pain management. *Pain Pract.* 2008;8(6):423–432.
 - Gallagher RM, Rosenthal LJ. Chronic pain and opiates: balancing pain control and risks in long-term opioid treatment. *Arch Phys Med Rehabil*. 2008;89(3 suppl 1):S77–S82.
 - McLean SA, Clauw DJ, Abelson JL, Liberzon I. The development of persistent pain and psychological morbidity after motor vehicle collision: integrating the potential role of stress response systems into a biopsychosocial model. *Psychosom Med*, 2005;67(5):783–790.
 - Katz NP, Adams EH, Chilcoat H, et al. Challenges in the development of prescription opioid abuse-deterrent formulations. *Clin J Pain*. 2007;23(8):648–660.
 - Kuehn BM. Opioid prescriptions soar: increase in legitimate use as well as abuse. JAMA. 2007;297(3):249–251.
 - Paulozzi LJ, Budnitz DS, Xi Y. Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiol Drug Saf.* 2006;15(9):618–627.
 - Touchet BK, Yates WR, Coon KA. Opioid contract use is associated with physician training level and practice specialty. *J Opioid Manag.* 2005;1(4):195–200.
 - Gagnon AM, Kahan M, Srivastava A. Opioid use and abuse: is there a problem? *Clin J Pain*. 2007;23(8):661–662.
 - Governale L. Outpatient prescription opioid utilization in the US, years 2000–2009. US Food and Drug Administration. 2010. http://www. fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ UCM220950.pdf. Accessed January 6, 2011.
 - 22. Ashburn MA, Lipman AG. Pain in society. In: Lipman AG, ed. Pain Management for Primary Care Clinicians. Bethesda, MD: American Society of Health-System Pharmacists; 2004.
 - Chou R, Fanciullo GJ, Fine PG, et al; American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10(2):113–130.
 - Katz NP, Adams EH, Benneyan JC, et al. Foundations of opioid risk management. *Clin J Pain*. 2007;23(2):103–118.

- Rich BA, Fine PG. Ethical and legal issues in pain management. In: Lipman AG, ed. *Pain Management for Primary Care Clinicians*. Bethesda, MD: American Society of Health-System Pharmacists; 2004; 281–300.
- Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R. Lost productive time and cost due to common pain conditions in the US workforce. *JAMA*. 2003;290(18):2443–2454.
- Soin A, Cheng J, Brown L, Moufawad S, Mekhail N. Functional outcomes in patients with chronic nonmalignant pain on long-term opioid therapy. *Pain Pract*. 2008;8(5):379–384.
- McCarberg B. Contemporary management of chronic pain disorders. J Fam Pract. 2004;53(10 suppl):S11–S22.
- 29. Chou R. 2009 Clinical Guidelines from the American Pain Society and the American Academy of Pain Medicine on the use of chronic opioid therapy in chronic noncancer pain: what are the key messages for clinical practice? *Pol Arch Med Wewn*. 2009;119(7–8):469–476.
- 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 TROUP study. *Pain*. 2008;138(2):440–449.
- Olsen Y, Daumit GL, Ford DE. Opioid prescriptions by U.S. primary care physicians from 1992 to 2001. J Pain. 2006;7(4):225–235.
- 32. Brennan Braden J, Fan MY, Edlund MJ, Martin BC, DeVries A, Sullivan MD. Trends in use of opioids by non-cancer pain type 2000–2005 among Arkansas Medicaid and HealthCore enrollees: results from the TROUP study. *J Pain*. 2008;9(11):1026–1035.
- 33. US Department of Health and Human Services Substance Abuse and Mental Health Services Administration Office of Applied Studies. Results from the 2009 National Survey on Drug Use and Health: Volume I. Summary of national findings. September 2010. http://oas.samhsa.gov/ NSDUH/2k9NSDUH/2k9ResultsP.pdf. Accessed January 6, 2011.
- Spiller H, Lorenz DJ, Bailey EJ, Dart RC. Epidemiological trends in abuse and misuse of prescription opioids. J Addict Dis. 2009;28(2):130–136.
- 35. The National Center on Addiction and Substance Abuse at Columbia University. Under the counter: the diversion and abuse of controlled prescription drugs in the U.S. July 2005. http://www.casacolumbia.org/ download.aspx?path = /UploadedFiles/tt3bl4lk.pdf. Accessed January 6, 2011.
- 36. Watkins A. The new faces of heroin addiction: teen use on the rise. The Adolescent Substance Abuse Knowledge Base. 2009. http://www. adolescent-substance-abuse.com/substance-abuse/the-new-faces-of-heroinaddiction-teen-use-on-the-rise.htm. Accessed February 10, 2011.
- Partnership for a Drug-Free America. The Partnership Attitude Tracking Survey (PATS): Teens 2008 Report. Released February 26, 2009. http:// www.doj.mt.gov/rxabuse/docs/2008PATSreport.pdf. Accessed January 6, 2011.
- Manchikanti L, Singh A. Therapeutic opioids: a ten-year perspective on the complexities and complications of the escalating use, abuse, and nonmedical use of opioids. *Pain Physician*. 2008;11(2 suppl):S63–S88.
- IMS Health. Full year 2008. http://www.rxlist.com/script/main/hp.asp. Accessed November 8, 2010.
- Inciardi JA, Surratt HL, Kurtz SP, Cicero TJ. Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. *Pain Med.* 2007;8(2):171–183.
- Centers for Disease Control and Prevention (CDC). Adult use of prescription opioid pain medications—Utah, 2008. *MMWR Morb Mortal Wkly Rep.* 2010;59(6):153–157.
- Wiedemer NL, Harden PS, Arndt IO, Gallagher RM. The opioid renewal clinic: a primary care, managed approach to opioid therapy in chronic pain patients at risk for substance abuse. *Pain Med*. 2007;8(7):573–584.
- Kamal-Bahl SJ, Stuart BC, Beers MH. Propoxyphene use and risk for hip fractures in older adults. *Am J Geriatr Pharmacother*. 2006;4(3):219–226.
- 44. Varrassi G, Marinangeli F, Piroli A, Coaccioli S, Paladini A. Strong analgesics: working towards an optimal balance between efficacy and side effects. *Eur J Pain.* 2010;14(4):340–342.

- 45. Ballantyne JC, Shin NS. Efficacy of opioids for chronic pain: a review of the evidence. *Clin J Pain*. 2008;24(6):469–478.
- Morley-Forster PK, Clark AJ, Speechley M, Moulin DE. Attitudes toward opioid use for chronic pain: a Canadian physician survey. *Pain Res Manag.* 2003;8(4):189–194.
- 47. Nwokeji ED, Rascati KL, Brown CM, Eisenberg A. Influences of attitudes on family physicians' willingness to prescribe long-acting opioid analgesics for patients with chronic nonmalignant pain. *Clin Ther.* 2007;29(suppl):2589–2602.
- Ponte CD, Johnson-Tribino J. Attitudes and knowledge about pain: an assessment of West Virginia family physicians. *Fam Med.* 2005;37(7):477–480.
- 49. Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drugrelated behaviors? A structured evidence-based review. *Pain Med.* 2008;9(4):444–459.
- 50. 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(2):131–146.
- 51. Turk DC, Swanson KS, Gatchel RJ. Predicting opioid misuse by chronic pain patients: a systematic review and literature synthesis. *Clin J Pain*.

2008;24(6):497–508.

- Passik SD, Hays L, Eisner N, Kirsh KL. Psychiatric and pain characteristics of prescription drug abusers entering drug rehabilitation. *J Pain Palliat Care Pharmacother*. 2006;20(2):5–13.
- Boscarino JA, Rukstalis M, Hoffman SN, et al. Risk factors for drug dependence among out-patients on opioid therapy in a large US healthcare system. *Addiction*. 2010;105(10):1776–1782.
- 54. Wasan AD, Butler SF, Budman SH, Benoit C, Fernandez K, Jamison RN. Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. *Clin* J Pain. 2007;23(4):307–315.
- Banta-Green CJ, Merrill JO, Doyle SR, Boudreau DM, Calsyn DA. Opioid use behaviors, mental health and pain–development of a typology of chronic pain patients. *Drug Alcohol Depend*. 2009;104(1–2):34–42.
- Passik SD, Kirsh KL, Casper D. Addiction-related assessment tools and pain management: instruments for screening, treatment planning, and monitoring compliance. *Pain Med.* 2008;9(S2):S145–S166.
- Moore TM, Jones T, Browder JH, Daffron S, Passik SD. A comparison of common screening methods for predicting aberrant drug-related behavior among patients receiving opioids for chronic pain management. *Pain Med.* 2009;10(8):1426–1433.

- Butler SF, Fernandez K, Benoit C, Budman SH, Jamison RN. Validation of the revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R). J Pain. 2008;9(4):360–372.
- Akbik H, Butler SF, Budman SH, Fernandez K, Katz NP, Jamison RN. Validation and clinical application of the Screener and Opioid Assessment for Patients with Pain (SOAPP). *J Pain Symptom Manage*. 2006;32(3):287–293.
- Smith HS, Kirsh KL, Passik SD. Chronic opioid therapy issues associated with opioid abuse potential. J Opioid Manag. 2009;5(5):287–300.
- 61. Fleming MF, Davis J, Passik SD. Reported lifetime aberrant drug-taking behaviors are predictive of current substance use and mental health problems in primary care patients. *Pain Med.* 2008;9(8):1098–1106.
- 62. D'Arcy Y, McCarberg B. Pain management: patients with a substance use disorder. *Nurse Pract*. 2007;32(9):36–44.
- Mitra S, Sinatra RS. Perioperative management of acute pain in the opioid-dependent patient. *Anesthesiology*. 2004;101(1):212–227.
- Webster LR, Fine PG. Approaches to improve pain relief while minimizing opioid abuse liability. J Pain. 2010;11(7):602–611.
- Abeles M, Solitar BM, Pillinger MH, Abeles AM. Update on fibromyalgia therapy. *Am J Med.* 2008;121(7):555–561.
- 66. Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. *Pain Med.* 2005;6(2):107–112.
- Breuer B, Pappagallo M, Tai JY, Portenoy RK. U.S. board-certified pain physician practices: uniformity and census data of their locations. *J Pain*. 2007;8(3):244–250.
- Meier B. Move to restrict pain killers puts onus on doctors. *New York Times*. July 28, 2010: B1. http://www.nytimes.com/2010/07/29/ business/29pain.html. Accessed November 8, 2010.
- Webster LR, Bath B, Medve RA. Opioid formulations in development designed to curtail abuse: who is the target? *Expert Opin Investig Drugs*. 2009;18(3):255–263.
- Katz N. Abuse-deterrent opioid formulations: are they a pipe dream? Curr Rheumatol Rep. 2008;10(1):11–18.
- Budman SH, Grimes Serrano JM, Butler SF. Can abuse deterrent formulations make a difference? Expectation and speculation. *Harm Reduct J.* 2009;68.
- 72. Young AM, Havens JR, Leukefeld CG. Route of administration for illicit prescription opioids: a comparison of rural and urban drug users. *Harm Reduct J.* 2010;7(1):24.
- McCabe SE, Cranford JA, Boyd CJ, Teter CJ. Motives, diversion and routes of administration associated with nonmedical use of prescription opioids. *Addict Behav.* 2007;32(3):562–575.
- Brennan MJ, Stanos S. Strategies to optimize pain management with opioids while minimizing risk of abuse. *PM R*. 2010;2(6):544–558.

Property of Postgaduate Not copy