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Opioid Treatment Guidelines

Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain

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Abstract: Use of chronic opioid therapy for chronic noncancer pain has increased substantially. The American Pain Society and the American Academy of Pain Medicine commissioned a systematic review of the evidence on chronic opioid therapy for chronic noncancer pain and convened a multidisciplinary expert panel to review the evidence and formulate recommendations. Although evidence is limited, the expert panel concluded that chronic opioid therapy can be an effective therapy for

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carefully selected and monitored patients with chronic noncancer pain. However, opioids are also associated with potentially serious harms, including opioid-related adverse effects and outcomes related to the abuse potential of opioids. The recommendations presented in this document provide guidance on patient selection and risk stratification; informed consent and opioid management plans; initiation and titration of chronic opioid therapy; use of methadone; monitoring of patients on chronic opioid therapy; dose escalations, high-dose opioid therapy, opioid rotation, and indications for discontinuation of therapy; prevention and management of opioid-related adverse effects; driving and work safety; identifying a medical home and when to obtain consultation; management of breakthrough pain; chronic opioid therapy in pregnancy; and opioid-related polices.

Perspective: ***Safe and effective chronic opioid therapy for chronic noncancer pain requires clinical skills and knowledge in both the principles of opioid prescribing and on the assessment and management of risks associated with opioid abuse, addiction, and diversion. Although evidence is limited in many areas related to use of opioids for chronic noncancer pain, this guideline provides recommendations developed by a multidisciplinary expert panel after a systematic review of the evidence.***

Key words: *Clinical practice guideline, opioids, opioid analgesics, risk assessment, monitoring, chronic pain.*

Editor's Note: The American Pain Society and the American Academy of Pain Medicine present this first of 3 articles in this 3-part report as a guideline for opioid treatment of noncancer pain.

Opioid analgesics are widely accepted for the treatment of severe acute pain and chronic pain related to active cancer or at the end of life. In contrast, the use of chronic opioid therapy (COT, see Appendix B, Glossary) to treat other types of chronic pain remains controversial. Chronic pain is defined by the *International Association for the Study of Pain* as "pain that persists beyond normal tissue healing time, which is assumed to be three months."[59] Chronic pain may occur in the context of numerous diseases and syndromes.[51,134] For the purposes of this guideline, all chronic pain disorders outside of cancer pain or pain at end of life are collectively labeled "chronic noncancer pain" (CNCP). CNCP conditions, including common conditions such as back pain, osteoarthritis, fibromyalgia, and headache, are extremely prevalent and account for very large costs. For back pain alone, total health care expenditures in 2004 and 2005 were estimated at $85 to $100 billion.[75] CNCP is a leading cause of disability[16,128] and can have deleterious effects on ability to work, functional status and other quality of life domains.

There are numerous treatments for CNCP and a comprehensive assessment is needed in every case to guide therapeutic decision making. Some patients with CNCP are appropriate for focused therapy with a small number of modalities. Patients with more complex cases, including those with disabling CNCP, tend to experience better outcomes if they are managed using a comprehensive approach that integrates strategies to improve pain with those that address the functional impairment and psychosocial factors that are often associated with CNCP.[88] Whether the plan of care is limited or is designed to be more comprehensive, opioid therapy may be a useful component of the management plan.[30,132] However, the selection of patients for an opioid trial, and decisions about chronic opioid therapy (COT), must weigh potential benefits of opioids against the risk of significant harms, including a wide range of adverse effects as well as adverse outcomes associated with abuse (refer to Appendix B, Glossary for definition) potential.

Opioid prescriptions have increased substantially over the last 20 years,[14,90] in part due to a growing consensus that opioid therapy is appropriate for some patients with CNCP.[132] An increase in prescription opioid misuse (see Glossary) and mortality associated with opioid use has also been observed, affecting adolescent and adults of all ages.[9] Clinicians and regulators must jointly seek a balanced approach to opioid use, acknowledging the legitimate medical need for opioids in some patients with CNCP, while concurrently recognizing the serious public health problem of abuse (see Appendix B, Glossary), addiction (see Appendix B, Glossary) and diversion (see Appendix B, Glossary), and implement procedures to reduce these risks.

The American Pain Society (APS), in partnership with the American Academy of Pain Medicine (AAPM), commissioned a multidisciplinary panel to develop evidence-based guidelines on COT for adults with CNCP. These recommendations are based on a systematic evidence review also commissioned by the APS and AAPM.[19]

Methods

Panel Composition

The APS and AAPM convened a multidisciplinary panel of 21 experts to review the evidence and formulate recommendations (see Appendix 1 for list of panel members). Two co-chairs (P.F. and G.F.) were selected by the APS and AAPM to lead the panel, which also included the Chair of the APS Clinical Practice Guidelines Committee (C.M.) and the APS Director of Clinical Guidelines Development (R.C.).

Target Audience and Scope

The intent of the guideline is to provide evidence-based recommendations for use of COT for CNCP in

both primary care and specialty settings. The target audience is all clinicians who provide care for adults with CNCP, including cancer survivors with chronic pain due to their cancer or its treatment. Management of cancer pain, pain at end of life, acute pain, postsurgical pain, labor pain, or CNCP in children and adolescents is outside the scope of this guideline. Separate APS guidelines address management of sickle cell pain[5] and cancer pain.[83]

Funding and Conflicts of Interest

Funding for the guideline was provided by the APS. The guideline was approved by the APS and AAPM, but the content of the guideline is the sole responsibility of the authors and panel members. All panelists were required to disclose conflicts of interest within the preceding 5 years at all face-to-face meetings and before submission of the guideline for publication, and recused themselves from votes if a conflict was present. Conflicts of interest of the authors and panel members are listed in Appendix 1.

Evidence Review

This guideline is informed by an evidence review conducted at the Oregon Evidence-based Practice Center and commissioned by APS and AAPM.[19] The panel developed the key questions, scope, and inclusion criteria used to guide the evidence review. Literature searches were conducted through November 2007. Investigators reviewed 8,034 abstracts from searches for systematic reviews and primary studies from multiple electronic databases, reference lists of relevant articles, and suggestions from expert reviewers. A total of 14 systematic reviews and 57 primary studies (not included in previously published systematic reviews) were included in the evidence report.[19]

Grading of the Evidence and Recommendations

The panel used methods adapted from the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group to rate the recommendations included in this guideline.[52] Each recommendation received a separate grade for the strength of the recommendation (strong or weak) and for the quality of evidence (high, moderate, or poor) (Appendix 2). In general, a strong recommendation is based on the panel's assessment that potential benefits of following the recommendation clearly outweigh potential harms and burdens. Given the available evidence, most clinicians and patients would choose to follow a strong recommendation. A weak rating is based on more closely balanced benefits to harms or burdens, or weaker evidence. Decisions to follow a weak recommendation could vary depending on specific clinical circumstances or patient preferences and values. For grading the quality of a body of evidence that supports a recommendation, we considered the type, number, size, and quality of studies; strength of associations or effects; and consistency of results among studies.[52]

Guideline Development Process

The guideline panel met in person on three occasions between September 2006 and January 2008. At the first meeting, the panel developed the scope and key questions used to guide the systematic evidence review. At the second meeting, the panel reviewed the results of the evidence review and drafted initial potential recommendation statements. In between the second and third meetings, panelists participated in a multi-stage Delphi process, in which the draft recommendations were ranked and revised. At each stage of the Delphi process, the lowest-ranked recommendations were eliminated. At the third meeting, the final set of recommendations and recommendation grades were finalized and approved. Although a two-thirds majority was required for a recommendation to be approved, unanimous agreement was achieved on all but two recommendations (5.2 and 5.3 each had 2 panelists voting against). After the third meeting, the guideline was written by various panel members and drafts distributed to the panel for feedback and revisions. Over twenty external peer reviewers were solicited for additional comments. After another round of revisions and panel approval, the guideline was submitted to the APS and AAPM Executive Committees for approval.

The APS intends to update its clinical practice guidelines regularly. This guideline and the evidence report used to develop it will be reviewed and updated by 2012, or earlier if critical new evidence becomes available.

Recommendations

1. Patient Selection and Risk Stratification

Recommendations

1.1 Before initiating COT, clinicians should conduct a history, physical examination and appropriate testing, including an assessment of risk of substance abuse, misuse, or addiction (strong recommendation, low-quality evidence).

1.2 Clinicians may consider a trial of COT as an option if CNCP is moderate or severe, pain is having an adverse impact on function or quality of life, and potential therapeutic benefits outweigh or are likely to outweigh potential harms (strong recommendation, low-quality evidence).

1.3 A benefit-to-harm evaluation including a history, physical examination, and appropriate diagnostic testing, should be performed and documented before and on an ongoing basis during COT (strong recommendation, low-quality evidence).

Proper patient selection is critical and requires a comprehensive benefit-to-harm evaluation that weighs the potential positive effects of opioids on pain and function against potential risks. Thorough risk assessment and stratification is appropriate in every case. This approach is justified by estimates of aberrant drug-related behaviors (see Appendix B, Glossary), drug abuse, or misuse

in patients with CNCP, which range from 0% to 50%, depending on the population evaluated and methods used to define and identify these outcomes.[57] Risk stratification pertaining to outcomes associated with the abuse liability of opioids—misuse, abuse, addiction and diversion—is a vital but relatively undeveloped skill for many clinicians.[96] However, all clinicians prescribing opioids should be knowledgeable about risk factors for opioid abuse and methods for assessing risk. Assessment of risks for opioid-associated adverse effects also should be performed, given their high prevalence.[86]

A thorough history and physical examination, including an assessment of psychosocial factors and family history, is essential for adequate risk stratification. Implicit in the recommendation to conduct a comprehensive benefit-to-harm analysis is the recognition that an opioid trial may not be appropriate. Clinicians should obtain appropriate diagnostic tests to evaluate the underlying pain condition, and should consider whether the pain condition may be treated more effectively with nonopioid therapy rather than with COT. For example, COT generally would not be appropriate before a trial of an anticonvulsant for trigeminal neuralgia,[7] a disease-modifying antirheumatic drug for rheumatoid arthritis,[27] a corticosteroid for polymyalgia rheumatica,[118] or various abortive and prophylactic therapies for migraine headache.

Reliable evidence on methods to accurately assess the potential benefits of COT is limited. However, randomized trials that demonstrate the benefits of COT are most applicable to patients with moderate or more severe pain who have not responded to nonopioid therapies.[42,63] Presence of poorly-defined pain conditions, a likely somatoform disorder, or unresolved compensation or legal issues may predict poorer response to all therapies, including COT.[103,114] Although neuropathic and non-neuropathic pain conditions appear in general to respond similarly to COT,[42,63,86] evidence that demonstrates the efficacy of COT for conditions with strong psychosocial contributors such as some types of chronic low back pain,[74] daily headache,[119] and fibromyalgia[48] is sparse. There is insufficient evidence to recommend use of an intravenous opioid trial to predict likelihood of benefit from COT.[63]

The factor that appears to be most strongly predictive of drug abuse, misuse, or other aberrant drug-related behaviors after initiation of COT is a personal or family history of alcohol or drug abuse.[28,35,60,72,85,111] Younger age and presence of psychiatric conditions are also associated with aberrant drug-related behaviors in some studies.[28,35,60,84,111] Preexisting constipation, nausea, pulmonary disease, and cognitive impairment probably predict risk for opioid-related adverse effects, though no studies have adequately evaluated the utility of these factors for use in risk stratification.

Clinicians should consider a trial of COT for CNCP when potential benefits are likely to outweigh risks, and there is no alternative therapy that is likely to pose as favorable a balance of benefits to harms. For example, a patient who is 60 years old, has chronic disabling osteoarthritis pain despite nonopioid therapies, and whose history reveals no significant psychiatric comorbidities, major medical comorbidities, or personal or family history of drug abuse or addiction would be assessed as having high potential benefits from COT relative to potential risks. COT could be prescribed to this patient in most clinical settings with routine monitoring (see Section 5). In contrast, a patient who is 30 years old with fibromyalgia and recent intravenous drug abuse would have high potential risks relative to benefits. COT in this context requires intensive structure, monitoring, and management by professionals with expertise in both addiction medicine and pain medicine and should be undertaken only if risks can be adequately managed (see Section 6). The selection of patients between these two extremes requires careful assessment and characterization of patient risk and structuring of care to match risk (see Section 5). In patients with a history of substance abuse or a psychiatric comorbidity, this may require assistance from persons with expertise in managing pain, addiction or other mental health concerns (see Section 6), and in some cases opioids may not be appropriate or should be deferred until the comorbidity has been adequately addressed.

Screening tools that assess the potential risks associated with COT based on patient characteristics are likely to be helpful for risk stratification, though more validation and prospective outcome studies are needed to understand how their use predicts and affects clinical outcomes. Tools that appear to have good content, face, and construct validity include the Screener and Opioid Assessment for Patients with Pain (SOAPP) Version 1 (Appendix 3),[10] the revised SOAPP (SOAPP-R),[12] the Opioid Risk Tool (ORT) (Appendix 4),[138] and the Diagnosis, Intractability, Risk, Efficacy (DIRE) instrument (Appendix 5).[4] DIRE is clinician-administered and is designed to assess potential efficacy as well as harms. The SOAPP Version 1, SOAPP-R and ORT are patient self-report questionnaires that assess risk of aberrant drug-related behaviors.

2. Informed Consent and Opioid Management Plans

Recommendations

2.1 When starting COT, informed consent should be obtained. A continuing discussion with the patient regarding COT should include goals, expectations, potential risks, and alternatives to COT (strong recommendation, low-quality evidence).

2.2 Clinicians may consider using a written COT management plan to document patient and clinician responsibilities and expectations and assist in patient education (weak recommendation, low-quality evidence).

Clinicians should inform patients about the risks and benefits associated with COT before initiating a trial of therapy.[30] In patients already on COT, clinicians should periodically review risks and benefits of therapy. Patients should be counseled about the potential for common opioid-related adverse effects (eg, constipation, nausea, sedation) as well as other serious risks (eg, abuse, addiction, overdose). Potential risks of long-term or high-dose

COT (eg, hyperalgesia (see Appendix B, Glossary), endocrinologic or sexual dysfunction) should also be discussed, though more evidence is needed to better understand and quantify these risks.[24,25,73,82] The goal of the consent process is to assist patients to make appropriate medical decisions that are consistent with their preferences and values. In some states, clinicians are required to document this discussion, though specific requirements vary.[95] A sample informed consent form is shown in Appendix 6.

It is important for clinicians to discuss a COT management plan before initiating a course of treatment and on an ongoing basis while patients are on therapy.[30] The COT management plan includes goals of therapy, how opioids will be prescribed and taken, expectations for clinic follow-up and monitoring (see Section 5), alternatives to COT, expectations regarding use of concomitant therapies, and potential indications for tapering or discontinuing COT, which may include failure to make progress toward therapeutic goals, intolerable adverse effects, or repeated or serious aberrant drug-related behaviors.[2] Patients should be counseled that opioids may be just one part of a multimodal treatment plan (see Section 9) to reduce pain intensity and improve quality of life, especially functional capacity. To avoid unrealistic patient expectations regarding likely benefits, patients should be counseled that total pain relief with COT is rare. Indeed, trials suggest that improvement averages less than 2 to 3 points on a 0 to 10 scale.[42,63]

Although evidence is lacking about the most effective methods to convey the COT management plan, written documentation can help clarify the plan with the patient, the patient's family, and other clinicians who may become involved in the patient's care. For patients at higher risk for misuse of opioid analgesics, use of clear written guidelines may be particularly helpful to reinforce expectations about the appropriate and safe use of opioids. Though the content of written COT management plans vary,[34] provisions may include: Obtaining opioids from one prescriber, filling opioids prescriptions at one designated pharmacy, random urine drug screens, office visits at a specified minimum interval, use of pill counts, limited prescriptions (in weekly or biweekly instead of monthly amounts) and enumeration of behaviors that may lead to discontinuation of opioids. However, there is insufficient evidence to guide specific recommendations on which provisions to include. A sample COT management plan is shown in Appendix 7.

There is increasing awareness that theft from medicine cabinets is a major source of diverted opioids. All patients should be encouraged to lock their medications (eg, using a medicine safe). Guidance is available on best methods for disposing of opioids.[89]

3. Initiation and titration of COT

Recommendations

3.1 Clinicians and patients should regard initial treatment with opioids as a therapeutic trial to determine whether COT is appropriate (strong recommendation, low-quality evidence).

3.2 Opioid selection, initial dosing, and titration should be individualized according to the patient's health status, previous exposure to opioids, attainment of therapeutic goals, and predicted or observed harms (strong recommendation, low-quality evidence). There is insufficient evidence to recommend short-acting versus long-acting opioids, or as-needed versus around-the-clock dosing of opioids.

An initial course of treatment with opioids for CNCP should be viewed as a short-term, therapeutic trial lasting from several weeks to several months. The decision to proceed with COT should be intentional and based on careful consideration of outcomes during the trial. Outcomes to consider include progress toward meeting therapeutic goals, presence of opioid-related adverse effects, changes in the underlying pain condition, changes in psychiatric or medical comorbidities, and the identification of aberrant drug-related behaviors, addiction, or diversion (see Section 5 on monitoring). In most cases, the therapeutic trial includes individualization of the dose through incremental dose escalations, as long as no serious harms are present. In patients who experience mild or moderate opioid-related adverse effects, a longer trial may be indicated because some adverse effects decrease with longer exposure. Some adverse effects can be managed with additional therapies (see Section 8). Suspected aberrant drug-related behaviors require further evaluation and action (see Section 6).

In patients who are opioid-naïve, or have modest previous opioid exposure, opioids should be started at a low dose and titrated slowly, to decrease risk of opioid-related adverse effects. However, there is insufficient evidence to recommend specific optimal starting doses and methods of dose titration. In general, opioid doses should be individualized based on risk for adverse outcomes and responses to therapy. Some patients, such as frail older persons or those with comorbidities, may benefit from more cautious initiation and titration of therapy. Short-acting opioids are probably safer for initial therapy since they have a shorter half-life and may be associated with a lower risk of inadvertent overdose. However, there is no direct evidence from randomized trials that demonstrates that any one opioid is superior to any other for initial therapy (see Section 4 for issues regarding methadone).[17] There is also insufficient evidence to guide recommendations for use of short-acting versus long-acting opioids,[17] or as-needed versus around-the-clock dosing. Proposed benefits of transitioning to long-acting opioids with around-the-clock dosing include more consistent control of pain, improved adherence and lower risk of addiction or abuse, though well-conducted studies have not examined these benefits.

4. Methadone

Recommendation

4.1 Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics

and should be initiated and titrated cautiously, by clinicians familiar with its use and risks (strong recommendation, moderate-quality evidence).

Use of methadone for CNCP has increased dramatically.[15] However, few trials have evaluated benefits and harms of methadone for CNCP.[17] In addition, a number of epidemiologic studies suggest an increased rate of methadone-associated deaths in the United States.[15,44,76,91] QTc prolongation and cardiac arrhythmias may occur in patients on methadone, particularly at higher doses, or with concomitant use of drugs that interact with methadone or that themselves prolong QTc.[21,23,68]

Clinicians who prescribe methadone should be familiar with its clinical pharmacology and associated risks. Methadone has a very long and highly variable half-life, which necessitates careful titration to avoid delayed adverse events, such as overdose. Although the half-life of methadone is usually estimated at 15 to 60 hours, in some reports the half-life is as high as 120 hours.[71] In a patient for whom the methadone half-life is 60 hours, it would take almost 12 days on a stable dose of methadone to approach a steady state (5 half-lives). Methadone should therefore be started at low doses and titrated slowly. Based on panel consensus, a safe starting dose in most opioid-naïve patients is 2.5 mg every 8 hours, with dose increases occurring no more frequently than weekly. In older patients or those with renal or hepatic comorbidities, less frequent dosing and more cautious dose titration are recommended.

In opioid-tolerant patients, conversion to methadone should be performed cautiously. Equianalgesic dose ratios for methadone relative to other opioids are variable and can range from 0.1% to 10% morphine equivalents (lower at higher doses). In patients on lower doses of other opioids, safe starting doses of methadone may be similar to those used for opioid-naïve patients. Starting methadone doses should generally not exceed 30 to 40 mg a day even in patients on high doses of other opioids. Several algorithms are available for converting from other opioids to methadone, though there is insufficient evidence to recommend a particular method, and much of the evidence is derived from studies of patients with cancer.[49,69,112] Because of its long half-life and variable pharmacokinetics, the panel recommends that methadone not be used to treat breakthrough pain or as an as-needed medication.

5. Monitoring

Recommendations

5.1 Clinicians should reassess patients on COT periodically and as warranted by changing circumstances. Monitoring should include documentation of pain intensity and level of functioning, assessments of progress toward achieving therapeutic goals, presence of adverse events, and adherence to prescribed therapies (strong recommendation, low-quality evidence).

5.2 In patients on COT who are at high risk or who have engaged in aberrant drug-related behaviors, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the COT plan of care (strong recommendation, low-quality evidence).

5.3 In patients on COT not at high risk and not known to have engaged in aberrant drug-related behaviors, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the COT plan of care (weak recommendation, low-quality evidence).

Clinicians should periodically reassess all patients on COT. Regular monitoring of patients once COT is initiated is critical because therapeutic risks and benefits do not remain static and can be affected by changes in the underlying pain condition, presence of coexisting disease, or changes in psychological or social circumstances. Monitoring is essential to identify patients who are benefiting from COT, those who might benefit more with restructuring of treatment or receiving additional services such as treatment for addiction, and those whose benefits from treatment are outweighed by harms. Insufficient evidence exists to guide precise recommendations on appropriate monitoring intervals. However, risk stratification (see Section 1) is useful for guiding the approach to monitoring. In patients at low risk for adverse outcomes and on stable doses of opioids, monitoring at least once every three to six months may be sufficient. Patients who may need more frequent or intense monitoring, at least for a period of time after initiation of therapy or changes in opioid doses, include those with a prior history of an addictive disorder, those in an occupation demanding mental acuity, older adults, patients with an unstable or dysfunctional social environment, and those with comorbid psychiatric or medical conditions. For patients at very high risk for adverse outcomes, monitoring on a weekly basis may be a reasonable strategy.

Monitoring that involves regular, repeated evaluations and addresses a variety of domains is likely to be more informative than infrequent, narrowly focused evaluations. Although there is insufficient evidence for specific recommendations about how to monitor patients on COT, there is general agreement that monitoring should routinely include assessment and documentation of pain severity and functional ability, progress toward achieving therapeutic goals, and presence of adverse effects.[98] In addition, clinicians should routinely carry out a thorough clinical assessment for presence of aberrant drug-related behaviors, substance use, and psychological issues. Because patient self-report may be unreliable for determining amount of opioid use, functionality, or aberrant drug-related behaviors,[31,67,110] pill counts, urine drug screening , family member or caregiver interviews, and use of prescription monitoring program data can be useful supplements. Although evidence is lacking on the accuracy and effects on clinical outcomes of formal screening instruments for identification of aberrant drug-related behaviors, use of tools with strong content, face and construct validity, such as the PADT (Appendix 8)[97,98] and COMM (Appendix 9)[11] are

recommended as an efficient method of assessment and documentation.

Periodic urine drug screening can be a helpful tool to monitor patients on COT.[65] Urine drug screening is likely to result in a higher yield in patients with risk factors for drug abuse or diversion. However, targeted (nonuniversal) urine drug screening will miss some proportion of patients who engage in aberrant drug-related behaviors, as predictors of such behaviors are relatively weak.[18] Random urine drug screens may be more informative than scheduled or routine testing, as patients may change behaviors when they expect to be tested, though there are no studies comparing these approaches. Although evidence on accuracy of urine drug screening to identify aberrant drug-related behaviors or diversion is lacking, and no evidence exists that demonstrates that screening improves clinical outcomes, absence of prescribed opioids or presence of unprescribed opioids or illicit drugs can be a marker for problematic issues that would not be apparent without urine drug screening.[67] Interpretation of urine drug screen results is a challenge, and requires an understanding of opioid drug metabolism, pharmacokinetics and limits of laboratory testing methods.[8] In fact, urine drug screen results usually do not suggest a definitive course of action, but rather should be interpreted in the context of individual patient circumstances.[55] Clinicians should consider a differential diagnosis for abnormal urine drug screen results, including drug abuse or addiction, self-treatment of poorly controlled pain, psychological issues, or diversion (which may be suggested by absence of prescribed opioids).

6. High-Risk Patients

Recommendations

6.1 Clinicians may consider COT for patients with CNCP and history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors only if they are able to implement more frequent and stringent monitoring parameters. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist (strong recommendation, low-quality evidence).

6.2 Clinicians should evaluate patients engaging in aberrant drug-related behaviors for appropriateness of COT or need for restructuring of therapy, referral for assistance in management, or discontinuation of COT (strong recommendation, low-quality evidence).

CNCP is common in patients with suspected aberrant drug-related behaviors, psychosocial comorbidities, and history of substance abuse.[115,129] Use of COT is challenging in these patients because they are more vulnerable to drug misuse, abuse, and addiction. In some patients, such as those actively using illicit drugs, potential benefits are outweighed by potential risks, and COT should not be prescribed outside of highly controlled and specialized settings (such as an opioid treatment program with directly observed therapy). In other patients, potential benefits of COT may outweigh potential risks. Although evidence is lacking on best methods for managing such patients, potential risks may be minimized by more frequent and intense monitoring compared with lower risk patients (see Section 5), authorization of limited prescription quantities, and consultation or co-management with persons who have expertise in addiction or mental health issues. In settings where local access to specialists is limited, clinicians may need to consider alternative methods (such as telemedicine or web-based resources) for obtaining consultative services, though there is no evidence evaluating risks and benefits compared with traditional face-to-face consultation. Clinicians should also be aware of and use prescription monitoring programs if they are available in their area of practice, as they can help identify patients who obtain drugs from multiple sources.[62]

The occurrence of aberrant drug-related behavior always suggests the need for re-evaluation, and perhaps a change in therapy. However, aberrant drug-related behaviors vary in seriousness. Clinicians should formulate a differential diagnosis when evaluating suspected aberrant drug-related behaviors (see Section 5).[41] The response to aberrant drug-related behavior reflects a clinical judgment about its seriousness, its cause or causes, the likelihood that behaviors of this type will recur, and the clinical context. Although evidence to guide optimal management strategies is lacking, anecdotal experience of panel members suggests that patients who are not assessed as being at high risk and engage in a relatively nonserious aberrant behavior, such as one or two episodes of unauthorized opioid escalations, can often be managed with patient education and enhanced monitoring. Patients who are repeatedly nonadherent and patients who engage in more serious aberrant behaviors (such as use of cocaine, use of unprescribed opioids, or obtaining opioids from multiple outside sources) may require consultation or referral (if not already done), major restructuring of therapy, and in many cases discontinuation of COT (see Section 7). In one study, four or more previous aberrant drug-related behaviors were a strong predictor of a current substance use disorder.[35] Patients who report a subjective sense of losing control regarding opioid use may also require restructuring of therapy, as this may predict future aberrant drug-related behaviors.[139] Patients who meet criteria for a substance use disorder should be referred for treatment of this serious comorbidity.

Restructuring of therapy may include more frequent or intense monitoring strategies, temporary or permanent tapering of opioid doses, or the addition of psychological therapies or other nonopioid treatments. In patients with opioid addiction who require ongoing pain treatment and do not respond to nonopioid analgesic interventions, structured opioid agonist treatment with methadone or buprenorphine by a licensed program may be an appropriate option. COT must be discontinued in patients who are known to be diverting opioids or in those engaging in seriously aberrant behaviors (such as injecting an oral formulation). Patients whose COT is to be discontinued may require referral or

consultation for assistance with opioid detoxification and management of withdrawal (see Section 7).

7. Dose Escalations, High-Dose Opioid Therapy, Opioid Rotation, and Indications for Discontinuation of Therapy

Recommendations

7.1 When repeated dose escalations occur in patients on COT, clinicians should evaluate potential causes and reassess benefits relative to harms (strong recommendation, low-quality evidence).

7.2 In patients who require relatively high doses of COT, clinicians should evaluate for unique opioid-related adverse effects, changes in health status, and adherence to the COT treatment plan on an ongoing basis, and consider more frequent follow-up visits (strong recommendation, low-quality evidence).

7.3 Clinicians should consider opioid rotation when patients on COT experience intolerable adverse effects or inadequate benefit despite dose increases (weak recommendation, low-quality evidence).

7.4 Clinicians should taper or wean patients off of COT who engage in repeated aberrant drug-related behaviors or drug abuse/diversion, experience no progress toward meeting therapeutic goals, or experience intolerable adverse effects (strong recommendation, low-quality evidence).

Management of treatment-refractory patients on high doses of COT is challenging. Although progressively higher opioid doses may improve symptom control in some patients, repeated dose escalations can also be a marker for a substance use disorder or diversion. In some patients, repeated dose escalations may have limited utility because of adverse effects, the lack of incremental benefit with higher doses, or other factors. Theoretically, opioids have no maximum or ceiling dose, but there is little evidence to guide safe and effective prescribing at higher doses and there is no standardized definition for what constitutes a "high" dose. By panel consensus, a reasonable definition for high dose opioid therapy is >200 mg daily of oral morphine (or equivalent), based on maximum opioid doses studied in randomized trials[42,63] and average opioid doses observed in observational studies.[105] Some studies suggest that hyperalgesia,[1,20] neuroendocrinologic dysfunction,[25,70] and possibly immunosuppression[113,116] may be more likely at higher opioid doses, though more evidence is needed to define these risks, their relationship to dose, and their relationship to clinical outcomes.

Clinicians should carefully reassess (see Section 5) all patients on COT who have repeated dose escalations. When opioid doses reach 200 mg daily of morphine (or equivalent), more frequent and intense monitoring is often appropriate, to sufficiently inform the decision to continue therapy or consider additional dose escalations. Opioid treatment may require restructuring (including weaning or discontinuation of COT) if assessments indicate reduced analgesia, function, or quality of life; aberrant drug-related behaviors; or the presence of intolerable adverse effects.

Opioid rotation (switching from one opioid to another opioid) is a potential strategy for patients on COT who experience intolerable adverse effects or inadequate benefit despite dose increases. The theory behind opioid rotation is based on concepts of incomplete cross-tolerance to the analgesic and nonanalgesic effects across opioids and a high degree of individual variation in response to different opioids. This could potentially lead to a better balance of benefits to harms when one opioid is changed to another.[80,108] However, well-designed studies that evaluate the benefits and harms of opioid rotation are lacking, and available studies in patients with CNCP show inconsistent results.[38-40] There is also insufficient evidence to guide specific recommendations for performing opioid rotation. Dose conversion tables and rotation protocols are available[102] and generally suggest that a switch to a new drug should be accompanied by a moderate (usually 25% to 50%) reduction in the calculated equianalgesic dose. However, this method does not apply to cases in which patients are being rotated to methadone (see Section 4).

Patients should be tapered or weaned off COT when they engage in serious or repeated aberrant drug-related behaviors or diversion, experience intolerable adverse effects, or make no progress toward meeting therapeutic goals. Although there is insufficient evidence to guide specific recommendations on optimal strategies, a taper or wean can often be achieved in the outpatient setting in patients without severe medical or psychiatric comorbidities. When available, opioid detoxification in a rehabilitation setting (outpatient or inpatient) can be helpful, especially for patients unable to reduce their opioid dose in a less structured setting. When aberrant drug-related behaviors are a continuing issue, the clinician may need to enforce weaning efforts. If the aberrant behaviors are thought to be due to addiction, addiction treatment resources should be made available and continued follow-up arranged to provide both support for nonopioid pain management and to motivate the patient to seek treatment for addiction.

Symptoms of opioid withdrawal can be very unpleasant, but are generally not life threatening. Approaches to weaning range from a slow 10% dose reduction per week to a more rapid 25% to 50% reduction every few days. Evidence to guide specific recommendations on the rate of reduction is lacking, though a slower rate may help reduce the unpleasant symptoms of opioid withdrawal.[22,109,131] Factors that may influence the rate of reduction include the reason driving the decision to discontinue COT, presence of medical and psychiatric comorbidities, the starting dose, and the occurrence of withdrawal symptoms as the process is initiated. Anecdotal clinical experience of panel members suggests that at high doses (eg, over 200 mg/d of morphine or equivalent), the initial wean can be more rapid. The rate of dose reduction often must be slowed when relatively low daily doses, such as 60 to 80 mg daily of morphine (or equivalent), are reached, due to occurrence

of more withdrawal symptoms. Patients weaned from COT because of lack of effectiveness may report improvements in well-being and function without any worsening in pain,[3] though other patients may experience pain hypersensitivity during opioid withdrawal.[1] Clinicians should continue to treat patients who are withdrawn from COT for their painful condition as well as for substance use or psychiatric disorders.

8. Opioid-Related Adverse Effects

Recommendation

8.1 Clinicians should anticipate, identify, and treat common opioid-associated adverse effects (strong recommendation, moderate-quality evidence).

An important goal of any COT management plan is to maintain a favorable balance of benefits relative to harms. Anticipation and treatment of opioid-associated adverse effects reduce the likelihood that patients will discontinue COT due to intolerable adverse effects, and may allow use of higher opioid doses if needed for uncontrolled pain.

Constipation is one of the most common opioid-related adverse effects.[86] Most patients develop some degree of constipation after opioid initiation or dose increases, and resolution of constipating effects of opioids often does not occur with continued exposure. In older adults or other patients with additional reasons to develop constipation, we recommend routinely considering initiation of a bowel regimen before the development of constipation. Though most evidence is anecdotal, bowel regimens including increased fluid and fiber intake, stool softeners, and laxatives are often effective. There is insufficient evidence to recommend oral opioid antagonists to prevent or treat opioid-induced bowel dysfunction in persons with CNCP, though randomized trials suggest some potential benefits over placebo.[100,137]

Nausea or vomiting is another common opioid-associated adverse effect that tends to diminish over days or weeks of continued opioid exposure. A number of antiemetic therapies, in both oral and rectal forms, are available to treat nausea or vomiting.

Sedation or clouded mentation after opioid initiation also tends to wane over time. When initiating or changing doses of opioids, patients should be counseled about driving and work and home safety (see Section 10). In addition, patients should be counseled on effects and risks of concomitant exposure to other drugs and substances with sedating effects. There is insufficient evidence to recommend specific pharmacologic therapies for persistent opioid-related sedation.

Chronic use of sustained-release oral opioids for CNCP was associated with hypogonadism and decreased levels of dehydroepiandrosterone sulfate in several cross-sectional studies.[24-26] Patients should be tested for such hormonal deficiencies if they report symptoms consistent with their presence, such as decreased libido, sexual dysfunction, or fatigue. Insufficient evidence exists to recommend routine monitoring of asymptomatic patients on COT for CNCP for hormonal deficiencies, or to guide specific treatment approaches if a deficiency is identified.

Other common opioid-related adverse effects include pruritus and myoclonus. Effective treatment strategies for either condition are largely anecdotal. Respiratory depression may occur when initial opioid doses are too high, opioids are titrated too rapidly, or opioids are combined with other drugs that are associated with respiratory depression or that may potentiate opioid-induced respiratory depression (such as benzodiazepines). Patients with sleep apnea or other underlying pulmonary conditions may be at higher risk for respiratory depression and opioids should be initiated and titrated carefully.

9. Use of Psychotherapeutic Cointerventions

Recommendation

9.1 As CNCP is often a complex biopsychosocial condition, clinicians who prescribe COT should routinely integrate psychotherapeutic interventions, functional restoration, interdisciplinary therapy, and other adjunctive nonopioid therapies (strong recommendation, moderate-quality evidence).

CNCP is often a complex condition that may involve biological, psychological, and environmental factors.[88] When pain is accompanied by comorbidities, impaired function, or psychological disturbances, COT is likely to be most effective as part of multimodality treatment that addresses all of these domains. Clinicians should routinely integrate therapies that target the psychosocial and functional factors that contribute to or are affected by CNCP.

Cognitive-behavioral therapy is the best-studied psychological therapy and is consistently shown to be effective for CNCP.[56,78,87,92,133] It often focuses on helping patients cope with chronic pain to improve function. Other potentially beneficial psychological therapies include progressive relaxation, biofeedback, and other techniques.[133] Functional restoration with specific behavioral interventions, pain education, and simulated or actual physical tasks in a supervised environment may enhance function and improve strength, endurance, flexibility, and cardiovascular fitness.[121] Interdisciplinary or multidisciplinary pain management approaches coordinate physical, vocational, or psychological components and are provided by at least two health care professionals with different clinical backgrounds, and may be the best method for providing multimodality therapy for the highly disabled CNCP patient.[36,53,64] The intensity and content of interdisciplinary therapy varies widely, but most involve an exercise program and some type of psychological therapy. More intensive interdisciplinary programs tend to be more effective than less intensive programs.[53] Barriers to obtaining interdisciplinary therapy include high costs, limited availability in the United States, and frequent lack of insurance coverage. In addition, patients are more likely to benefit if highly

motivated to participate, because interdisciplinary rehabilitation generally requires a high degree of engagement and commitment of time and effort.

10. Driving and Work Safety

Recommendation

10.1 Clinicians should counsel patients on COT about transient or lasting cognitive impairment that may affect driving and work safety. Patients should be counseled not to drive or engage in potentially dangerous activities when impaired or if they describe or demonstrate signs of impairment (strong recommendation, low-quality evidence).

Opioids may cause somnolence, clouded mentation, decreased concentration, and slower reflexes or incoordination, especially when initiating therapy, increasing doses, or when opioids are taken with other drugs or substances that affect the central nervous system.[86,101,126] These effects could impair patients' abilities to drive or work safely. However, epidemiologic studies suggest that motor vehicle accidents, fatalities, and citations for impaired driving are not disproportionally associated with opioid use.[32,33] Other studies indicate that patients who initiate opioids or are on COT perform similarly to patients not on COT on standardized driving tests.[13,43,45,79,117] Shortcomings of the evidence include a reliance on cross-study comparisons (eg, rates of opioid use in persons involved in motor vehicle accidents compared with estimates of opioid use in the general population), use of simulated and other controlled driving tests that may not completely mirror real-world driving conditions, and probable selection bias, as patients experiencing central nervous system opioid-related adverse effects are probably less likely to drive or to participate in studies that evaluate driving ability. No studies have evaluated the effects of COT on work safety.

As a public health measure and for the individual patient's safety, clinicians should counsel all patients initially prescribed COT not to drive or engage in potentially dangerous work or other activities when impaired. Patients should be educated about the greater risk of impairment when starting opioid therapy, when increasing doses, and when taking other drugs or substances that may have central nervous effects, including alcohol. Clinicians should counsel patients not to drive or engage in potentially dangerous activities if they describe or demonstrate signs of impairment, and should refer to state laws regarding physician-reporting requirements to local authorities in these situations. In the absence of signs or symptoms of impairment, no evidence exists to suggest that patients maintained on COT should be restricted from driving or engaging in most work activities. Some studies suggest that COT may improve cognitive functioning due to better control of pain.[61,130] However, clinicians should be aware that certain professions (such as bus drivers and pilots) may be subject to additional regulations and laws regarding use of opioids.

11. Identifying a Medical Home and When to Obtain Consultation

Recommendations

11.1 Patients on COT should identify a clinician who accepts primary responsibility for their overall medical care. This clinician may or may not prescribe COT, but should coordinate consultation and communication among all clinicians involved in the patient's care (strong recommendation, low-quality evidence).

11.2 Clinicians should pursue consultation, including interdisciplinary pain management, when patients with CNCP may benefit from additional skills or resources that they cannot provide (strong recommendation, moderate-quality evidence).

Studies show that patients do better when they have continuous access to a clinician who provides comprehensive care for the large majority of their health care needs and who coordinates care when the services of other health care professionals are needed.[127] Having a clinician who accepts primary responsibility for their overall medical care is likely to be particularly important for patients with CNCP, as they use health care services more frequently[122] and have more comorbidities[136] than those without CNCP. US adults with a primary care clinician, rather than a specialist, as their main health care provider had 33% lower costs of care and were 19% less likely to die at a given age compared with a matched cohort, after adjusting for demographic and health characteristics.[37] Having a primary care clinician is a powerful predictor of longevity.[124]

The attributes of effective primary care were described recently in a model known as the patient-centered primary care medical home.[99] With their multiple and complex health care needs, patients with CNCP require the coordinated and comprehensive services offered through a medical home. The medical home model does not necessarily require the primary care clinician to prescribe and monitor COT. In fact, patients with CNCP may need additional or special services that may not be available in their medical home. In such cases, consultation with other professionals is essential. In particular, pain centers that provide access to an array of pain therapies and specialists trained to assess, prescribe, and monitor COT can be highly valuable. Nonetheless, the primary care clinician should continue to coordinate consultation and communication among all clinicians involved in the patient's treatment.

12. Breakthrough Pain

Recommendation

12.1 In patients on around-the-clock COT with breakthrough pain, clinicians may consider as-needed opioids based upon an initial and ongoing analysis of therapeutic benefit versus risk (weak recommendation, low-quality evidence).

Patients prescribed stable doses of around-the-clock COT for CNCP frequently experience periods of increased

pain (ie, breakthrough pain).[6,106] Breakthrough pain (see Appendix B, Glossary) should be assessed separately from the baseline pain, and can be related to progression of the underlying condition, or a new or unrelated pain condition. Appropriate evaluation of breakthrough pain may require additional diagnostic testing, follow-up visits, or consultation in order to identify the etiology of the pain or the factors precipitating it. Management of breakthrough pain should include consideration of specific therapies directed at the cause of the pain or the precipitating factors, or nonspecific symptomatic therapies intended to lessen the impact of breakthrough pain when it occurs.

There is insufficient evidence to guide recommendations regarding optimal treatment strategies for breakthrough pain in patients with CNCP. Limited evidence from short-term trials suggest that short-acting or rapid onset, as-needed opioids may be effective in this setting, but more studies are needed to evaluate the long-term benefits and harms of this strategy, and to compare effects of different short-acting or rapid onset opioids.[104,125] Clinicians should weigh carefully the potential benefits versus risks when considering the addition of an as-needed opioid for treatment of breakthrough pain, and consider both nonopioid drug therapies and nonpharmacologic treatments as other options. Although there is no evidence on the risk of aberrant drug-related behavior in relation to the availability of medication prescribed for breakthrough pain, it is reasonable to assume that access to a short-acting drug may increase the risk of such behavior in those already engaging in them or at high risk to do so. In patients at low risk for aberrant drug-related behaviors, a trial of an as-needed opioid with routine follow-up and monitoring may be a reasonable strategy. In patients at higher risk for aberrant drug-related behaviors, a trial of an as-needed opioid should only occur in conjunction with more frequent monitoring and follow-up. In all cases, clinicians should carefully assess for aberrant drug-related behaviors and progress toward meeting therapeutic goals, and periodically reassess relative benefits to risks of the as-needed opioid to make appropriate decisions regarding continuation of this therapy.

13. Opioids in Pregnancy

Recommendation

13.1 Clinicians should counsel women of childbearing potential about the risks and benefits of COT during pregnancy and after delivery. Clinicians should encourage minimal or no use of COT during pregnancy, unless potential benefits outweigh risks. If COT is used during pregnancy, clinicians should be prepared to anticipate and manage risks to the patient and newborn (strong recommendation, low-quality evidence).

Managing CNCP in pregnant women is challenging. COT in this setting affects at least two patients, one of whom (the fetus) is unable to consent to treatment. In addition, due to the paucity of research that has been done, or is likely to be done for ethical reasons, it is difficult to evaluate benefits and risks of COT in pregnancy. Most of the literature on pregnancy and opioids has focused on women in methadone maintenance treatment, or women who used opioids for analgesia during labor, rather than COT for CNCP.

Although there are survey data that associate the use of COT during pregnancy with adverse newborn outcomes including low birth weight, premature birth, hypoxic-ischemic brain injury, and neonatal death,[54] it is difficult to separate effects of opioid use from other maternal factors that may contribute to these adverse newborn outcomes.[29] Other neonatal complications associated with maternal opioid use include prolonged QT syndrome and opioid withdrawal syndrome. The risks of adverse neonatal outcomes may be lower when women are on methadone for chronic pain management rather than for opioid dependence treatment.[123] Higher doses of antenatal methadone in tolerant mothers do not seem to increase complication rates.[77]

Given potential risks of opioids during pregnancy, clinicians should counsel women about risks and benefits of COT and recommend minimal or no use of opioids unless potential benefits outweigh risks (eg, severe disabling pain only controllable with opioids). Clinicians who care for pregnant women on COT must be prepared to address the additional risks. While antenatal harms may be difficult to predict and prevent, opioid withdrawal can be expected in up to half of newborns of opioid-dependent mothers. If the mother is receiving COT at or near the time of delivery, a professional who is experienced in the management of neonatal withdrawal should be available.

14. Opioid Policies

Recommendation

14.1 Clinicians should be aware of current federal and state laws, regulatory guidelines, and policy statements that govern the medical use of COT for CNCP (strong recommendation, low-quality evidence).

Surveys show that clinicians have a poor or limited understanding of the laws, regulations, and other policies that govern the prescribing, dispensing, or administration of controlled substances, including opioid analgesics.[46,107] Little research has been conducted to determine the extent that clinicians' knowledge of policies impacts healthcare practice and patient care.[47] However, clinicians are more vulnerable to regulatory investigation or discipline if they fail to comply with practice standards or regulations. Clinicians who prescribe COT for CNCP should be aware of the substantial policy changes that have occurred in recent years, and take steps to understand their responsibilities under federal and state laws, regulations, and other governmental policies that govern such practice. Resources are available to provide clinicians with information regarding opioid-prescribing policies in all 50 states and the District of Columbia.[93-95]

Conclusions

Use of COT for CNCP has been steadily increasing for 2 decades. Guidelines based on the best available

evidence and developed by multidisciplinary panels of experts are critical for promoting the effective and safe use of COT for CNCP. Although evidence is limited, an expert panel convened by APS and AAPM concludes that COT can be an effective therapy for carefully selected and monitored patients with CNCP. However, opioids are also associated with potentially serious harms, including opioid-related adverse effects and outcomes related to the abuse potential of opioids. The guidelines presented in this document are based on the underlying assumption that safe and effective therapy requires clinical skills and knowledge in both the principles of opioid prescribing and on the assessment and management of risks associated with opioid abuse, addiction, and diversion.

Although these guidelines are based on a systematic review of the evidence on COT for CNCP, the panel identified numerous research gaps. In fact, the panel did not rate any of its 25 recommendations as supported by high quality evidence. Only 4 recommendations were viewed as supported by even moderate quality evidence. Nonetheless, the panel came to unanimous consensus on almost all of its recommendations. Optimally balancing benefits and risks of COT for CNCP is dependent on careful patient evaluation and structuring of opioid therapy to accommodate identified risk, appropriate initiation and titration of COT, regular and comprehensive monitoring while on COT, and anticipation and management of opioid-related adverse effects. Other areas of strong consensus include recommendations to use therapies targeting psychosocial factors and to identify a medical home for all chronic pain patients. Critical research gaps are present in methods for providing informed consent, effective components of opioid management plans, balancing risks and benefits of high-dose opioid therapy, utility of opioid rotation, and treatment of breakthrough pain. More research is also needed on how policies that govern prescribing and use of COT affect clinical outcomes.

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Note: Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. As part of a shared decision making approach, it may be appropriate for the clinician to inform a patient that a particular recommendation may not be applicable, after considering all circumstances pertinent to that individual.

Supplementary Data

Supplementary data accompanying this article is available online at www.jpain.org, www.sciencedirect.com, and at doi:10.1016/j.jpain.2008.10.008. The supplementary data include Appendices 1–9.

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Appendix A

American Pain Society and American Academy of Pain Medicine Opioids Guidelines Panel Members; Discipline and Affiliation

Director, APS Clinical Guidelines Project, Roger Chou, MD – Internal Medicine, Oregon Health and Sciences University – Oregon Evidence-based Practice Center.

Co-chairs: Gilbert J. Fanciullo, MD, MS – Anesthesiology/Pain Medicine, Dartmouth-Hitchcock Medical Center, Department of Anesthesiology, Pain Management Center.

Perry G. Fine, MD, Anesthesiology/Pain Medicine and Palliative Care, University of Utah, Pain Research Center.

Chair, APS Clinical Practice Guidelines Committee: Christine Miaskowski, RN, PhD, FAAN, Registered Nurse/Pain Medicine, University of San Francisco, Department of Physiological Nursing.

Panel: Jeremy A. Adler, MS, PA-C, Physician Assistant, Pacific Pain Medicine Consultants.

Jane C. Ballantyne, MD, Anesthesiology/Pain Medicine, Massachusetts General Hospital, Department of Anesthesia and Critical Care.

Pamela Davies, MS, ARNP, Nurse Practitioner/Pain Medicine, Seattle Cancer Care Alliance (Formerly Internal medicine, Veterans Affairs Medical Center, Seattle).

Marilee I. Donovan, PhD, RN, Registered Nurse/Pain Medicine, Kaiser Permanente Northwest, Pain Management Clinic.

David A. Fishbain, MD, FAPA, Psychiatry/Pain Medicine, University of Miami, School of Medicine, Neurological Surgery and Anesthesiology.

Kathy M. Foley, MD, Neurology/Pain Medicine and Palliative Care, Memorial Sloan-Kettering Cancer Center, Pain and Palliative Care Service, Department of Neurology.

Jeffrey Fudin, BS, PharmD, DAAPM, Clinical Pharmacy, Samuel S. Stratton Department of Veterans Affairs Medical Center, and Albany College of Pharmacy & Health Sciences.

Aaron M. Gilson, PhD, Health Policy, University of Wisconsin Paul P. Carbone Comprehensive Cancer Center, Pain and Policy Studies Group.

Alexander Kelter, MD, Public Health, California Department of Health Services, Epidemiology and Prevention for Injury Control (EPIC) Branch (retired 2005).

Alexander Mauskop, MD, FAAN, Neurology, New York Headache Center, State University of New York, Downstate Medical Center.

Patrick G. O'Connor, MD, MPH, Internal Medicine, Yale University School of Medicine and Yale-New Haven Hospital, Section of General Internal Medicine.

Steven D. Passik, PhD, MA, Psychology/Addiction, Memorial Sloan-Kettering Cancer Center, Department of Psychiatry and Behavioral Sciences.

Gavril W. Pasternak, MD, PhD, Neuropharmacology, Memorial Sloan-Kettering Cancer Center, Laboratory of Molecular Neuropharmacology.

Russell K. Portenoy, MD, Neurology/Pain Medicine and Palliative Care, Beth Israel Medical Center, Department of Pain Medicine and Palliative Care.

Ben A. Rich, JD, PhD, Law/Ethics, University of California, Davis, School of Medicine, Division of Bioethics.

Richard G. Roberts, MD, JD, FAAFP, FCLM, Family Practice, University of Wisconsin, School of Medicine and Public Health.

Knox H. Todd, MD, MPH, FACEP, Emergency Medicine, Beth Israel Medical Center - Pain and Emergency Medicine Institute.

Appendix B. Glossary

Term	*Definition*
Aberrant drug-related behavior	A behavior outside the boundaries of the agreed on treatment plan which is established as early as possible in the doctor-patient relationship.[50]
Abuse	Any use of an illegal drug, or the intentional self-administration of a medication for a nonmedical purpose such as altering one's state of consciousness, for example, getting high.[66]
Addiction	A primary, chronic, neurobiologic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.[120]
Breakthrough pain	Transient or episodic exacerbation of pain that occurs in patients with pain that is otherwise considered stable but persistent[81]
Chronic opioid therapy	Daily or near-daily use of opioids for at least 90 days, often indefinitely (adapted from Von Korff et al).[135]
Diversion	The intentional transfer of a controlled substance from legitimate distribution and dispensing channels.[66]
Hyperalgesia	An increased response to a stimulus which is normally painful.[58]
Misuse	Use of a medication (for a medical purpose) other than as directed or as indicated, whether willful or unintentional, and whether harm results or not.[66]
Physical dependence	A state of adapation manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.[120]
Tolerance	A state of adapation in which exposure to a drug induces changes that result in a diminution of one or more opioid effects over time.[120]

Appendix 1. List of Panel Members and Conflict of Interest Statements

Director, APS Clinical Guidelines Project

Roger Chou, MD

Oregon Health & Sciences University - Oregon Evidence-based Practice Center

- No conflicts to report

Co-chairs

Gilbert J. Fanciullo, MD, MS

Dartmouth-Hitchcock Medical Center - Deptartment of Anesthesiology, Pain Management Center

Fee Income:

- Medtronic: Research grant; Speaker, Consultant
- Janssen: Research support
- Teva Pharmaceuticals: Expert Witness
- Pfizer: Educational support for Fellows in Dartmouth Fellowship Program

Perry G. Fine, MD

University of Utah - Pain Research Center

Fee Income:

- Combined honoraria income (exceeding $10,000) from serving on advisory boards related to opioid analgesics for Alpharma, Cephalon, Endo Pharmaceuticals, GlaxoSmithKline, Lilly, Merck, NIH, Ortho-McNeil (J & J), Purdue Pharma, and Wyeth
- Total income of above sources over last three years estimated at $30,000

Ownership interests:

- 17,500 shares in ZARS Pharma, a privately owned company that develops opioid delivery systems

Chair, APS Guidelines

Christine Miaskowski, PhD, RN, FAAN

University of San Francisco - Department of Physiological Nursing

Fee Income:

- Consultant/Speaker' Bureaus for Anesta, Cephalon, Endo,GlaxoSmithKline, Merck, and Pricara

Panel

Jeremy A. Adler, MS, PA-C

Pacific Pain Medicine Consultants

Fee Income:

- Advisory Board member: Alpharma
- Speaker's Bureau: Alpharma, Elan, Endo, Pfizer, and Victory pharmaceutical companies

Jane C. Ballantyne, MD

Massachusetts General Hospital - Department of Anesthesia and Critical Care

Fee Income:

- Harvard International Outreach in Geneva & Bern, Switzerland – 4 weeks sponsored by Novartis, August 2005
- Evidence Base of Acute Pain Management Panel of Experts – results published in *Anesthesia & Analgesia*, sponsored by Orthopedic Review, November 2005
- Hydromorphone Expert Panel/Advisory – sponsored by Endo Pharmaceuticals, May 2006
- Harvard Medical School received $1,500, 000 from Purdue Pharma used to sponsor research and education programs at Massachusetts General Hospital Pain Unit

Appendix 1. Continued

Pamela Davies, MS, ARNP
Seattle Cancer Care Alliance
Fee Income:
- Received honorarium payments from Alpharma and Endo Pharmaceuticals for work as Clinical Advisor
- Received honorarium from Endo Pharmaceuticals for work at University of Washington, School of Nursing Continuing Education
- Total of all honoraria in last 3 years: approximately $5,000

Marilee I. Donovan, PhD, RN
Kaiser Permanente Northwest - Pain Management Clinic
Employment:
- Manager of Kaiser-Permanente Northwest region Pain Management Clinic
- Application for ROI to develop predictors of addiction
- Department accepts test equipment from vendors who then sell department equipment and supplies for interventional pain management procedures
- Consultant to JCAHO re: pain standards
- Clinical lead for outcomes process for Kaiser-Permanente Chronic Pain Guidelines

David A. Fishbain, MD, FAPA
University of Miami - School of Medicine, *Neurological Surgery and Anesthesiology*
- No conflicts to report

Kathy M. Foley, MD
Memorial Sloan-Kettering Cancer Center - Pain & Palliative Care Service, Department of Neurology
- No conflicts to report

Jeffrey Fudin, BS, PharmD, DAAPM
Samuel S. Stratton Department of Veterans Affairs Medical Center, and Albany College of Pharmacy & Health Sciences
Fee Income:
- Speakers Bureaus for Advisory Boards: Abbott (less than $10,000), Alpharma (less than $10,000), Calloway Labs, Janssen, and Pricara (division of Ortho-McNeil)
- Janssen: Research support
- Teva Pharmaceuticals: Expert Witness

Appendix 1. Continued

Aaron M. Gilson, PhD
University of Wisconsin Paul P. Carbone Comprehensive Cancer Center - Pain & Policy Studies Group
Fee Income:
- Consulting responsibilities for the American Cancer Society
- Honorarium payment for presentations at the Pharmacy Society of Wisconsin and the Federation of State Medical Boards of the U.S., and from Janssen Pharmaceuticals.
- The Pain & Policy Studies Group at The University of Wisconsin receives unrestricted educational grants from Alpharma, Endo Pharmaceuticals, and Purdue Pharma

Research Funding:
- Robert Wood Johnson Foundation, Federation of State Medical Boards of the U.S.
- Research projects at the Pain & Policy Studies Group at The University of Wisconsin are funded by grants from the American Cancer Society, Susan B. Komen for the Cure, U.S. Cancer Pain Relief Committee, and through a cooperative agreement with the Lance Armstrong Foundation
- Project funding is pending for R03 project at the Pain & Policy Studies Group

Alexander Kelter, MD
California Department of Health Services - Epidemiology & Prevention for Injury Control (EPIC) Branch (retired 2005)
- No conflicts to report

Alexander Mauskop, MD, FAAN
New York Headache Center
State University of New York, Downstate Medical Center
- No conflicts to report

Patrick G. O'Connor, MD, MPH
Yale University School of Medicine and Yale-New Haven Hospital - Section of General Internal Medicine
- No conflicts to report

Steven D. Passik, PhD, MA
Memorial Sloan-Kettering Cancer Center - Department of Psychiatry and Behavioral Sciences
Fee Income:
- Consultant/Speaker' Bureaus for Alpharma, Cephalon, Endo, King, Ligand, Lilly, and, Pricara pharmaceutical companies
- Honoraria for speaking on pain/addiction and risk management from Ligand, Cephalon, Endo, Alpharma, Purdue, and Mallinckrodt pharmaceutical companies

Research Funding:
- Have received grant/research support from Cephalon, Lilly, Amgen, Janssen, and Ligand companies

Gavril W. Pasternak, MD, PhD
Memorial Sloan-Kettering Cancer Center - Laboratory of Molecular Neuropharmacology
Fee Income:
- Consultant/Scientific Advisory Boards for Sarentis, Traxon, EpiCept, Limmerick, and QrxPahrma companies
- Honoraria from Adolor, Endo, Cephalon, and Ortho-McNeill pharmaceutical companies

Research Funding:
Have received grant/research support from Sarentis for preclinical evaluation of drug candidates

Appendix 1. Continued

Russell K. Portenoy, MD
Beth Israel Medical Center - Department of Pain Medicine & Palliate Care
Fee Income:
- Consulting agreements with an extensive list of pharmaceutical companies, estimated to work with 4-5 within three year period (complete list available upon request)

Research Funding:
- Department at Beth Israel Medical Center has received research funding in amounts ranging from less than $10,000 to over $100,000 funding from several pharmaceutical companies, foundations, and other sources (complete list available upon request)

Ben A. Rich, JD, PhD
University of California, Davis - School of Medicine, Division of Bioethics
Fee Income:
- Speaker honoraria payments from Purdue Pharma, PharmaCon, Pharmacia/Pfizer
- Expert consultant/review payment from Purdue Pharma

Richard G. Roberts, MD, JD, FAAFP, FCLM
University of Wisconsin - School of Medicine and Public Health
Fee Income:
- Advisor Board membership payments (less than $10,000 each) from Endo, Ortho-McNeill, and Pfizer

Knox H. Todd, MD, MPH, FACEP
Beth Israel Medical Center - Pain and Emergency Medicine Institute
Fee Income:
- Consulting payments from Johnson & Johnson, Alpharma, ALZA, and Ortho-McNeill pharmaceutical companies

Research Funding:
- Board of Director member for the American Chronic Pain Association, which has received research funding from Cephalon

Appendix 2. Grading Evidence and Recommendations (GRADE)

Grading evidence and recommendations - operationalization of GRADE methods[52]

High-quality Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least two consistent, higher-quality randomized controlled trials*, or multiple, consistent observational studies with no significant methodological flaws showing large effects).
Moderate-quality Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least one higher-quality trial* with >100 subjects; two or more higher-quality trials* with some inconsistency; at least two consistent, lower-quality trials*, or multiple, consistent observational studies with no significant methodological flaws showing at least moderate effects).
Low-quality Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher quality studies, important flaws in study design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

*Or prospective studies on risk prediction or studies of diagnostic accuracy when appropriate

Appendix 3. Risk Assessment Tool – Screener and Opioid Assessment for Patients with Pain (SOAPP)

Screener and Opioid Assessment for Patients with Pain (SOAPP)® Version 1.0 - 14Q

The Screener and Opioid Assessment for Patients with Pain (SOAPP)® Version 1.0 is a tool for clinicians to help determine how much monitoring a patient on long-term opioid therapy might require. Physicians remain reluctant to prescribe opioid medication because of concerns about addiction, misuse, and other aberrant medication-related behaviors, as well as liability and censure concerns. Despite recent findings suggesting that most patients are able to successfully remain on long-term opioid therapy without significant problems, physicians often express a lack of confidence in their ability to distinguish patients likely to have few problems on long-term opioid therapy from those requiring more monitoring.

SOAPP® version 1.0 is a quick and easy-to-use questionnaire designed to help providers evaluate the patients' relative risk for developing problems when placed on long-term opioid therapy. Version 1.0 -14Q is:

- A brief paper and pencil questionnaire
- Developed based on expert consensus regarding important concepts likely to predict which patients will require more or less monitoring on long-term opioid therapy (content and face valid)
- Preliminary reliability data (coefficient α) from 175 patients chronic pain patients
- Preliminary validity data from 100 patients (predictive validity)
- Simple scoring procedures
- 14 items
- 5 point scale
- <8 minutes to complete
- Ideal for documenting decisions about the level of monitoring planned for a particular patient or justifying referrals to specialty pain clinic.
- The SOAPP® is for clinician use only. The tool is not meant for commercial distribution.
- The SOAPP® is **NOT** a lie detector. Patients determined to misrepresent themselves will still do so. Other clinical information should be used with SOAPP® scores to decide on a particular patient's treatment.
- The SOAPP® is **NOT** intended for all patients. The SOAPP® should be completed by chronic pain patients being considered for opioid therapy.
- It is important to remember that all chronic pain patients deserve treatment of their pain. Providers who are not comfortable treating certain patients should refer those patients to a specialist.

 The SOAPP® was developed with a grant from the National Institutes of Health and an educational grant from Endo Pharmaceuticals.

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Appendix 3. Continued

SOAPP® Version 1.0-14Q

Name: _____ Date: _____

The following are some questions given to all patients at the Pain Management Center who are on or being considered for opioids for their pain. Please answer each question as honestly as possible. This information is for our records and will remain confidential. Your answers alone will not determine your treatment. Thank you.

Please answer the questions below using the following scale:

0 = Never, 1 = Seldom, 2 = Sometimes, 3 = Often, 4 = Very Often

1. How often do you have mood swings?	0 1 2 3 4
2. How often do you smoke a cigarette within an hour after you wake up?	0 1 2 3 4
3. How often have any of your family members, including parents and grandparents, had a problem with alcohol or drugs?	0 1 2 3 4
4. How often have any of your close friends had a problem with alcohol or drugs?	0 1 2 3 4
5. How often have others suggested that you have a drug or alcohol problem?	0 1 2 3 4
6. How often have you attended an AA or NA meeting?	0 1 2 3 4
7. How often have you taken medication other than the way that it was prescribed?	0 1 2 3 4
8. How often have you been treated for an alcohol or drug problem?	0 1 2 3 4
9. How often have your medications been lost or stolen?	0 1 2 3 4
10. How often have others expressed concern over your use of medication?	0 1 2 3 4

Appendix 3. Continued

0 = Never, 1 = Seldom, 2 = Sometimes, 3 = Often, 4 = Very Often

11. How often have you felt a craving for medication?	0 1 2 3 4
12. How often have you been asked to give a urine screen for substance abuse?	0 1 2 3 4
13. How often have you used illegal drugs (for example, marijuana, cocaine, etc.) in the past five years?	0 1 2 3 4
14. How often, in your lifetime, have you had legal problems or been arrested?	0 1 2 3 4

Please include any additional information you wish about the above answers. Thank you.

Appendix 3. Continued

Scoring Instructions for the SOAPP® Version 1.0-14Q

To score the SOAPP® V.1- 14Q, simply add the ratings of all the questions:

A score of 7 or higher is considered positive.

Sum of Questions	SOAPP® Indication
> or = 7	+
< 7	-

What does the Cutoff Score Mean?

For any screening test, the results depend on what cutoff score is chosen. A score that is good at detecting patients at-risk will necessarily include a number of patients that are not really at risk. A score that is good at identifying those at low risk will, in turn, miss a number of patients at risk. A screening measure like the SOAPP® generally endeavors to minimize the chances of missing high-risk patients. This means that patients who are truly at low risk may still get a score above the cutoff. The table below presents several statistics that describe how effective the SOAPP® is at different cutoff values. These values suggest that the SOAPP® is a sensitive test. This confirms that the SOAPP® is better at identifying who is at high risk than identifying who is at low risk. Clinically, a score of 7 or higher will identify 91% of those who actually turn out to be at high risk. The Negative Predictive Values for a cutoff score of 7 is .90, which means that most people who have a negative SOAPP® are likely at low-risk. Finally, the Positive likelihood ratio suggests that a positive SOAPP® score (at a cutoff of 7) is nearly 3 times (2.94 times) as likely to come from someone who is actually at high risk (note that, of these statistics, the likelihood ratio is least affected by prevalence rates). All this implies that by using a cutoff score of 7 will ensure that the provider is least likely to miss someone who is really at high risk. However, one should remember that a low SOAPP® score suggests the patient is really at low-risk, while a high SOAPP® score will contain a larger percentage of false positives (about 30%), while at the same time retaining a large percentage of true positives. This could be improved, so that a positive score has a lower false positive rate, but only at the risk of missing more of those who actually do show aberrant behavior.

SOAPP® Cutoff Score	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ration
Score 7 or above	.91	.69	.71	.90	2.94	.13
Score 8 or above	.86	.73	.75	.86	3.19	.19
Score 9 or above	.77	.80	.77	.80	3.90	.28

Appendix 4. Risk Assessment Tool – Opioid Risk Tool (ORT)

Date _____

Patient Name _____

OPIOID RISK TOOL

		Mark each box that applies	Item Score If Female	Item Score If Male
1. Family History of Substance Abuse	Alcohol	[ ]	1	3
	Illegal Drugs	[ ]	2	3
	Prescription Drugs	[ ]	4	4
2. Personal History of Substance Abuse	Alcohol	[ ]	3	3
	Illegal Drugs	[ ]	4	4
	Prescription Drugs	[ ]	5	5
3. Age (Mark box if 16 – 45)		[ ]	1	1
4. History of Preadolescent Sexual Abuse		[ ]	3	0
5. Psychological Disease	Attention Deficit Disorder Obsessive Compulsive Disorder Bipolar Schizophrenia	[ ]	2	2
	Depression	[ ]	1	1
TOTAL		**[ ]**		

Total Score Risk Category Low Risk 0 – 3 Moderate Risk 4 – 7 High Risk $\geq$8

Reproduced with permission from Lynn Webster[137]

Appendix 5. Risk Assessment Tool - Score Diagnosis, Intractability, Risk Efficacy (D.I.R.E.)

D.I.R.E. Score: Patient Selection for Chronic Opioid Analgesia

For each factor, rate the patient's score from 1-3 based on the explanations in the right hand column

Score	Factor	Explanation
	Diagnosis	1 = Benign chronic condition with minimal objective findings or no definite medical diagnosis. Examples: fibromyalgia, migraine headaches, non-specific back pain. 2 = Slowly progressive condition concordant with moderate pain, or fixed condition with moderate objective findings. Examples: failed back surgery syndrome, back pain with moderate degenerative changes, neuropathic pain. 3 = Advanced condition concordant with severe pain with objective findings. Examples: severe ischemic vascular disease, advanced neuropathy, severe spinal stenosis.
	Intractability	1 = Few therapies have been tried and the patient takes a passive role in his/her pain management process. 2 = Most customary treatments have been tried but the patient is not fully engaged in the pain management process, or barriers prevent (insurance, transportation, medical illness). 3 = Patient fully engaged in a spectrum of appropriate treatments but with inadequate response.
	Risk	(R= Total of P+C+R+S below)
	Psychological:	1 = Serious personality dysfunction or mental illness interfering with care. Example: personality disorder, severe affective disorder, significant personality issues. 2 = Personality or mental health interferes moderately. Example: depression or anxiety disorder. 3 = Good communication with clinic. No significant personality dysfunction or mental illness.
	Chemical Health:	1 = Active or very recent use of illicit drugs, excessive alcohol, or prescription drug abuse. 2 = Chemical coper (uses medications to cope with stress) or history of CD in remission. 3 = No CD history. Not drug-focused or chemically reliant.
	Reliability:	1 = History of numerous problems: medication misuse, missed appointments, rarely follows through. 2 = Occasional difficulties with compliance, but generally reliable. 3 = Highly reliable patient with meds, appointments & treatment.
	Social Support:	1 = Life in chaos. Little family support and few close relationships. Loss of most normal life roles. 2 = Reduction in some relationships and life roles. 3 = Supportive family/close relationships. Involved in work or school and no social isolation.
	Efficacy score	1 = Poor function or minimal pain relief despite moderate to high doses. 2 = Moderate benefit with function improved in a number of ways (or insufficient info- hasn't tried opioid yet or very low doses or too short of a trial). 3 = Good improvement in pain and function and quality of life with stable doses over time.

_____Total score = D + I + R + E

Score 7-13: Not a suitable candidate for long-term opioid analgesia
Score 14-21: Good candidate for long-term opioid analgesia

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Appendix 6. Sample Informed Consent form

Consent for Chronic Opioid Therapy

A consent form from the **American Academy of Pain Medicine**

Dr. _____ is prescribing opioid medicine, sometimes called narcotic analgesics, to me for a diagnosis of _____.

This decision was made because my condition is serious or other treatments have not helped my pain.

I am aware that the use of such medicine has certain risks associated with it, including, but not limited to: sleepiness or drowsiness, constipation, nausea, itching, vomiting, dizziness, allergic reaction, slowing of breathing rate, slowing of reflexes or reaction time, physical dependence, tolerance to analgesia, addiction and possibility that the medicine will not provide complete pain relief.

I am aware about the possible risks and benefits of other types of treatments that do not involve the use of opioids. The other treatments discussed included:

_____

_____

_____

I will tell my doctor about all other medicines and treatments that I am receiving.

I will not be involved in any activity that may be dangerous to me or someone else if I feel drowsy or am not thinking clearly. I am aware that even if I do not notice it, my reflexes and reaction time might still be slowed. Such activities include, but are not limited to: using heavy equipment or a motor vehicle, working in unprotected heights or being responsible for another individual who is unable to care for himself or herself.

I am aware that certain other medicines such as nalbuphine (Nubain ™), pentazocine (Talwin™), buprenorphine (Buprenex™), and butorphanol (Stadol™), may reverse the action of the medicine I am using for pain control. Taking any of these other medicines while I am taking my pain medicines can cause symptoms like a bad flu, called a withdrawal syndrome. I agree not to take any of these medicines and to tell any other doctors that I am taking an opioid as my pain medicine and cannot take any of the medicines listed above.

I am aware that addiction is defined as the use of a medicine even if it causes harm, having cravings for a drug, feeling the need to use a drug and a decreased quality of life. I am aware that the chance of becoming addicted to my pain medicine is very low. I am aware that the development of addiction has been reported rarely in medical journals and is much more common in a person who has a family or personal history of addiction. I agree to tell my doctor my complete and honest personal drug history and that of my family to the best of my knowledge.

Appendix 6. Continued

I understand that physical dependence is a normal, expected result of using these medicines for a long time. I understand that physical dependence is not the same as addiction. I am aware physical dependence means that if my pain medicine use is markedly decreased, stopped or reversed by some of the agents mentioned above, I will experience a withdrawal syndrome. This means I may have any or all of the following: runny nose, yawning, large pupils, goose bumps, abdominal pain and cramping, diarrhea, irritability, aches throughout my body and a flu-like feeling. I am aware that opioid withdrawal is uncomfortable but not life threatening.

I am aware that tolerance to analgesia means that I may require more medicine to get the same amount of pain relief. I am aware that tolerance to analgesia does not seem to be a big problem for most patients with chronic pain, however, it has been seen and may occur to me. If it occurs, increasing doses may not always help and may cause unacceptable side effects. Tolerance or failure to respond well to opioids may cause my doctor to choose another form of treatment.

(**Males only**) I am aware that chronic opioid use has been associated with low testosterone levels in males. This may affect my mood, stamina, sexual desire and physical and sexual performance. I understand that my doctor may check my blood to see if my testosterone level is normal.

(**Females Only**) If I plan to become pregnant or believe that I have become pregnant while taking this pain medicine, I will immediately call my obstetric doctor and this office to inform them. I am aware that, should I carry a baby to delivery while taking these medicines, the baby will be physically dependent upon opioids. I am aware that the use of opioids is not generally associated with a risk of birth defects. However, birth defects can occur whether or not the mother is on medicines and there is always the possibility that my child will have a birth defect while I am taking an opioid.

I have read this form or have it read to me. I understand all of it. I have had a chance to have all of my questions regarding this treatment answered to my satisfaction. By signing this form voluntarily, I give my consent for the treatment of my pain with opioid pain medicines.

Patient signature _____ Date _____

Witness to above _____

Approved by the AAPM Executive Committee on January 14, 1999.

PHYSICIANS DEDICATED TO RELIEVING PAIN
the AMERICAN ACADEMY *of* PAIN MEDICINE
the voice of pain medicine

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Web site www.painmed.org

Appendix 7. Sample Medical Agreement

the AMERICAN ACADEMY of PAIN MEDICINE
the voice of pain medicine

SAMPLE FOR ADAPTATION AND REPRODUCTION ON PHYSICIAN LETTERHEAD

PLEASE CONSULT WITH YOUR ATTORNEY

Long-term Controlled Substances Therapy for Chronic Pain

SAMPLE AGREEMENT

*A consent form from the **American Academy of Pain Medicine***

The purpose of this agreement is to protect your access to controlled substances and to protect our ability to prescribe for you.

The long-term use of such substances as opioids (narcotic analgesics), benzodiazepine tranquilizers, and barbiturate sedatives is controversial because of uncertainty regarding the extent to which they provide long-term benefit. There is also the risk of an addictive disorder developing or of relapse occurring in a person with a prior addiction. The extent of this risk is not certain.

Because these drugs have potential for abuse or diversion, strict accountability is necessary when use is prolonged. For this reason the following policies are agreed to by you, the patient, as consideration for, and a condition of, the willingness of the physician whose signature appears below to consider the initial and/or continued prescription of controlled substances to treat your chronic pain.

1. All controlled substances must come from the physician whose signature appears below or, during his or her absence, by the covering physician, unless specific authorization is obtained for an exception. (Multiple sources can lead to untoward drug interactions or poor coordination of treatment.)
2. All controlled substances must be obtained at the same pharmacy, where possible. Should the need arise to change pharmacies, our office must be informed. The pharmacy that you have selected is:

   _____ phone: _____.
3. You are expected to inform our office of any new medications or medical conditions, and of any adverse effects you experience from any of the medications that you take.
4. The prescribing physician has permission to discuss all diagnostic and treatment details with dispensing pharmacists or other professionals who provide your health care for purposes of maintaining accountability.
5. You may not share, sell, or otherwise permit others to have access to these medications.
6. These drugs should not be stopped abruptly, as an abstinence syndrome will likely develop.
7. Unannounced urine or serum toxicology screens may be requested, and your cooperation is required. Presence of unauthorized substances may prompt referral for assessment for addictive disorder.

Appendix 7. Continued

8. Prescriptions and bottles of these medications may be sought by other individuals with chemical dependency and should be closely safeguarded. It is expected that you will take the highest possible degree of care with your medication and prescription. They should not be left where others might see or otherwise have access to them.

9. Original containers of medications should be brought in to each office visit.

10. Since the drugs may be hazardous or lethal to a person who is not tolerant to their effects, especially a child, you must keep them out of reach of such people.

11. Medications may not be replaced if they are lost, get wet, are destroyed, left on an airplane, etc. If your medication has been stolen and you complete a police report regarding the theft, an exception may be made.

12. Early refills will generally not be given.

13. Prescriptions may be issued early if the physician or patient will be out of town when a refill is due. These prescriptions will contain instructions to the pharmacist that they not be filled prior to the appropriate date.

14. If the responsible legal authorities have questions concerning your treatment, as might occur, for example, if you were obtaining medications at several pharmacies, all confidentiality is waived and these authorities may be given full access to our records of controlled substances administration.

15. It is understood that failure to adhere to these policies may result in cessation of therapy with controlled substance prescribing by this physician or referral for further specialty assessment.

16. Renewals are contingent on keeping scheduled appointments. Please do not phone for prescriptions after hours or on weekends.

17. It should be understood that any medical treatment is initially a trial, and that continued prescription is contingent on evidence of benefit.

18. The risks and potential benefits of these therapies are explained elsewhere [and you acknowledge that you have received such explanation].

19. You affirm that you have full right and power to sign and be bound by this agreement, and that you have read, understand, and accept all of its terms.

_____ _____

Physician Signature Patient Signature

_____ _____

Date Patient Name (Printed)

Approved by the AAPM Executive Committee on April 2, 2001.

AAPM
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Glenview, IL 60025-1485
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Web site http://www.painmed.org/

Appendix 8. Monitoring Tool – Pain Assessment and Documentation Tool (PADT)

A

PROGRESS NOTE
Pain Assessment and Documentation Tool (PADT™)

Patient Stamp Here

Patient Name: _____ Record #: _____

Assessment Date: _____

Current Analgesic Regimen

Drug name	Strength (eg, mg)	Frequency	Maximum Total Daily Dose

The PADT is a clinician-directed interview; that is, the clinician asks the questions, and the clinician records the responses. The Analgesia, Activities of Daily Living, and Adverse Events sections may be completed by the physician, nurse practitioner, physician assistant, or nurse. The Potential Aberrant Drug-Related Behavior and Assessment sections must be completed by the physician. Ask the patient the questions below, except as noted.

Analgesia

If zero indicates "no pain" and ten indicates "pain as bad as it can be," on a scale of 0 to 10, what is your level of pain for the following questions?

1. What was your pain level on average during the past week? (Please circle the appropriate number)

No Pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as it can be**

2. What was your pain level at its worst during the past week?

No Pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as it can be**

3. What percentage of your pain has been relieved during the past week? (Write in a percentage between 0% and 100%.) _____

4. Is the amount of pain relief you are now obtaining from your current pain reliever(s) enough to make a real difference in your life?
❑ Yes ❑ No

5. **Query to clinician:** Is the patient's pain relief clinically significant?
❑ Yes ❑ No ❑ Unsure

Activities of Daily Living

Please indicate whether the patient's functioning with the current pain reliever(s) is Better, the Same, or Worse since the patient's last assessment with the PADT.* (Please check the box for Better, Same, or Worse for each item below.)

	Better	Same	Worse
1. Physical functioning	❑	❑	❑
2. Family relationships	❑	❑	❑
3. Social relationships	❑	❑	❑
4. Mood	❑	❑	❑
5. Sleep patterns	❑	❑	❑
6. Overall functioning	❑	❑	❑

* If the patient is receiving his or her first PADT assessment, the clinician should compare the patient's functional status with other reports from the last office visit.

(Continued on reverse side)

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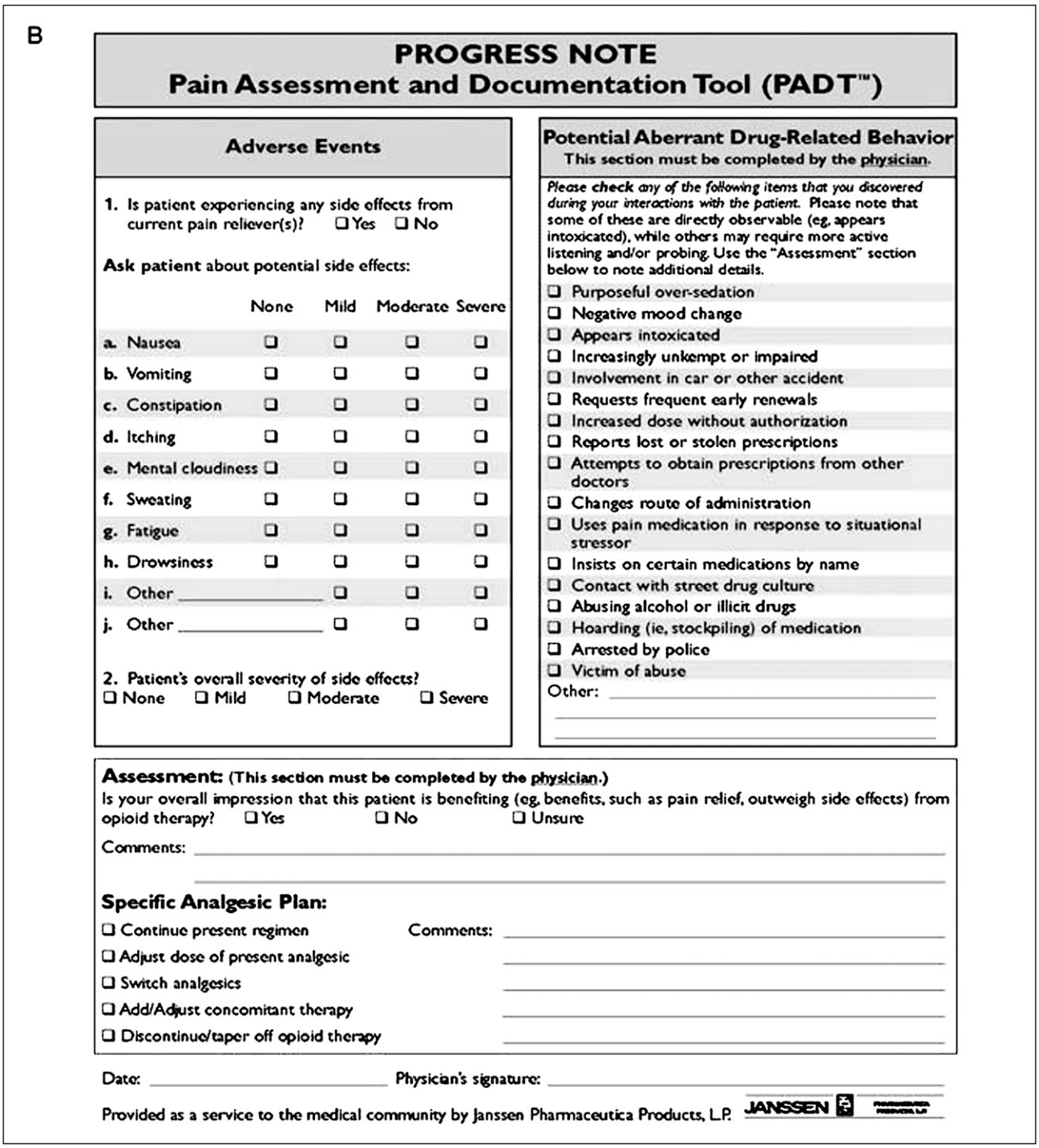
Appendix 8. Continued



B

PROGRESS NOTE
Pain Assessment and Documentation Tool (PADT™)

Adverse Events

1. Is patient experiencing any side effects from current pain reliever(s)? ❑ Yes ❑ No

Ask patient about potential side effects:

	None	Mild	Moderate	Severe
a. Nausea	❑	❑	❑	❑
b. Vomiting	❑	❑	❑	❑
c. Constipation	❑	❑	❑	❑
d. Itching	❑	❑	❑	❑
e. Mental cloudiness	❑	❑	❑	❑
f. Sweating	❑	❑	❑	❑
g. Fatigue	❑	❑	❑	❑
h. Drowsiness	❑	❑	❑	❑
i. Other _____	❑	❑	❑	❑
j. Other _____	❑	❑	❑	❑

2. Patient's overall severity of side effects?
❑ None ❑ Mild ❑ Moderate ❑ Severe

Potential Aberrant Drug-Related Behavior
This section must be completed by the physician.

Please check any of the following items that you discovered during your interactions with the patient. Please note that some of these are directly observable (eg, appears intoxicated), while others may require more active listening and/or probing. Use the "Assessment" section below to note additional details.

- ❑ Purposeful over-sedation
- ❑ Negative mood change
- ❑ Appears intoxicated
- ❑ Increasingly unkempt or impaired
- ❑ Involvement in car or other accident
- ❑ Requests frequent early renewals
- ❑ Increased dose without authorization
- ❑ Reports lost or stolen prescriptions
- ❑ Attempts to obtain prescriptions from other doctors
- ❑ Changes route of administration
- ❑ Uses pain medication in response to situational stressor
- ❑ Insists on certain medications by name
- ❑ Contact with street drug culture
- ❑ Abusing alcohol or illicit drugs
- ❑ Hoarding (ie, stockpiling) of medication
- ❑ Arrested by police
- ❑ Victim of abuse

Other: _____

Assessment: (This section must be completed by the physician.)

Is your overall impression that this patient is benefiting (eg, benefits, such as pain relief, outweigh side effects) from opioid therapy? ❑ Yes ❑ No ❑ Unsure

Comments: _____

Specific Analgesic Plan:

- ❑ Continue present regimen — Comments: _____
- ❑ Adjust dose of present analgesic
- ❑ Switch analgesics
- ❑ Add/Adjust concomitant therapy
- ❑ Discontinue/taper off opioid therapy

Date: _____ Physician's signature: _____

Provided as a service to the medical community by Janssen Pharmaceutica Products, L.P. JANSSEN

Appendix 9. Monitoring Tool – Current Opioid Misuse Measure (COMM)

Current Opioid Misuse Measure (COMM)™

The Current Opioid Misuse Measure (COMM)™ is a brief patient self-assessment to monitor chronic pain patients on opioid therapy. The COMM™ was developed with guidance from a group of pain and addiction experts and input from pain management clinicians in the field. Experts and providers identified six key issues to determine if patients already on long-term opioid treatment are exhibiting aberrant medication-related behaviors:

- *Signs & Symptoms of Intoxication*
- *Emotional Volatility*
- *Evidence of Poor Response to Medications*
- *Addiction*
- *Healthcare Use Patterns*
- *Problematic Medication Behavior*

The COMM™ will help clinicians identify whether a patient, currently on long-term opioid therapy, may be exhibiting aberrant behaviors associated with misuse of opioid medications. In contrast, the Screener and Opioid Assessment for Patients with Pain (SOAPP®) is intended to predict which patients, being considered for long-term opioid therapy, may exhibit aberrant medications behaviors in the future. Since the COMM™ examines concurrent misuse, it is ideal for helping clinicians monitor patients' aberrant medication-related behaviors over the course of treatment. The COMM™ is:

- A quick and easy to administer patient-self assessment
- 17 items
- Simple to score
- Completed in less than 10 minutes
- Validated with a group of approximately 500 chronic pain patients on opioid therapy
- Ideal for documenting decisions about the level of monitoring planned for a particular patient or justifying referrals to specialty pain clinic.
- The COMM™ is for clinician use only. The tool is not meant for commercial distribution.
- The COMM™ is **NOT** a lie detector. Patients determined to misrepresent themselves will still do so. Other clinical information should be used with COMM™ scores to decide if and when modifications to particular patient's treatment plan is needed.
- It is important to remember that all chronic pain patients deserve treatment of their pain. Providers who are not comfortable treating certain patients should refer those patients to a specialist.

 The COMM™ was developed with a grant from the National Institutes of Health and an educational grant from Endo Pharmaceuticals.

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Appendix 9. Continued

COMM™

Please answer each question as honestly as possible. Keep in mind that we are only asking about the **past 30 days**. There are no right or wrong answers. If you are unsure about how to answer the question, please give the best answer you can.

Please answer the questions using the following scale:	Never	Seldom	Sometimes	Often	Very Often
	0	1	2	3	4
1. In the past 30 days, how often have you had trouble with thinking clearly or had memory problems?	O	O	O	O	O
2. In the past 30 days, how often do people complain that you are not completing necessary tasks? (i.e., doing things that need to be done, such as going to class, work or appointments)	O	O	O	O	O
3. In the past 30 days, how often have you had to go to someone other than your prescribing physician to get sufficient pain relief from medications? (i.e., another doctor, the Emergency Room, friends, street sources)	O	O	O	O	O
4. In the past 30 days, how often have you taken your medications differently from how they are prescribed?	O	O	O	O	O
5. In the past 30 days, how often have you seriously thought about hurting yourself?	O	O	O	O	O
6. In the past 30 days, how much of your time was spent thinking about opioid medications (having enough, taking them, dosing schedule, etc.)?	O	O	O	O	O

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Appendix 9. Continued

Please answer the questions using the following scale:	Never	Seldom	Sometimes	Often	Very Often
	0	1	2	3	4
7. In the past 30 days, how often have you been in an argument?	O	O	O	O	O
8. In the past 30 days, how often have you had trouble controlling your anger (e.g., road rage, screaming, etc.)?	O	O	O	O	O
9. In the past 30 days, how often have you needed to take pain medications belonging to someone else?	O	O	O	O	O
10. In the past 30 days, how often have you been worried about how you're handling your medications?	O	O	O	O	O
11. In the past 30 days, how often have others been worried about how you're handling your medications?	O	O	O	O	O
12. In the past 30 days, how often have you had to make an emergency phone call or show up at the clinic without an appointment?	O	O	O	O	O
13. In the past 30 days, how often have you gotten angry with people?	O	O	O	O	O
14. In the past 30 days, how often have you had to take more of your medication than prescribed?	O	O	O	O	O
15. In the past 30 days, how often have you borrowed pain medication from someone else?	O	O	O	O	O
16. In the past 30 days, how often have you used your pain medicine for symptoms other than for pain (e.g., to help you sleep, improve your mood, or relieve stress)?	O	O	O	O	O

Appendix 9. Continued

Please answer the questions using the following scale:	Never	Seldom	Sometimes	Often	Very Often
	0	1	2	3	4
17. In the past 30 days, how often have you had to visit the Emergency Room?	O	O	O	O	O

Appendix 9. Continued

Scoring Instructions for the COMM™

To score the COMM™, simply add the rating of all the questions. A score of 9 or higher is considered a positive

Sum of Questions	COMM Indication
> or = 9	+
< 9	-

As for any scale, the results depend on what cutoff score is chosen. A score that is sensitive in detecting patients who are abusing or misusing their opioid medication will necessarily include a number of patients that are not really abusing or misusing their medication. The COMM™ was intended to over-identify misuse, rather than to mislabel someone as responsible when they are not. This is why a low cut-off score was accepted. We believe that it is more important to identify patients who have only a possibility of misusing their medications than to fail to identify those who are actually abusing their medication. Thus, it is possible that the COMM™ will result in false positives – patients identified as misusing their medication when they were not.

The table below presents several statistics that describe how effective the COMM™ is at different cutoff values. These values suggest that the COMM™ is a sensitive test. This confirms that the COMM™ is better at identifying who is misusing their medication than identifying who is not misusing. Clinically, a score of 9 or higher will identify 77% of those who actually turn out to be at high risk. The Negative Predictive Values for a cutoff score of 9 is .95, which means that most people who have a negative COMM™ are likely not misusing their medication. Finally, the Positive likelihood ratio suggests that a positive COMM™ score (at a cutoff of 9) is over 2 times (2.26 times) as likely to come from someone who is actually misusing their medication (note that, of these statistics, the likelihood ratio is least affected by prevalence rates). All this implies that by using a cutoff score of 9 will ensure that the provider is least likely to miss someone who is really misusing their prescription opioids. However, one should remember that a low COMM™ score suggests the patient is really at low-risk, while a high COMM™ score will contain a larger percentage of false positives (about 34%), while at the same time retaining a large percentage of true positives. This could be improved, so that a positive score has a lower false positive rate, but only at the risk of missing more of those who actually do show aberrant behavior.

COMM™ Cutoff Score	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ration
Score 9 or above	.77	.66	.66	.95	2.26	.35