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VA/DoD clinical practice guideline for management of opioid therapy for chronic pain.

Bibliographic Source(s)

Management of Opioid Therapy for Chronic Pain Working Group. VA/DoD clinical practice guideline for management of opioid therapy for chronic pain. Washington (DC): Department of Veterans Affairs, Department of Defense; 2010 May. 159 p.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Veterans Health Administration, Department of Defense. VA/DoD clinical practice guideline for the management of opioid therapy for chronic pain. Washington (DC): Veterans Health Administration, Department of Defense; 2003 Mar. Various p. [51 references]

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

Drug Withdrawal

- November 19, 2010 – Propoxyphene (Darvon, Darvocet): The U.S. Food and Drug Administration notified healthcare professionals that Xanodyne Pharmaceuticals has agreed to withdraw propoxyphene, an opioid pain reliever used to treat mild to moderate pain, from the U.S. market at the request of the FDA, due to new data showing that the drug can cause serious toxicity to the heart, even when used at therapeutic doses.

Additional Notice

- August 1, 2013 – Acetaminophen: The U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients that acetaminophen has been associated with a risk of rare but serious skin reactions. Acetaminophen is a common active ingredient to treat pain and reduce fever; it is included in many prescription and over-the-counter (OTC) products. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fever and pain/body aches (e.g., non-steroidal anti-inflammatory drugs, or NSAIDS, such as ibuprofen and naproxen) also carry the risk of causing serious skin reactions, which is already described in the warnings section of their drug labels.

Scope

Disease/Condition(s)

Chronic pain

Guideline Category

Evaluation
Management
Treatment

Clinical Specialty

Anesthesiology
Family Practice
Internal Medicine
Neurology
Pharmacology
Physical Medicine and Rehabilitation

Psychiatry
Rheumatology

Intended Users

Advanced Practice Nurses
Health Care Providers
Nurses
Pharmacists
Physician Assistants
Physicians
Substance Use Disorders Treatment Providers

Guideline Objective(s)

- To update the evidence base of the 2003 guideline
- To promote evidence-based management of individuals with chronic pain
- To identify the critical decision points in management of patients with chronic pain who are candidates for opioid therapy
- To improve patient outcomes (i.e., reduce pain, increase functional status, and enhance the quality of life)
- To decrease the incidence of complications
- To allow flexibility so that local policies or procedures, such as those regarding referrals to or consultation with substance abuse specialty, can be accommodated

Target Population

- Adults (18 or older) with chronic pain conditions who are treated in any Department of Veterans Affairs (VA) or Department of Defense (DoD) clinical setting
- Special populations: Patients with polytrauma, traumatic brain injury (TBI), mild traumatic brain injury (mTBI), post-traumatic stress disorder (PTSD), substance misuse, and psychiatric co-morbidity

Interventions and Practices Considered

Evaluation

1. Comprehensive history and physical examination (age, gender, present illness, past medical and surgical history, past psychiatric history, substance use history, family and social history, medications, allergies, mental status examination, review of diagnostic studies, evaluation of occupational risks)
2. Adequate trial of non-opioid therapy
3. Urine drug test (UDT)
4. Assessment for suicide risk
5. Complete assessment of pain using numerical rating scale (NRS) 0-10
6. Assessment of contraindications to opioid therapy

Treatment and Management

1. Patient and family education regarding treatment options
2. Written opioid plan care agreement (OPCA) that defines the responsibilities of the patient and the provider
3. Identification of appropriate opioid therapy using medication that provides the best pain relief with the fewest adverse effects at the lowest effective dose
4. Timely, accurate, and thorough documentation of drug therapy in compliance with the federal Controlled Substances Act (CSA)
5. Assessment of patient status and response to therapy (adverse effects, patient adherence, and drug efficacy)
6. Adjustment of therapy (management of side effects and non-adherence)
7. Modification of the treatment plan to achieve minimal harm and adverse effects
8. Discontinuation of opioid therapy in cases of:
    - Severe unmanageable adverse effects

- Serious non-adherence to the treatment plan or unsafe, criminal, or dangerous behaviors
- Misuse suggestive of addiction to prescribed medication
- Lack of effectiveness of therapy or a desire on the part of the patient to discontinue therapy

9. Referral to addiction/substance specialist or to specialty care
10. Appropriate long-term surveillance
11. Management of special populations (history of substance use, buprenorphine-treated patients, patient with sleep apnea)

Pharmacological Treatment

Short-acting Opioids

1. Codeine (alone or in combination with acetaminophen [APAP] or aspirin [acetylsalicylic acid (ASA)])
2. Hydrocodone (in combination with APAP, ASA, or ibuprofen [IBU])
3. Hydromorphone
4. Morphine
5. Oxycodone (alone or in combination with APAP or ASA)
6. Oxymorphone
7. Propoxyphene* (alone or in combination with APAP)
8. Tapentadol
9. Tramadol (alone or in combination with APAP)

***Note from the National Guideline Clearinghouse (NGC)**: On November 19, 2010, the U.S. Food and Drug Administration (FDA) notified healthcare professionals that Xanodyne Pharmaceuticals has agreed to withdraw propoxyphene, an opioid pain reliever used to treat mild to moderate pain, from the U.S. market at the request of the FDA, due to new data showing that the drug can cause serious toxicity to the heart, even when used at therapeutic doses. See the FDA Web site for more information.

Long-acting Opioids

1. Fentanyl Transdermal System
2. Methadone
3. Morphine controlled release (CR), sustained release (SR), extended release (ER)
4. Oxycodone CR
5. Oxymorphone ER
6. Tramadol ER

Major Outcomes Considered

- Pain reduction
- Complication rates
- Functional status
- Quality of life
- Adverse effects of therapeutic interventions
- Mortality

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Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

An initial global literature search identified a few comprehensive systematic reviews (SRs) that employed a rigorous and methodical search for evidence on the key questions related to opioid therapy (OT) in adults. The work group (WG) decided to adopt the results of these systematic reviews and to focus the additional searches on topics that were not addressed by the published SRs. Therefore, the Search Questions developed by the WG were divided into

two (2) categories. First were comprehensive (full) searches of topic areas that had either not been addressed in the previous version of this guideline or had been included but not fully developed. The search for these questions covered the period since the last Department of Veterans Affairs/Department of Defense (VA/DoD) clinical practice guideline (CPG) (2002 through 2009). The second group was limited (update) searches on topics which had been adequately addressed by the published SR of American Pain Society/American Academy of Pain Medicine (APS/AAPM), (2009) and for which new research findings were probable. The updating search for these questions covered the periods from June 2008 to March 2009.

Generally speaking, full searches were conducted on specific topics concerning potential adverse effects and their management, sub-populations with higher risk of harm caused by OT, and specific interventions involved in providing an OT trial. These included:

- Risks and benefits of OT for patients with sleep apnea, cardiac disease, substance use disorder and suicidal potential
- Approaches to addressing common adverse effects
- Breakthrough pain in non-cancer versus cancer, pre-medication
- Benefits & harms of OT in patients with comorbidities (e.g., traumatic brain injury [TBI], post-traumatic stress disorder [PTSD])
- Enhancements of care and Care Models

Limited (update) searches were conducted on:

- Risks & benefits of OT for patients with substance use disorder (SUD)
- Patient education
- Treatment and consent agreements
- Aberrant behavior: evaluation, predictors, and treatment
- Discontinuing or tapering OT
- Breakthrough pain; acute exacerbations or new acute pain
- Long acting opioids

All questions specified (adapted from the Evidence-Based Medicine toolbox, Center for Evidence-Based Medicine, [http://www.cebm.net]):

- **P**opulation – Characteristics of the target patient population
- **I**ntervention – Exposure, diagnostic, or prognosis
- **C**omparison – Intervention, exposure, or control used for comparison
- **O**utcome – Outcomes of interest

These specifications served as the preliminary criteria for selecting studies. See PICO Questions to Guide Literature Search (page 101 of the original guideline document) for a complete listing and categorization of the questions.

Selection of Evidence

The evidence selection process was designed to identify the best available evidence to address each key question and ensure maximum coverage of studies at the top of the hierarchy of study types. Published, peer-reviewed randomized controlled studies (RCTs), as well as meta-analyses and systematic reviews that included randomized controlled studies, were considered to constitute the strongest level of evidence in support of guideline recommendations. This decision was based on the judgment that RCTs provide the clearest, most scientifically sound basis for judging comparative efficacy. The WG made this decision while recognizing the limitations of RCTs, particularly considerations of generalizability with respect to patient selection and treatment quality. When available, the search sought out critical appraisals already performed by others that described explicit criteria for deciding what evidence was selected and how it was determined to be valid. The sources that have already undergone rigorous critical appraisal include Cochrane Reviews, Best Evidence, Technology Assessment, and Agency for Healthcare Research and Quality (AHRQ) systematic evidence reports.

In addition to Medline/PubMed, the following databases were searched: Cinahl/Medline/Embase/PsycINFO (OVID), Database of Abstracts of Reviews of Effectiveness (DARE), and Cochrane Central Register of Controlled Trials. For Medline/PubMed searches, limits were set for language (English), and type of research (RCT, systematic reviews and meta-analysis). For prognostic and diagnostic questions (e.g., does test improve outcome?); cohort or other prospective non-RCT designs were considered.

The following inclusion criteria were used to select the articles identified in the literature search for possible inclusion:

- Published in United States, United Kingdom, Europe, Australia, Japan, New Zealand
- Full articles only published in English
- Study populations: age limited to adults 18 years of age or older; all races, ethnicities, and cultural groups

Since the initial global search revealed only a limited number of randomized trials, the inclusion criteria were expanded to include prospective trials, cohort studies and in some cases, where these were not available, also epidemiologic and observational studies.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

I	At least one properly done randomized controlled trial (RCT)
II-1	Well-designed controlled trial without randomization
II-2	Well-designed cohort or case-control analytic study, preferably from more than one source
II-3	Multiple time series evidence with/without intervention, dramatic results of uncontrolled experiment
III	Opinion of respected authorities, descriptive studies, case reports, and expert committees

Overall Quality

Good	High-grade evidence (I or II-1) directly linked to health outcome
Fair	High-grade evidence (I or II-1) linked to intermediate outcome; **or** Moderate-grade evidence (II-2 or II-3) directly linked to health outcome
Poor	Level III evidence or no linkage of evidence to health outcome

Net Effect of the Intervention

Substantial	More than a small relative impact on a frequent condition with a substantial burden of suffering; **or** A large impact on an infrequent condition with a significant impact on the individual patient level
Moderate	A small relative impact on a frequent condition with a substantial burden of suffering; **or** A moderate impact on an infrequent condition with a significant impact on the individual patient level
Small	A negligible relative impact on a frequent condition with a substantial burden of suffering; **or** A small impact on an infrequent condition with a significant impact on the individual patient level

Zero or Negative	Negative impact on patients; **or** No relative impact on either a frequent condition with a substantial burden of suffering, or an infrequent condition with a significant impact on the individual patient level

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Preparation of Evidence Tables (Reports) and Evidence Rating

The results of the searches were organized in evidence reports, and copies of the original studies were provided to the work group (WG) for further analysis. Each reference was appraised for scientific merit, clinical relevance, and applicability to the populations served by the Department of Veterans Affairs (VA) and Department of Defense (DoD) health care systems.

Evidence-based practice involves integrating clinical expertise with the best available clinical evidence derived from systematic research. A group of research analysts read and coded each article that met inclusion criteria. The articles were assessed for methodological rigor and clinical importance. Clinical experts from the VA and DoD WG reviewed the results and evaluated the strength of the evidence, considering quality of the body of evidence (made up of the individual studies) and the significance of the net benefit (potential benefit minus possible harm) for each intervention.

The overall strength of each body of evidence that addresses a particular Key Question was assessed using methods adapted from the U.S. Preventive Services Task Force. To assign an overall quality [QE] of the evidence (good, fair, or poor), the number, quality, and size of the studies; consistency of results between studies; and directness of the evidence were considered. Consistent results from a number of higher-quality studies across a broad range of populations; supports with a high degree of certainty that the results of the studies are true and therefore the entire body of evidence would be considered "good" quality. A "fair" quality was assigned to the body of evidence indicating that the results could be due to true effects or to biases present across some or all of the studies. For a "poor" quality body of evidence, any conclusion is uncertain due to serious methodological shortcomings, sparse data, or inconsistent results. (See the "Rating Scheme for the Strength of the Evidence" field).

The Strength of Recommendation [SR] was then determined based on the Quality of the Evidence [QE], and the clinical significance of the net benefit [NE] for each intervention, as demonstrated by the body of evidence. Thus, the grade (i.e., A, B, C, D or I) assigned to guideline recommendations reflects both variables: the Quality of the evidence and the potential clinical benefit that the intervention may provide to patients (see the "Rating Scheme for the Strength of the Recommendations" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The update of the Department of Veterans Affairs/Department of Defense (VA/DoD) Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain was developed following the steps described in "Guideline for Guidelines," an internal working document of the VA/DoD Evidence Based Practice Working Group, that requires an ongoing review of guideline works in progress.

The Offices of Quality and Performance and Patient Care Services of the VA, the U.S. Deputy Assistant Under-Secretary for Health, and the Army Medical Command of the DoD identified clinical leaders to champion the guideline development process. During a preplanning conference call, the clinical leaders defined the scope of the

guideline and identified a group of clinical experts from the VA and DoD to form the Opioid Therapy (OT) for Chronic Pain Working Group (WG). For this guideline these WG participants were drawn from the fields of primary care, pain management, physical medicine (PM&R), anesthesiology, internal medicine, rheumatology, neurology, psychiatry, psychology, pharmacy, nursing, social work, and addiction specialists from diverse geographic regions, and both VA and DoD health care systems.

The WG participated in two face-to-face meetings to reach consensus about the guideline algorithm and recommendations and to prepare a draft update document. The draft continued to be revised by the Working Group through numerous conference calls and individual contributions to the document.

Recommendations for the performance or inclusion of specific procedures or services were derived through a rigorous methodological approach that included the following:

- Determining appropriate criteria such as effectiveness, efficacy, population benefit, or patient satisfaction
- Reviewing literature to determine the strength of the evidence in relation to these criteria
- Formulating the recommendations and grading the level of evidence supporting the recommendation

The WG developed a set of researchable questions within the focus area of the guideline and identified associated key terms after orientation to the guideline scope and to goals that had been identified. This ensured that the guideline development work outside of meetings focused on issues that practitioners considered important and produced criteria for the literature search and selection of included studies that formed the body of evidence for this guideline update.

Lack of Evidence—Consensus of Experts

Where existing literature was ambiguous or conflicting, or where scientific data was lacking on an issue, recommendations were based on the clinical experience of the Working Group.

This update of the OT Guideline is the product of many months of diligent effort and consensus building among knowledgeable individuals from the VA, DoD, and academia, as well as guideline facilitators from the private sector. An experienced moderator facilitated the multidisciplinary Working Group. The list of participants is included in Appendix H of the original guideline document.

Rating Scheme for the Strength of the Recommendations

Final Grade of Recommendation

	The Net Benefit of the Intervention			
Quality of Evidence	**Substantial**	**Moderate**	**Small**	**Zero or negative**
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	I

Strength of Recommendations Rating System

A	A strong recommendation that the clinicians provide the intervention to eligible patients. *Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.*
B	A recommendation that clinicians provide (the service) to eligible patients. *At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.*
C	No recommendation for or against the routine provision of the intervention is made. *At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D	Recommendation is made against routinely providing the intervention to asymptomatic patients. *At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.*
I	The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. *Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.*

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

Not stated

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Recommendations

Major Recommendations

Note from the Department of Veterans Affairs and the Department of Defense (VA/DoD) and the National Guideline Clearinghouse (NGC): The recommendations for the management of opioid therapy for chronic pain are presented in one major algorithm. The recommendations are provided below. See the original guideline document for the algorithm and evidence tables associated with selected recommendations, including level and quality of evidence, strength of recommendation, and supporting evidence citations.

The strength of recommendation grading (A, B, C, D, I) is defined at the end of the "Major Recommendations" field.

1. **Assessment**
   - A. **Patient with Chronic Pain**

     Recommendations

     1. A trial of opioid therapy (OT) is indicated for a patient with chronic pain who meets all of the following criteria:
        - a. Moderate to severe pain that has failed to adequately respond to indicated non-opioid and non-drug therapeutic interventions
        - b. The potential benefits of OT are likely to outweigh the risks (i.e., no absolute contraindications)
        - c. The patient is fully informed and consents to the therapy
        - d. Clear and measurable treatment goals are established
     2. The ethical imperative is to provide the pain treatment with the best benefit-to-harm profile for the individual patient.

     Note: For more information on identifying patients who should be referred to a pain specialist or pain clinic see the Web-based educational program "Opioids in the Management of Acute and Chronic Pain," available at http://www1.va.gov/PAINMANAGEMENT/docs/OpioidBrochure06REV.doc.

   - B. **Obtain Comprehensive Assessment Including: History, Physical Examination, and a Review of Diagnostic Studies**

     Objective

     Perform and document a benefit-to-harm evaluation, which includes history, physical examination, and appropriate diagnostic testing before initiating OT.

     Recommendations

     0. A comprehensive patient assessment should be completed to identify clinical conditions

that may interfere with the appropriate and safe use of OT. The comprehensive assessment should include:

a. Medical history
- Age, sex
- History of present illness, including a complete pain assessment (see Annotation C below)
- History of injury, if applicable
- Past medical and surgical history
- Past psychiatric history (including depression, anxiety, other emotional disorders, risk of suicide including family history and previous suicidal attempts)
- Medications (including current and past analgesics, their effectiveness, side effects, and tolerability, as well as drugs that may interact with OT)
- Substance use history (personal, family, peer group)
- Family history
- Social history (including employment, cultural background, social network, marital history, and legal history, other behavioral patterns [i.e., impulse behaviors])
- Review of systems
- Allergies
- Abuse (sexual, physical, and mental)

b. Physical examination
- A general examination
- A pain-focused musculoskeletal and neurologic examination
- Mental Status Examination (MSE) (including level of alertness, ability to understand and follow instruction, and suicidal ideation)

c. Review of diagnostic studies and assessments

d. Evaluation of occupational risks and ability to perform duty

2. Information from the pain history and physical exam should be reviewed to ensure that the patient has had an adequate therapeutic trial of non-opioid medication therapies.

3. A urine drug test (UDT) (also referred to as urine drug screen [UDS]) should be used to screen for the presence of illegal drugs, unreported prescribed medication, or unreported alcohol use prior to starting therapy. **[B]**

4. Patients on chronic OT should be assessed for suicide risk at onset of therapy and regularly thereafter. High suicide risk is a relative contraindication for OT.

5. OT should be used only after careful consideration of the risks and benefits

C. **Complete Assessment of Pain; Determine Cause of Pain, if Possible**

Objective

Obtain pain-related data required to manage the pain intervention.

Recommendations

0. Pain intensity should be evaluated at each visit.

1. Intensity of pain should be measured using a numerical rating scale (0-10 scale) for each of the following:
- Current pain
- Least pain in last week
- "Usual" or "average" pain in the last week

The patient's response to current pain treatments should be assessed using questions such as:

- "What is your intensity of pain after taking (use of) your current treatment/medication?"
- "How long does your pain relief last after taking your treatment/medication?"
- "How does taking your treatment/medication affect your functioning?

Note: some interventions may temporarily increase pain, so it may not be appropriate to ask these questions.

Other attributes of pain should be assessed as part of the comprehensive pain assessment:

- Onset and duration, location, radiation, description (quality), aggravating and alleviating factors, behavioral manifestations of pain, and impact of pain
- Temporal patterns and variations (e.g., diurnal, monthly, seasonal)
- Current and past treatments for pain
- Patient's expectations for pain relief

If possible, determine the type of pain:

- Differentiate between nociceptive and neuropathic pain
- Consider further evaluation if needed (such as imaging, electrodiagnostic studies [EDS] or consultation)
- Ask specifically whether the patient suffers from headache

Assessment of function, to obtain a baseline, should include: (Consistent evaluation tool is helpful in providing evaluation of response to OT over time):

- Cognitive function (attention, memory, and concentration)
- Employment
- Enjoyment of life
- Emotional distress (depression and anxiety)
- Housework, chores, hobbies, and other day to day activities
- Sleep
- Mobility
- Self-care behaviors
- Sexual function

Information from the pain history and physical exam should be reviewed to ensure that the patient has had an adequate trial of non-opioid therapy.

2. **Determination of the Appropriateness of OT**

D. **Are There Contraindications to OT That Cannot Be Resolved?**

Objective

Avoid inappropriate or harmful therapy.

Recommendations

1. OT should NOT be initiated in the following situations (absolute contraindications):
   a. Severe respiratory instability
   b. Acute psychiatric instability or uncontrolled suicide risk
   c. Diagnosed non-nicotine substance use disorder (SUD) (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV] criteria) not in remission and not in treatment
   d. True allergy to opioid agents (cannot be resolved by switching agents)
   e. Co-administration of drug capable of inducing life-limiting drug-drug interaction
   f. QTc interval >500 millisecond for using methadone
   g. Active diversion of controlled substances (providing the medication to someone for whom it was not intended)
   h. Prior adequate trials of specific opioids that were discontinued due to

intolerance, serious adverse effects that cannot be treated, or lack of efficacy

2. OT trial can be initiated with caution in the following situations. Consider consultation with appropriate specialty care to evaluate if potential benefits outweigh the risks of therapy.
   a. Patient receiving treatment for diagnosed SUD (DSM-IV criteria). (See Annotation P1)
   b. Medical condition in which OT may cause harm:
      - Patient with obstructive sleep apnea not on continuous positive airway pressure (CPAP)
      - Patients with central sleep apnea (See Annotation P2)
      - Chronic pulmonary disease (mild-moderate asthma, chronic obstructive pulmonary disease [COPD])
      - Cardiac condition (QTc interval 450-500 milliseconds) that may increase risk of using methadone
      - Known or suspected paralytic ileus
      - Respiratory depression in unmonitored setting
   c. Risk for suicide or unstable psychiatric disorder
   d. Complicated pain
      - Headache not responsive to other pain treatment modalities
   e. Conditions that may impact adherence to OT:
      - Inability to manage OT responsibly (e.g., cognitively impaired)
      - Unwillingness or inability to comply with treatment plan
      - Unwillingness to adjust at-risk activities resulting in serious re-injury
      - Social instability
      - Mental health disorders
3. Consider consultation with an appropriate specialist if legal or clinical problems indicate need for more intensive care related to opioid management. (See Annotation E – Indications for Consultation).

E. **Indication for Referral/Consultation for Evaluation and/or Treatment?**

Recommendations

0. Refer to an **Advanced Pain Provider**, or interdisciplinary pain clinic or program for evaluation and treatment a patient with persistent pain and any of the following conditions:
   . Complex pain conditions or polytrauma
   a. Significant medical comorbidities that may negatively impact OT
   b. Situation requires management beyond the comfort level of the primary provider
2. Refer to **Substance Use Disorder (SUD) Specialty Provider** for evaluation and treatment patient whose behavior suggests addiction to substances (excluding nicotine).
3. Consider consultation with a **SUD specialist** to evaluate the risk of recurrent substance abuse or to assist with ongoing management.
4. Refer to **Behavioral Health Specialty** for evaluation and treatment a patient with any of the following conditions:
   . Psychosocial problems or comorbidities that may benefit from behavioral disease/case management
   a. Uncontrolled, severe psychiatric disorders or those who are emotionally unstable
   b. Patients expressing thoughts or demonstrating behaviors suggestive of suicide risk
5. Refer patients with significant headache to a neurologist for evaluation and treatment.

6. Consider consultation with occupational health specialty if patient's occupation requires a high level of cognitive function.

F. **Determine Appropriate Setting for OT**

Recommendations

0. The clinician should assess the ability of the patient being considered for OT to be able to adhere to treatment requirements, as these patients are likely to do well and benefit from OT.
1. The appropriateness of OT as a treatment modality for chronic pain and the level of risk for adverse outcomes should be determined based on the initial and ongoing assessment of the patient.
2. For patients with history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors, initiation of a trial of OT in the primary care setting should only be considered if more frequent and stringent monitoring can be provided. In such situations, clinicians should strongly consider consultation with a mental health or addiction specialist.
3. Young patients (less than 25 years old) are at higher risk for diversion and abuse and may benefit from more stringent monitoring.
4. The clinician should consider referring patients who have unstable co-occurring disorders (substance use, mental health illnesses, or aberrant drug related behaviors) and who are at higher risk for unsuccessful outcomes (see Annotation E in the original guideline document).

Note: The level of risk in a certain clinical condition or situation, and the treatment setting are summarized in Table 2 in the original guideline document.

G. **Educate Patient and Family about Treatment Options; Share Decisions about Goals and Expected Outcomes of Therapy**

Objective

Reduce barriers and address concerns regarding opioids so that the patient and caregiver/family can make informed decisions about pain management, patient outcomes, and adherence to therapy.

Recommendations

0. Involve the patient and family/caregiver in the educational process, providing written educational material in addition to discussion with patient/family.
1. Discuss the *opioid pain care agreement (OPCA)* in detail, and reinforce in subsequent visits (See Annotation H below and in the original guideline document).
2. Provide, and document in the medical record, patient education on the following topics:
   - General information: goals and expectations, addiction, tolerance, physical dependency, withdrawal symptoms
   - Patient responsibilities: prescriptions, adherence to treatment plan, obtaining medications from a single prescriber (or clinic) and single pharmacy, pain diary, feedback to the provider
   - Legal issues
   - Instruction on how to take medication: importance of dosing and timing, interaction with other drugs
   - Prophylactic treatment of adverse effects and management of constipation
   - Discussion of an individualized comprehensive care plan that may include, in addition to OT, physical therapy, occupational therapy, cognitive-behavioral therapy, acupuncture, manipulation, complementary and alternative medicine, other non-pharmacologic therapies, and other non-opioid agent

Discuss a Written Opioid Pain Care Agreement with Patient and Family

Objective

Define the responsibilities of the patient and the provider for the management of OT.

Recommendations

Discuss a trial of opioid therapy with the patient, and obtain the patient's informed consent in a shared decision-making discussion. Document the informed consent discussion.

Review and discuss a written Opioid Pain Care Agreement (OPCA) with the patient who is expected to receive daily opioid therapy for the treatment of chronic pain. The signed agreement can serve as documentation of an informed consent discussion. (For a sample agreement, see Appendix C in the original guideline document)

The responsibilities during therapy, of the provider and the patient, should be discussed with the patient and family. A discussion of patient responsibilities should be patient-centered and address the following issues:

- Goals of therapy – Partial pain relief and improvement in physical, emotional, and/or social functioning
- The requirement for a single prescribing provider or treatment team
- The limitation on dose and number of prescribed medications
- Proscription against the patient changing dosage without discussing with provider
- Monitoring patient adherence – Discuss the role of random urine drug testing, the use of "pill counts"
- A prohibition on use with alcohol, other sedating medications, or illegal drugs without discussing with provider
- Agreement not to drive or operate heavy machinery until abatement of medication-related drowsiness
- Responsibility to keep medication safe and secure
- Prohibition of selling, lending, sharing or giving any medication to others
- Limitations on refills: only by appointment, in person, and no extra refills for running out early (exceptions should be considered on an individual basis)
- Compliance with all components of overall treatment plan (including consultations and referrals)
- Adverse effects and safety issues such as the risk of dependence and addictive behaviors
- The option of sharing information with family members and other providers, as necessary, with the patient's consent
- Need for periodic re-evaluation of treatment
- Reasons for stopping opioid therapy
- Consequences of non-adherence with the treatment agreement

Patient refusal to sign an agreement should be documented in the medical record. Consider patient's refusal to sign an agreement as part of the initial and ongoing assessments of the patient's ability to adhere to the treatment plan and the level of risk for adverse outcomes (see Table 2, Annotation F in the original guideline document). The prescription of therapy, in such cases, should be based on the individual patient and the benefits versus harm involved with therapy. The rationale for prescribing opioids without a signed agreement should be documented.

Determine and Document Treatment Plan

Objective

Identify and describe key elements of the opioid treatment plan.

Recommendations

The treatment plan should be individually tailored to the patient's circumstances and to the characteristics of the patient's pain.

Consider the use of other treatment approaches (such as supervised therapeutic exercise, biofeedback, and cognitive behavior approaches), which should be coordinated with the OT.

Consider establishing a referral and interdisciplinary team approach, if indicated.

Establish a follow-up schedule to monitor the treatment and patient progress.

The treatment plan and patient preferences should be documented in the medical record.

OT Treatment Goals

Treatment goals should be relevant to the individual patient and may include the following domains:

Improvement of physical function (e.g., increase range of motion, standing, walking)

Improvement of general functional status (e.g., increase activities of daily living, social—recreational activities, home—domestic activities)

Increase in self-management of the persistent pain

Improvement of vocational/disability status (e.g., improvement in work function, return to work, start job training; start classes)

Reduction/discontinuation of opioids and other pharmacologic medications

Reduction of health care utilization for the chronic pain condition (e.g., reduce medical procedures, inpatient admissions, outpatient office and emergency room visits)

Reduction of pain level (e.g., reduce visual analog scale scores, verbal rating scores, verbal descriptor scores)

Reduction of emotional distress associated with chronic pain

Achieve above goals while reducing the risk of misuse, and optimize treatment to avoid harm.

3. **Starting the OT Trial**

J. **Candidate for Trial of OT with Consent**

OT is a therapeutic trial. Prior to such a trial, the provider should determine that the potential benefits are likely to outweigh the potential harms, and the patient should be fully informed and should consent to the therapy. As treatment is administered, close monitoring of outcomes (pain reduction, physical and psychosocial functioning, satisfaction, adverse effects, or any aberrant drug-related behaviors) along with careful titration and appropriate management of adverse outcomes, can establish successful long-term therapy.

A trial of OT consists of three phases: initiation, titration, and maintenance. The **initiation** phase (see Annotation K1) involves selecting an appropriate opioid agent and dose for the individual patient, after considering the information obtained in the comprehensive assessment of the patient. The **titration** phase (see Annotation K2) involves adjustment of the dosage to achieve the desired clinical outcomes (pain relief, improved function, and patient satisfaction with minimal or tolerable adverse effects). The patient has entered the **maintenance** phase (see Annotation K3) when the required daily dose remains relatively stable. This may be the longest phase of the OT trial. Worsening pain after a period of stable maintenance may indicate disease progression, increased activity level, environmental factors (exposure to cold or reduced barometric pressure), development of psychosocial stressors, tolerance, or development of hyperalgesia. Additional evaluation may be indicated to determine the cause.**Supplemental** doses of non-opioids, short-acting opioids, or both should be considered during treatment (see Annotation K4).

4. K1. **Initiation Phase**
5. *Objective*

6. Start OT using an appropriate drug and formulation for the patient at a relatively low dose to gauge initial response, minimize adverse effects, and allow the patient to develop tolerance before making further dosage increases.

7. *Recommendations*
8. General Strategy for OT Initiation Phase
   10. Chronic pain is often a complex biopsychosocial condition. Clinicians who prescribe OT should routinely integrate psychotherapeutic interventions, functional optimization, interdisciplinary therapy, and other adjunctive non-opioid pain therapies.
   11. Provide written and verbal education to the patient about the specific medication, anticipated adverse effects, dosing and administration, possible excessive sedation and symptoms of opioid withdrawal.
   12. With patient consent, obtain a urine drug test (UDT) prior to initiating an OT trial and randomly at follow-up visits to confirm the appropriate use of opioids. A patient can refuse urine drug testing. The provider should take into consideration a patient's refusal to undergo urine drug testing as part of the ongoing assessment of the patient's ability to adhere to the treatment plan and the level of risk for adverse outcomes (see Annotation F, Table 2 in the original guideline document).
   13. There is no evidence to recommend for or against the selection of any specific opioid:
      a. Using a shared decision-making process, select a specific opioid formulation, based on experience and knowledge that matches the individual's needs and specific medical conditions
      b. Consider patient preference, and agent that allows administration by the least invasive route
      c. Consider the ease of drug administration, patient's prior experience with, and level of tolerance to opioid medications, potential risk for misuse, abuse patterns, and local formulary guidance
      d. Transdermal fentanyl should be avoided in opioid naïve patients.
   5. Start the OT trial with a low dose and with one medication at a time.
   6. Initiate a bowel regimen to prevent and treat constipation, which is anticipated with all opioids.

   For possible choices of opioids, see Table 3: Use of Opioids for Chronic Pain in Special Populations in the original guideline document.

   Initiation Strategy for Continuous, Persistent Daily Pain
   7. For continuous chronic pain, an agent with a long duration of action, such as controlled-release morphine or methadone is recommended.
   8. Alternatively, short-acting opioids can be started, and later converted to long-acting opioids. (See Annotation K2 - Titration)
   9. Treatment of continuous chronic pain should be initiated with opioids on a defined and scheduled basis.

   Initiation Strategy for Episodic Pain (Intermittent Pain That Occurs Few Times a Week)
   10. For episodic chronic pain, consider short-acting opioids (such as morphine, oxycodone, or hydrocodone), trying one medication at a time on a PRN (as needed) basis. Long-acting opioids should not be used on a PRN basis.

   Cautions for Use of Methadone in Patients with Chronic Pain

   Methadone is characterized by complicated and variable pharmacokinetics and pharmacodynamics and should be initiated and titrated cautiously by clinicians who are familiar with its use and risks, or who can

methadone be considered as an alternative first-line drug for OT in the primary care setting.

11. When using methadone:
    a. Inform patients of the arrhythmia risk
    b. Ask patients about heart disease, arrhythmia, and syncope
    c. Obtain an electrocardiogram (ECG) to measure the QTc interval before starting methadone and once the dose is stabilized (maintenance phase). Measure the QTc annually thereafter if the patient history is positive for risk factors for prolonged QTc interval, or has known prolonged QTc interval. Perform additional electrocardiography if the methadone dosage exceeds 100 mg/day, or if the patient has unexplained syncope or seizures
    d. If the QTc interval is greater than 450 ms, but less than 500 ms, reevaluate and discuss with the patient the potential risks and benefits of therapy, and the need for monitoring the QTc more frequently
    e. If the QTc interval exceeds 500 ms, discontinue or taper the methadone dose and consider using an alternative therapy. Other contributing factors, such as drugs that cause hypokalemia, or QT prolongation should be eliminated whenever possible
    f. Be aware of interactions between methadone and other drugs that may prolong QTc interval, or slow the elimination of methadone, and educate patients about drug interaction.

K2. **Titration Phase**

Objective

Adjust the dose of opioid in an individualized and safe manner to achieve satisfactory pain control and a tolerable adverse effect profile.

Recommendations

<u>The General Strategy for Titration</u>

12. Maintain close communication with patients and families, explicitly discussing the criteria for evaluating the effects of analgesic medications; doing so can help in defusing the anxiety that often accompanies visits to the physician.
13. Ask the patient to keep records of the time and dose of medication, the degree of pain relief, and the occurrence of adverse effects.
14. Documentation is essential, and should demonstrate the evaluation process—including consultation, prescriptions, and periodic review of patient status. Any change and consequent patient response should be documented in the record.
15. Follow up with the patient in no longer than 2 to 4 weeks after dosage modifications, or other treatment adjustments, basing the frequency of follow-up on the clinical situation (also see Annotation K3 – Maintenance Phase).
16. Assess the patient for changes in biopsychosocial and spiritual domains but especially the diagnosis, trajectory of disease, and effect of adjuvant therapies.
17. As with initial opioid selection and dosing, titration should be individualized according to the patient's age, health status, previous exposure to opioids, level of pain, comorbidities, potential drug interactions, the particular opioid formulation, the level (setting) of care, attainment of therapeutic goals, and predicted or observed harms.
18. If necessary, the daily dose may be increased by 25% to 100%. In general, smaller increments are appropriate for elderly or frail patients, those with likely low opioid tolerance, and patients experiencing unsatisfactory pain relief in the presence of some adverse effects. Larger increments may be used in patients with severe uncontrolled pain or likely high level of opioid tolerance. If the new dose is well tolerated but ineffective, additional increases in dose can be considered.
19. To ensure that the full effect from a dosage change has been manifested, and to avoid potential toxicity due to rapid accumulation of a drug, do not increase the dose more frequently than every

five half-lives. In the case of methadone, upward dosage titration should not occur more frequently than every 7 days and perhaps longer (e.g., every 1 to 2 months), and only if there is no problem with daytime sedation, taking into consideration that there is wide interpatient variability in half-lives and responsiveness. (See Tables in Appendix E and F in the original guideline document)

20. If possible, titrate only one drug at a time while observing the patient for additive effects. Maintain patients on as few medications as possible to minimize drug interactions and adverse events. Discontinue medications, especially adjuvant medications, which do not add substantially to patient function or comfort. Continue close assessment of patients prescribed multiple centrally acting/psychoactive medications.
21. If a medication provides less than satisfactory pain reduction despite increasing the dose as tolerated to a reasonable level (less than 200 mg/day morphine equivalent), evaluate for potential causes such as non-adherence and drug interactions (see Appendix E, Table E6 in the original guideline document [Drug Interactions]), and consider changing to an alternate opioid medication.
22. Medication may be increased until limited by adverse effects or clear evidence of lack of efficacy. If a high dose of medication (greater than 200 mg/day morphine equivalent) provides no further improvement in function, consider consultation rather than further increasing the dose.
23. During the titration phase, reasonable supplemental (rescue) doses of a short acting opioid may be considered. (See Annotation K-4-Supplemental Dosing)
24. Consider one or more of the following adjustments in therapy when there is an apparent loss of analgesic effect
    a. Further optimize adjuvant therapies
    b. Re-titrate the dose
        - Increase dose by 25-100%.
        - <u>Do not</u> increase the dose more frequently than every 5 half lives (for methadone or fentanyl no more than once a week), to ensure that the full effect from a dosage change has been manifested and to avoid potential toxicity due to rapid accumulation of a drug.
        - If possible, titrate only one drug at a time, while observing the patient for additive effects. Inappropriate or ineffective medications should be tapered while titrating an appropriate pharmacologic regimen.
        - Medication may be increased until treatment goals are met, intolerable adverse effects occur, or there is clear evidence of lack of efficacy.

        Rotate to another opioid
        - Rotation between opioids may help to improve efficacy, reduce side effects, and reduce dose escalation in some patients who are receiving long-term OT.
        - Rotate to another agent based on equianalgesic table and titrate (see Appendix E, Table E6 in the original guideline document for conversion factors)

        Refer or consult with advanced pain care (pain or palliative care specialist/pharmacist).
        - If the dose of opioid is large (more than 200mg/day morphine equivalent)
        - If opioid induced hyperalgesia or opioid tolerance is suspected

        Discontinue OT (See Annotation X).

<u>Converting Short-Acting Opioids to Long-acting Opioids</u>

14. For a patient with continuous pain an agent with a long duration of action, such as controlled-release morphine or methadone, is recommended.
15. If short-acting opioids are effective and well tolerated, it may be possible to achieve equivalent pain relief with fewer daily doses of medication by substituting an equivalent dose of long-acting opioid medication (such as methadone, morphine controlled release [CR], oxycodone CR, or transdermal fentanyl). These long-acting medications may provide steadier serum levels and smoother pain control. They can be supplemented with doses of short-acting medication to control

pain exacerbation.

16. The conversion to a long-acting opioid should be based on an equianalgesic conversion (see Appendix E, Table E6 in the original guideline document for conversion factors) and consideration of the incomplete cross-tolerance between opioids. To allow for incomplete cross-tolerance, in most cases, the starting conversion dose should be 50% to 67% of the calculated equianalgesic dose.

    A notable exception to this general rule is methadone, which has relatively little cross-tolerance with other opioids and should be started at a conversion dose that is based on the previous morphine-equivalent dose. Inexperienced clinicians should consult with an expert before initiating methadone, even in an opioid tolerant patient (see Appendix E, Table E6 and Appendix F in the original guideline document for Methadone Dosing Recommendations).

General Recommendations for Opioid Rotation

17. Base the method of rotating opioids on the clinical situation. Either of the following two methods may be used:

    . Step-wise Rotation: Reduce the old opioid dose by 25% to 50% decrements and replace the amount removed with an equianalgesic conversion dose of the new opioid. This method may be preferable when switching large doses of opioids. A disadvantage of this method is that the causative opioid(s) of new or worsening adverse effects during rotation would be difficult to identify.

    a. Single-step Rotation: Stop the old opioid and start the new opioid in an equianalgesic conversion dose. This method may be preferable when the old agent must be stopped immediately because of a hypersensitivity reaction. A disadvantage of this method is that pain may worsen if the new agent has a delayed peak analgesic effect (e.g., methadone) while the old agent has a relatively short offset of effects.

    See Appendix E, Table E6, in the original guideline document for equianalgesic doses and conversion methods.

K3. **Maintenance Phase**

Objective

Maintain reliable pain control and/or improvement in function by repeating the effective, satisfactorily tolerated dose in a routine schedule.

Recommendations

18. Maintain the lowest effective and well-tolerated dose. The optimal opioid dose is the one that achieves the goals of pain reduction and/or improvement in functional status and patient satisfaction with tolerable adverse effects.
19. Recognize that the dose may need to be titrated up or down on basis of the patient's current biopsychosocial situation. (See Annotation K2 – Titration Phase)
20. Assess patients at least every 1 to 6 months based on the following:

    Individualize and adjust visit frequencies based on patient characteristics, comorbidities, level of risk for potential drug misuse (i.e., diversion, addiction, abuse, and aberrant drug-related behavior), type of pain, and type and dose of opioids. No specific visit frequency applies to all patients

    Select a frequency that allows close follow-up of the patient's adverse effects, pain status, and appropriate use of medication

    The patient should be able to request an early evaluation

    Any change in the efficacy of the maintenance dose requires a face to face encounter for assessment prior to modifying therapy

4. Monthly renewal of the prescription for opioid medication can be facilitated by:
   . Phone call, email, or mail-in requests
   a. A structured program (e.g., opioid renewal clinic) staffed by advanced care providers (e.g., pharmacists, nurse practitioners, PA-Cs, psychologists, RNs) with appropriate co-signatures
5. In addition to the maintenance opioid analgesic, supplemental doses of short-acting opioids may be considered. (See Annotation K4 – Supplemental Therapy)
6. Assess and re-educate patient's adherence with safely storing opioid medications.

K4. **Supplemental Therapy**

Recommendations

7. Evaluate worsening or new pain symptoms to determine the cause and the best treatment approach.
8. Encourage the use of non-pharmacologic modalities (e.g., pacing activities, relaxation, heat, cognitive behavioral therapy).
9. Carefully evaluate the potential benefits, side effects, and risks when considering supplemental opioids.
10. Consider supplemental short-acting opioid, non-opioid, or a combination of both agents on an as-needed basis.
11. Avoid the use of rapid-onset opioids as supplemental OT in chronic pain, unless the time course of action of the preparation matches the temporal pattern of pain intensity fluctuation.
12. Avoid use of long-acting agents for acute pain or on an as-needed basis in an outpatient setting.
13. When using combination products, do not exceed maximum recommended daily doses of acetaminophen, aspirin, or ibuprofen.
14. Avoid the use of mixed agonist-antagonist opioids, as these agents may precipitate withdrawal in patients who have physical opioid dependence.
15. Whenever possible, use the same opioid for supplemental therapy as the long-acting opioid to avoid confusion about the cause of any adverse effects that may develop.
16. When using short-acting pure agonist opioids (alone or in combination with non-opioid analgesics) for supplemental therapy, give opioid doses equivalent to about 10-15%, the every four hourly equivalent, or 1/6th of the total daily opioid dose, as needed.

Rescue Therapy

11. Use rescue short-acting opioids to assist with pain management during the titration process and to help determine the long-term daily opioid dose.

Breakthrough Pain Therapy

12. Do not use routinely for chronic pain. If necessary, use breakthrough pain therapy sparingly.
13. Consider adjusting the long-acting opioid regimen if pain exacerbations are interfering with patient function due to severity, frequency, or diurnal variations in pain intensity.

Incident Pain Therapy

14. Educate and reassure patient, emphasizing realistic expectations about limitations of chronic OT, the normal cyclic nature of chronic pain, and the importance of pacing activities.
15. Consider providing preemptive analgesia for preventing incident pain (e.g., 8 to 12 doses per month of short-acting opioid preparation).

L. **Document Therapy**

Recommendations

1. When writing a prescription for OT, be certain to record the name of the drug, the strength, the number of dosage units (written numerically and in text) and how the drug is to be taken. (In the case of methadone, indicate on the prescription that it is for pain as opposed to detoxification).
2. Follow local regulations.

4. **Assessment of Patient Status and Response to Therapy**

M1. **Assess for Adverse Effects**

Objective

Identify adverse effects and tolerability problems that may potentially change the treatment plan.

Recommendations

1. Evaluate patient for opioid adverse effects: constipation, nausea, vomiting, headache, dyspepsia, pruritus, dizziness, tiredness, dry mouth, sweating, hyperalgesia, sexual dysfunction, and sedation.
2. Many adverse effects spontaneously resolve with continued administration and development of tolerance. Consider individual levels of tolerability to different opioid agents.
3. If not already done, anticipate and consider preventive treatment for common adverse effects, particularly constipation and nausea.
4. Keep in mind that slowly titrating the opioid dose, modifying the dosage regimen, treating symptoms, and rotating the opioid agents may successfully treat most adverse effects.
5. Consider evaluation of possible drug-to-drug interactions with other medications that have been prescribed for the patient (see Appendix E in the original guideline document for a table of drug interactions).

M2. **Assess Adherence**

Objective

Determine whether patient is adhering to the essential components of the treatment plan and the reason for any non-adherence.

Recommendations

6. At every visit and telephone contact for opioid renewal, assess and document adherence with appropriate use of opioid analgesics, including evidence of misuse, abuse, or addiction.
   a. Evaluate how and when the patient is taking medication, use of other medications including nonprescription and herbal preparations, and use of alcohol and illicit drugs.
   b. Screening aids such as random pill counts, adherence checklists, or instruments such as the Screener and Opioid Assessment for Patients with Pain (SOAPP), may be used to assist the provider in assessing adherence.
   c. With patient consent, obtain a Urine Drug Test (UDT) before initiating OT trial and randomly at follow-up visits to confirm the appropriate use of opioids (See Annotation M3).
   d. Assess and document adherence to other components of the treatment plan, such as follow up with referrals, tests, and other therapies.
   e. Assess patients for behaviors that are predictive of addiction including repeated minor variations in adherence that may indicate an increased likelihood of addiction or serious non-adherence.
   f. Assess patient's adherence and reeducate regarding the importance of safely storing opioid medications.
   g. Assess and document patient motivation and barriers to adherence.
2. Based on the clinical assessment the provider should determine whether aberrant behavior is present and respond with appropriate action.
3. If the clinician is not sure of the meaning of the behavior, more frequent clinic visits, addiction or mental health specialist consultations, or periodic drug screens might be employed.
4. When aberrant behaviors are present, providers should not stigmatize or judge patients but instead simply inform the individual that the behavior is unsafe and needs evaluation and adjustment in treatment through increased structure and monitoring or referral.
5. A continuing pattern of repeated episodes of non-adherence following treatment changes designed to maximize adherence should increase prescriber concerns and consideration of potential

cessation of OT.

6. Consider involving family members or significant others in identifying solutions to non-adherence and in monitoring future adherence when possible. This may include a change in the patient's living situation that would provide greater structure (e.g., nursing home, assisted living facility), potentially enhance compliance, and reduce non-adherence

M3. **Urine Drug Tests (UDTs)**

Recommendations

7. Inform patients that drug testing is a routine procedure for all patients starting or on OT, and is an important tool for monitoring the safety of their treatment.
8. With patient consent, obtain a UDT in all patients prior to initiation of OT. **[B]**
9. With patient consent monitor all patients on OT with periodic random UDTs to confirm adherence to the treatment plan. Increase the frequency of UDTs based on risk level for aberrant drug-related behaviors and following each dose increase. **[B]**
10. Take into consideration a patient's refusal to take a UDT as part of the ongoing assessment of the patient's ability to adhere to the treatment plan and the level of risk for adverse outcomes (see Annotation F).
11. When interpreting UDT results take into account other clinical information (e.g., past SUD, other risk factors, aberrant drug-related behaviors, and other conditions indicating risk.)
12. Understanding of lab methods for drug testing and reporting are necessary to interpret UDT results (i.e., screen versus confirmatory test, substances tested, cut-off levels for tests). Maintain a close working relationship with the clinical laboratory to answer any questions about the UDT or for confirming the results.

M4. **Assess and Identify Any Complications, Co-occurring Conditions, or Other Indications for Consultation or Referral**

Objective

Identify and assess any complications, co-morbidities, or other indications for consultation or referral that are not necessarily related to active non-adherence behaviors.

Recommendations

13. Evaluate and assess the patient for the following problems or other indications for consultation or referral:
    a. Patient with complex pain conditions
    b. Patient with significant medical comorbidities that may negatively impact OT
    c. Patient with significant concurrent psychiatric illnesses
    d. Patient who is unable to tolerate increased pain or physical withdrawal symptoms arising from opioid tapering when OT is being discontinued
    e. Opioid induced hyperalgesia or opioid tolerance suspected (i.e., pain increases or changes while on chronic stable opioid dosing and with an unchanged underlying medical condition causing the pain)
    f. Patient with conditions requiring management beyond the expertise level of the primary provider

M5. **Assess Effectiveness (Pain, Function, and Satisfaction)**

Objective

Assess whether OT is meeting the patient's and clinician's expected goals of pain relief and/or functional improvement, and patient satisfaction, and whether OT should be continued.

Recommendations

14. Evaluate pain intensity at each visit.

a. Intensity of pain should be measured in the following manner using a Numerical Rating Scale (NRS) (0–10) and include the following:

- Current pain
- Least pain in last week
- "Usual" or "Average" pain in the last week

The patient's response to current pain medications should be assessed each visit using questions such as:

- "What is your intensity of pain after taking your current treatment/medication?"
- "How long does your pain relief last after taking your medication?"

2. Evaluate pain-related function using objective documentation whenever possible, such as physical therapy progress notes, employment records, exercise diaries, family reports, clinician observations (e.g., walking distance), or validated instruments or NRS on a monthly basis during the titration phase and every six months after the patient is on stable opioids. Assessment of function may include:

- Employment
- Enjoyment of life
- Emotional distress (depression and anxiety)
- Housework, chores, hobbies, and other day to day activities
- Sleep
- Mobility
- Self-care behaviors
- Sexual function

Assess overall patients' satisfaction with pain therapy at each visit.

Emphasis should be given to capitalizing on improved analgesia by gains in physical and social function; OT should be considered complementary to other analgesic and rehabilitative approaches.

Note: The VA Pain Outcomes Toolkit recommends several optional instruments for functional status assessment. (See the Department of Veterans Affairs Web site: http://www1.va.gov/PAINMANAGEMENT/docs/Outcomes.doc).

5. **Adjustment of Therapy**

N1. **Address Adverse Effects**

Objective

Modify treatment to achieve effective pain control while minimizing adverse effects and medication intolerance.

Recommendations

A General Strategy to Minimize Adverse Effects

1. Adverse effects can usually be minimized through the use of low starting doses, slow titration rates, prophylactic and symptomatic treatments, and specific patient education provided at initiation of therapy.
2. Symptomatic treatment should be augmented with slow dosage titration, dose modification, and/or opioid rotation to minimize the adverse effects as follows:
   a. Titrate slowly, temporarily reducing or holding doses if necessary, or modify the dosage regimen to allow the patient to develop tolerance to the adverse effects.
   b. If these measures fail to minimize the adverse effects, consider rotating to another opioid agent.
3. If adverse effects are unmanageable and therapy is a greater detriment than benefit as determined by discussion with the patient and family, OT should be discontinued.

Constipation

4. Initial bowel regimens should generally consist of a bowel stimulant and a stool softener as well

as general measures, such as increased fluid intake, increased dietary fiber, and adequate exercise.

5. Routinely initiate a stimulant-based bowel regimen at commencement of chronic OT.
6. If the initial regimen is inadequate, mild hyperosmotic, saline, and emollient laxatives may be added.
7. If possible, reduce or discontinue other drugs that may cause or contribute to constipation.
8. Bulk-producing laxatives, such as psyllium and polycarbophil, are not recommended and are relatively contraindicated as they may exacerbate constipation and lead to intestinal obstruction in patients with poor fluid intake.
9. Assess patients for constipation symptoms at every office visit.

Nausea and Vomiting

10. Consider prophylactic antiemetic therapy at initiation of therapy.
11. Rule out other causes of nausea, and/or treat based on cause including
    a. Stimulation of chemoreceptor trigger zone: dopamine or serotonin antagonist
    b. Slowed gastrointestinal (GI) motility: metoclopramide
    c. Nausea associated with motion: dimenhydrinate or scopolamine

Itching

12. Rule out an allergic reaction.
13. Itching may resolve spontaneously despite continuation of OT. If the itching does not spontaneously resolve, consider treatment with antihistamines.

Sedation

14. Rule out other causes.
15. Reduce dose (with or without addition of a co-analgesic). Excessive sedation within the first few days of initiating opioids may require temporarily holding one or two doses and restarting at a lower dose to prevent respiratory depression.
16. Add or increase non-opioid or non-sedating adjuvant for additional pain relief so that the opioid can be reduced.
17. If the above measures fail to relieve sedation adequately, consider rotating to another opioid agent.
18. Consider adding caffeine or a prescription psychostimulant medication.

Confusion or Minor Deterioration of Cognitive Function

19. Rule out other causes.
20. Consider reducing or stopping (tapering) the dose.
21. Add or increase non-opioid or non-sedating adjuvant for additional pain relief so that the opioid can be reduced.
22. Rotate opioid agent.
23. If patient continues to deteriorate during titration phase and presents with symptoms of delirium, OT should be discontinued.
24. If patient develops increased confusion or major cognitive changes (delirium) during the maintenance phase, consider hospitalization to investigate the cause and to continue treatment safely.

Opioid-Induced Endocrinopathy

25. Ask all patients on opioids for chronic pain about symptoms of opioid-induced endocrinopathy (i.e., hypogonadism) on each visit.
26. If opioid-induced endocrinopathy symptoms are present, and not accounted for by another disorder or illness (e.g., depression, chronic disease), laboratory evaluation and consultation with an endocrinologist should be considered.
27. Insufficient data exists to recommend routine laboratory screening for endocrinopathy in asymptomatic patients on OT.

Immune Dysfunction

28. There is insufficient evidence to make recommendations regarding OT and immune dysfunction.

Osteoporosis

29. Consider monitoring bone density in patients at risk for osteoporosis (See Table 6: "Risk Factors for Osteoporosis" in the original guideline document), as patients with fractures associated with hypogonadism often have no other symptoms associated with hypogonadism.

N2. **Severe Unmanageable Adverse Effects**

Objective

Determine whether adverse effects warrant adjustment of OT or discontinuation of OT.

Recommendations

30. If a medication causes unmanageable adverse effects, consider changing to an alternate opioid medication.
31. When therapy is a greater detriment than benefit as determined in consultation with the patient and family, OT should be discontinued.

N3. **Serious Non-Adherence – Illegal, Criminal, or Dangerous Behaviors**

Objective

Address serious non-adherence behaviors promptly.

Recommendations

32. Address safety issues immediately and apply legal mandates as appropriate.
33. Dangerous or illegal behaviors may require immediate cessation of the OT with consideration of appropriate treatment of potential withdrawal symptoms.
34. Document and refer to behavior health specialty those patients demonstrating behaviors suggestive of suicide.
35. For a patient with evidence of diversion or dangerous or suicidal behavior the clinician should discontinue OT, refer as appropriate for emergency psychiatric evaluation, and flag the chart.
36. Consider notifying law enforcement about suspected criminal behaviors such as prescription fraud or diversion. Consult with counsel prior to doing so to clarify current confidentiality laws and regulations (e.g., VA/military police, risk manager, and/or regional counsel).
37. Carefully document the details of the situation in the clinical record, or not, as advised by risk management and/or legal counsel.

N4. **Minor Non-adherence or Medication Misuse**

Objective

Educate patient, adjust clinical structure and behavioral interventions, and otherwise revise treatment to address relatively minor behavioral problems so that appropriate OT can be continued.

Recommendations

38. Consider adjustment of the initial treatment agreement, with emphasis upon specific adherence issues that have been identified; a more structured approach may be required. Possible responses to minor non-adherence might include:
    a. Reviewing, discussing, and restating the treatment plan
    b. Reviewing the written opioid treatment agreement and incorporating any needed revisions
    c. Recommending consultation with a pain, addictions, or behavior health specialist
    d. Administration of medications under supervision or with the assistance of others
    e. Change of medication, medication dose, or amount dispensed
    f. More frequent clinic contacts (telephonic, physician extenders, or clinic visits)
    g. Instituting periodic or random urine toxicology screens

2. Consider setting up a grievance procedure with the patient.
3. Consider involving family members or significant others in identifying solutions to non-adherence and in monitoring future adherence when possible. This may include change in the patient's living situation that would provide greater structure (e.g., nursing home, assisted living facility) and might enhance compliance and reduce non-adherence.

N5. **Moderate Non-Adherence: Persistent Aberrant Behavior, Co-morbidities or Other Indications for Consultation or Referral for Evaluation and Management**

Objective

Address moderate (Level II) non-adherence behaviors.

Recommendations

4. Consider consultation with, or referral to, a behavioral health specialist if exacerbation of an underlying psychotic disorder is an issue, if the non-adherent behaviors may be due to changes in mood or increased suicidality, or if there is evidence of increased and poorly controlled anger and tendency to violent behaviors (see Annotation O2).
5. Consider referral to an addiction specialist if the non-adherent behaviors are those associated with possible addiction (see Annotation O1).
6. Patients presenting with persistent or troublesome aberrant behavior who do not respond to intervention by primary care should be referred for evaluation and management of OT to a more structured care environment (e.g., Pharmacy Pain Management Clinic/Opioid Renewal Pain Care Clinic/Pain Medicine Clinic).
7. If such programs are not available, consider continuing OT with increased frequency of monitoring and screening, performing a comprehensive behavioral assessment, and addressing co-morbidities.

6. **Consultation/Referral**

O1. **Consultation or Referral to *SUD/Addiction Specialty* for Evaluation and Treatment of Non-Adherence Behaviors, or Misuse Suggestive of Addiction to Prescribed Medication, Including Addiction**

Recommendations

1. Consider consultation or referral to **addiction specialty** for evaluation and treatment in the following conditions:
   a. Demonstration of behaviors suggesting addiction to prescribed opioids or SUDs
   b. Patients with a significant chronic, or substantiated pain, who develop addiction behaviors in the context of chronic OT
   c. Uncontrolled SUD (excluding nicotine)
   d. Behaviors characteristic of compulsive drug use (addiction) to either opioids or other drugs or alcohol should be referred to an addiction specialty
   e. Complex conditions who manifest behaviors characteristic of addiction with multiple co-occurring psychiatric disorders
   f. Need for tapering of opioids or unable to tolerate tapering after discontinuation of OT.
2. Consider consultation with a **SUD specialist** to evaluate the risk of recurrent substance abuse or to assist with ongoing management.
3. Refer patient for psychosocial treatments specific to prescription medication addiction/abuse. These can include addiction counselors comfortable with such topics, and self-help organizations (Pills Anonymous/PA, the National Chronic Pain Outreach association, and other similar organizations).

O2. **Consider Consultation or Referral to Specialty Care for Complications, Co-occurring Conditions, or Other Indications**

Patients on OT should have one designated provider who accepts primary responsibility for their overall medical care. This clinician may or may not prescribe OT, but should coordinate

consultation and communication among all clinicians involved in the patient's care.

Recommendations

4. Consider referral to a **Pain Medicine Specialist** in the following situations:
    a. Patient with complex pain conditions or polytrauma
    b. Patient with significant medical comorbidities that may negatively impact OT
    c. Patient who is unable to tolerate increased pain or physical withdrawal symptoms arising from opioid tapering when OT is being discontinued
    d. Opioid induced hyperalgesia or opioid tolerance is suspected
    e. High dose of medication (greater than 200 mg/day morphine equivalent) provides no further improvement in function
    f. Patient requiring management beyond the expertise of the primary provider
2. Consider Referral to/consultation with a **Behavioral Health Provider** for evaluation and treatment in the following conditions:
    a. Exacerbation of an underlying psychotic disorder
    b. Uncontrolled, severe psychiatric disorder or those who are emotionally unstable
    c. Demonstration of high-risk behaviors suggestive of suicide ideation
    d. Psychosocial problems or comorbidities that may benefit from disease or case management
    e. Adverse behavioral or cognitive effects of OT
    f. Co-occurring trauma related conditions (mild traumatic brain injury [mTBI], TBI, post traumatic stress disorder [PTSD])

7. **Follow-Up**

P. **Follow-up at Appropriate Intervals**

Objective

Evaluate pain as a guide to further intervention.

Recommendations

1. Schedule follow-up visits at least every 2 to 4 weeks after any change in medication regimen and at least once every 1-6 months for the duration of the therapy (maintenance).
2. Assess at each visit:
    a. Comfort (degree of analgesia)
    b. Opioid-related adverse effects
    c. Functional status (physical and psychosocial)
    d. Adherence to opioid treatment agreement and other aspects of treatment plan
    e. Obtain laboratory studies (especially liver or kidney function screens), and/or order drug screens as indicated
    f. Use of self-report instruments (diary, opioid log) may be helpful but should not be required.
3. Documentation is essential and the medical record for each encounter should specifically address comfort, function, adverse-effects, and treatment plan adherence.

8. **Discontinue OT**

Q. **Indication to Discontinue OT**

Recommendations

1. OT should be tapered off and discontinued if any of the following situations occur:
    a. The medication fails to show partial analgesia with incremental dose titration
    b. Trials with different agents provide inadequate analgesia
    c. There is other evidence that the pain may not be opioid responsive
    d. Real or potential harms outweigh real or potential benefits

e. Patient request

2. Consider decreasing the opioid dose when pain level decreases in stable patients. (See Annotation X –Tapering)

R. **Is Patient Willing to Engage In Addiction Therapy**

Recommendations

0. Document, and offer referral to addiction specialty for patients demonstrating behaviors suggesting addiction to prescribed opioids or SUDs.

1. Discuss pharmacotherapy options with all patients with opioid and/or alcohol dependence.

2. If there are clearly unsafe or illegal behaviors, opioid prescribing should stop immediately and withdrawal should be addressed.

S. **Address Safety and Misuse; Begin Process to Discontinue Opioid Use**

Recommendations

0. Attempt to maintain contact with any patient who withdraws from treatment due to a disagreement.

1. Refer patients with comorbid psychiatric disorders to appropriate mental health providers.

2. Identify and document any co-occurring disorders (CODs) in patients with SUDs:

a. Psychiatric history, including symptoms and their relation to substance use, current and past diagnoses, treatments and providers

b. Infectious diseases (human immunodeficiency virus [HIV], hepatitis C, sexually transmitted disease)

c. For patients using nicotine offer and recommend tobacco use cessation treatment

d. Medical CODs that may be related to or affected by substance use (e.g., diabetes, cardiovascular disease, digestive disorders, skin infections, respiratory disorders, dementia, cerebrovascular disease)

4. Individuals with SUD should be assessed for any significant, unmet psychosocial needs or situational stressors. These include but are not limited to:

a. Inadequate or no housing

b. Financial difficulties, especially if unable to meet basic needs

c. Problematic family relationships or situations (including caregiver burden or domestic violence)

d. Poor social support

e. Religious and spiritual problems

f. Occupational problems

g. Difficulties with activities of daily living or instrumental activities of daily living

T. **Discontinue OT; Taper Medication**

Objective

Maintain patient safety and comfort during the initial phase of opioid abstinence.

Recommendations

0. Decisions regarding tapering schedule should be made on an individual basis. Sometimes faster or slower tapering may be warranted.

1. For those patients who are at high risk of aberrant behaviors (parasuicidal acts, dealing/selling medications, or those with severe impulse control disorders), tapering opioid in a primary care setting is not appropriate and those patients should be referred to an addiction or pain specialist with expertise dealing with difficult cases.

2. Patients with complicated withdrawal symptoms should be referred to a pain specialist or a center specializing in withdrawal treatment.
3. Patient being tapered due to development of addiction should be referred for SUD treatment. Opioid detoxification in a primary care setting followed by ongoing substance use treatment may be appropriate.

U. **Educate on Withdrawal Symptoms, Taper Medications**

Objective

Prepare the patient to discontinue opioids with a minimum of withdrawal symptoms.

Recommendations

0. Complete evaluation of treatment, co-morbidity, psychological condition, and other relevant factors should be completed prior to the initiation of the taper.
1. Clear written and verbal instructions should be given to patients/family to educate them about the slow taper protocol that will minimize abstinence (withdrawal) syndromes.
2. Patients who are unable to tolerate the taper as described should be considered for referral to, or consultation with, a pain specialist, substance use specialist or other expert.
3. Withdrawal management for addicted patients is not part of this guideline. Refer to the National Guideline Clearinghouse (NGC) summary of the VA/DoD Clinical Practice Guideline for Management of Substance Use Disorders.

Protocol for Tapering

- Taper by 20% to 50% per week (of original dose), for patients who are not addicted. The goal is to minimize adverse/withdrawal effects
- The rapid detoxification literature indicates that a patient needs 20% of the previous day's dose to prevent withdrawal symptoms.
- Decisions regarding tapering schedule should be made on an individual basis. Sometimes faster or slower tapering may be warranted.
- Some experts suggest that the longer the person has been on opioids, the slower the taper should be.
- Remain engaged with the patient through the tapering process, and provide psychosocial support as needed.
- Consider using adjuvant agents, such as antidepressants to manage irritability, sleep disturbance, or antiepileptics for neuropathic pain. (Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain. [2007] available at: http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf).
- Do not treat withdrawal symptoms with opioids or benzodiazepines after discontinuing opioids. (Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain [2007] available at:http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf)

Follow-up as Indicated

Objective

Provide appropriate long-term surveillance.

Recommendations

0. Do not abandon a patient under any circumstances.
1. Maintain contact with any patient who withdraws from treatment due to a disagreement.
2. Refer patients with comorbid psychiatric disorders to appropriate mental health providers.

9. **Management of OT in Special Populations**

W. **OT in Patient with History of Substance Use**

Recommendations

1. Use caution when using opioids in patients with history of SUDs. **[B]**
2. Use an integrated treatment approach addressing both pain **[B]** and SUD issues with appropriate information sharing. **[C]**
3. Patients on opioid agonist therapy for DSM-IV diagnosis of opioid dependence who have a co-occurring chronic pain disorder should be treated for pain considering the following options:
   a. Use non-pharmacologic interventions
   b. Use other non-opioid pharmacologic treatment modalities
   c. Cautious use of OT by using another opioid agonist with slow titration and careful communication with the SUD opioid agonist therapy prescribers. **[B]**
4. Perform urine drug testing as an adjunctive tool at regular intervals. **[B]**

Management of Buprenorphine-Treated Patients Transferred from Another Provider

5. Management of OT in patients on sublingual (SL) buprenorphine (with or without naloxone) for DSM-IV diagnosis of opioid dependence:
   a. SL buprenorphine is FDA-approved for treatment of opioid dependence and can only be prescribed by a qualified and Drug Enforcement Administration (DEA)-waivered physician for this purpose
   b. Patients on SL buprenorphine should not receive full agonist opioids concomitantly for routine pain control
   c. Nonopioid and nonpharmacologic strategies for pain management should be maximized
   d. In the event of anticipated pain (i.e., an elective procedure or surgery), SL buprenorphine should be stopped for 48 hours before the scheduled event
   e. For unanticipated pain (trauma, emergency surgery or procedure), the care team managing the acute pain should be notified that the patient is prescribed SL buprenorphine and when the last dose was taken.

OT and Risk for Sleep Apnea

Recommendations

0. Be vigilant for sleep apnea during OT. If clinical suspicion exists for the presence of sleep apnea in a patient on OT, sleep study should be considered. **[B]**.
1. Patients on OT who present with sleep disorder confirmed by a sleep study should be assessed for the appropriateness of continuing OT and should be evaluated for the risks (based on the severity of the sleep-disordered breathing) versus benefits of OT. If OT is continued, it should be titrated cautiously. Patients found to have sleep-disordered breathing should be followed with a repeated sleep study. **[C]**
2. Patient with abnormal sleep study should be educated about the significant additional risks including breathing disruption, and instructed to avoid alcohol, or any central nervous system (CNS)-depressant medication. **[A]**
3. The type of sleep apnea should be evaluated to determine if it is obstructive or central. Continuous positive airway pressure (CPAP) may worsen central sleep apnea. **[D]**
4. Patients with sleep apnea who are on OT may benefit from a reduction in the dose of their opioids.
5. Discontinuation of OT should be considered if the sleep apnea is severe or life threatening.
6. Consider more careful monitoring of OT in patients treated with methadone and/or benzodiazepines. **[B]**

Definitions:

Quality of Evidence

I	At least one properly done randomized controlled trial (RCT)
II-1	Well-designed controlled trial without randomization
II-2	Well-designed cohort or case-control analytic study, preferably from more than one source
II-3	Multiple time series evidence with/without intervention, dramatic results of uncontrolled experiment
III	Opinion of respected authorities, descriptive studies, case reports, and expert committees

Overall Quality

Good	High-grade evidence (I or II-1) directly linked to health outcome
Fair	High-grade evidence (I or II-1) linked to intermediate outcome; **or** Moderate-grade evidence (II-2 or II-3) directly linked to health outcome
Poor	Level III evidence or no linkage of evidence to health outcome

Net Effect of the Intervention

Substantial	More than a small relative impact on a frequent condition with a substantial burden of suffering; **or** A large impact on an infrequent condition with a significant impact on the individual patient level
Moderate	A small relative impact on a frequent condition with a substantial burden of suffering; **or** A moderate impact on an infrequent condition with a significant impact on the individual patient level
Small	A negligible relative impact on a frequent condition with a substantial burden of suffering; **or** A small impact on an infrequent condition with a significant impact on the individual patient level
Zero or Negative	Negative impact on patients; **or** No relative impact on either a frequent condition with a substantial burden of suffering, or an infrequent condition with a significant impact on the individual patient level

Final Grade of Recommendation

	The Net Benefit of the Intervention			
Quality of Evidence	**Substantial**	**Moderate**	**Small**	**Zero or negative**
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	I

Strength of Recommendations Rating System

A	A strong recommendation that the clinicians provide the intervention to eligible patients. *Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.*
B	A recommendation that clinicians provide (the service) to eligible patients. *At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.*
C	No recommendation for or against the routine provision of the intervention is made. *At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D	Recommendation is made against routinely providing the intervention to asymptomatic patients. *At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.*
I	The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. *Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.*

Clinical Algorithm(s)

An algorithm for the Management of Opioid Therapy for Chronic Pain is provided in the original guideline document.

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Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The guideline is based on an exhaustive review of the literature. Where existing literature was ambiguous or conflicting, or where scientific data were lacking on an issue, recommendations were based on the clinical experience of the Working Group.

The type of supporting evidence is identified for selected recommendations (see the "Major Recommendations" field).

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Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Improved use of opioids to treat chronic non-cancer pain
- Improved patient outcomes (i.e., reduction in pain, increase in functional status, and enhanced quality of life)
- Decrease in the incidence of complications

Potential Harms

- Typical opioid adverse effects are common. They include constipation, nausea, vomiting, somnolence, headache, dyspepsia, hyperalgesia, sexual dysfunction, pruritus, dizziness, tiredness, dry mouth, sweating, sedation, osteoporosis, sexual dysfunction, and endocrine dysfunction.
- Opioids may also cause adverse cognitive effects (e.g., confusion, deterioration of cognitive function), hallucinations/dysphoria, depression, endocrinopathy, osteoporosis, immune dysfunction, and central sleep apnea.

See Appendix E of the original guideline for more information regarding potential harms of specific opioid drugs used to manage chronic pain.

Subgroups Most Likely to Be Harmed

Older patients are more likely to experience difficulty with common adverse effects of opioids such as constipation and respiratory depression.

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Contraindications

Contraindications

Opioid therapy (OT) should not be used in the following situations (absolute contraindications):

- Severe respiratory instability
- Acute psychiatric instability or uncontrolled suicide risk
- Diagnosed non-nicotine substance use disorder (Diagnostic and Statistical Manual of Mental Disorders,

Fourth Edition [DSM-IV] criteria) not in remission and not in treatment
- True allergy to opioid agents (cannot be resolved by switching agents)
- Co-administration of drug capable of inducing life-limiting drug-drug interaction
- QTc interval >500 millisecond for using methadone
- Active diversion of controlled substances (providing the medication to someone for whom it was not intended)
- Prior adequate trials of specific opioids that were discontinued due to intolerance, serious adverse effects that cannot be treated, or lack of efficacy

OT can be used with caution (relative contraindications) in the following situations:

- Patient receiving treatment for diagnosed substance use disorder (DSM-IV criteria)
- Medical condition in which OT may cause harm:
  - Patient with obstructive sleep apnea not on continuous positive airway pressure [CPAP]
  - Patients with central sleep apnea
  - Chronic pulmonary disease (mild-moderate asthma, chronic obstructive pulmonary disease [COPD])
  - Cardiac condition (QTc interval 450-500 milliseconds) that may increase risk of using methadone
  - Known or suspected paralytic ileus
  - Respiratory depression in unmonitored setting
- Risk for suicide or unstable psychiatric disorder
- Complicated pain
  - Headache not responsive to other pain treatment modalities
- Conditions that may impact adherence to OT:
  - Inability to manage opioid therapy responsibly (e.g., cognitively impaired)
  - Unwillingness or inability to comply with treatment plan
  - Unwillingness to adjust at-risk activities resulting in serious re-injury
  - Social instability
  - Mental health disorders

See Appendix E of the original guideline for more information on contraindications.

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Qualifying Statements

Qualifying Statements

- The Department of Veterans Affairs (VA) and The Department of Defense (DoD) guidelines are based on the best information available at the time of publication. They are designed to provide information and assist in decision-making. They are not intended to define a standard of care and should not be construed as one. Also, they should not be interpreted as prescribing an exclusive course of management.
- Variations in practice will inevitably and appropriately occur when providers take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in any particular clinical situation.
- Opioid treatment of pain has been, and remains, severely hampered because of actual and legal constraints related to substance abuse and diversion. The guideline algorithm and recommendations suggest a structured goal-directed approach to chronic opioid treatment, which aims to select and monitor patients carefully, and wean therapy if treatment goals are not reached.

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Implementation of the Guideline

Description of Implementation Strategy

Implementation

The guideline and algorithms are designed to be adapted by individual facilities in considering needs and resources. The algorithms serve as a guide that providers can use to determine best interventions and timing of care for their patients to optimize quality of care and clinical outcomes. This should not prevent providers from using their own clinical expertise in the care of an individual patient. Guideline recommendations are intended to support clinical decision-making and should never replace sound clinical judgment.

Although this guideline represents the state of the art practice on the date of its publication, medical practice is evolving and this evolution requires continuous updating of published information. New technology and more research will improve patient care in the future. The clinical practice guideline can assist in identifying priority areas for research and optimal allocation of resources. Future studies examining the results of clinical practice guidelines such as these may lead to the development of new practice-based evidence.

Implementation Tools

Chart Documentation/Checklists/Forms
Clinical Algorithm
Quick Reference Guides/Physician Guides
Resources
Staff Training/Competency Material
Tool Kits

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

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Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness
Patient-centeredness
Safety

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Identifying Information and Availability

Bibliographic Source(s)

Management of Opioid Therapy for Chronic Pain Working Group. VA/DoD clinical practice guideline for management of opioid therapy for chronic pain. Washington (DC): Department of Veterans Affairs, Department of Defense; 2010 May. 159 p.

Adaptation

In completing this guideline update, the Working Group relied heavily on the following evidence-based guideline:

Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. (APS/AAPM)*The Journal of Pain* 2009 Feb;10(2):113-230.

Date Released

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Guideline Developer(s)

Department of Defense - Federal Government Agency [U.S.]
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United States Government

Guideline Committee

Management of Opioid Therapy for Chronic Pain Working Group

Composition of Group That Authored the Guideline

Working Group Members (VA): Michael E. Clark*, PhD; Rollin M. Gallagher*, MD, MPH (*Co-Chair*); Francine Goodman*, Pharm. D; Susan J. Hagan, MSN; Timothy Lee, MD; Shannon Miller, MD; Jack M. Rosenberg*, MD (*Co-Chair*); Nancy L. Wiedemer*, RN, CRNP

Working Group Members (DoD): Jeffrey Barr*, Maj, USAF, MC (*Co-Chair*); Thomas Brooks, LTC, AN, USA; Allison J. Franklin, MAJ, MC, USA; Kevin T. Galloway, LTC, AN, USA; Sushma Jani, MD; James E. McCrary, Lt Col, USAF, MC; Patrick A. Sherman, MAJ, MS, USA; James J. Staudenmeier, COL, MC, USA; Shana Trice, Pharm. D

Office of Quality and Performance, VHA: Carla Cassidy, RN, MSN, NP

Quality Management Division, U.S. Army Medical Command: Ernest Degenhardt, MSN, RN, ANP-FNP; Marjory Waterman, MN, RN

Facilitator: Oded Susskind*, MPH

Healthcare Quality Informatics, Inc.: Martha D'Erasmo, MPH; Rosalie Fishman, RN, MSN, CPHQ; Joanne Marko, MS, SLP

*Members of the CORE Editorial Panel

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Veterans Health Administration, Department of Defense. VA/DoD clinical practice guideline for the management of opioid therapy for chronic pain. Washington (DC): Veterans Health Administration, Department of Defense; 2003 Mar. Various p. [51 references]

Guideline Availability

Electronic copies: Available from the Department of Veterans Affairs Web site.

Print copies: Available from the Department of Veterans Affairs, Veterans Health Administration, Office of Quality and Performance (10Q) 810 Vermont Ave. NW, Washington, DC 20420.

Availability of Companion Documents

The following is available:

- VA/DoD clinical practice guideline for the management of opioid therapy for chronic pain. Guideline summary. Washington (DC): Department of Veterans Affairs (U.S.); 2010. May. 74 p. Electronic copies: Available in Portable Document Format (PDF) from the Department of Veterans Affairs Web site.

Print copies: Department of Veterans Affairs, Veterans Health Administration, Office of Quality and Performance (10Q) 810 Vermont Ave. NW, Washington, DC 20420.

The following are also available:

- Opioids in the management of acute and chronic pain: independent study. VA opioid web course. Washington (DC): Department of Veterans Affairs (U.S.). Employee education system. Available from the Department of Veterans Affairs Web site.
- VA methadone dosing and safety information paper. Washington (DC): Department of Veterans Affairs (U.S.). 4 p. Available from the Department of Veterans Affairs Web site.

- VA fentanyl transdermal patch dosing and safety information paper. Washington (DC): Department of Veterans Affairs (U.S.). 4 p. Available from the Department of Veterans Affairs Web site.

Additional pain management resources are available from the Department of Veterans Affairs Web site.
A sample opioid pain care agreement is available in the Appendices of the original guideline document.
The VHA Pain Outcomes Toolkit is also available from the Department of Veterans Affairs Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on August 2, 2004. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on July 15, 2005 following the FDA advisory on Duragesic. This summary was updated by ECRI Institute on April 1, 2009 following the FDA advisory on Reglan (metoclopramide). This NGC summary was updated by ECRI Institute on October 11, 2010. This summary was updated by ECRI Institute on March 16, 2011 following the U.S. Food and Drug Administration advisory on acetaminophen-containing prescription products. This summary was updated by ECRI Institute on October 28, 2013 following the U.S. Food and Drug Administration advisory on Acetaminophen.

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