QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians 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 the setting of any particular clinical situation.

These guidelines are not intended to represent TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

Version 3.0 – 2017
Prepared by:
The Opioid Therapy for Chronic Pain Work Group

With support from:
The Office of Quality, Safety and Value, VA, Washington, DC &
Office of Evidence Based Practice, U.S. Army Medical Command

Version 3.0 – 2017

Based on evidence reviewed through December 2016
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I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the “…Health Executive Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration and Military Health System,” by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This CPG is intended to provide healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with chronic pain who are on or being considered for long-term opioid therapy (LOT).

In 2010, the VA and DoD published the *Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain* (2010 OT CPG), which was based on evidence reviewed through March 2009. Since the release of that guideline, there has been growing recognition of an epidemic of opioid misuse and opioid use disorder (OUD) in America, including among America’s Veterans, as documented in the Background section. At the same time, there is a mounting body of research expanding detailing the lack of benefit and severe harms of LOT.

Consequently, a recommendation to update the 2010 OT CPG was initiated in 2015. The updated CPG, titled *Clinical Practice Guideline for Opioid Therapy for Chronic Pain* (OT CPG), includes objective, evidence-based information on the management of chronic pain. It is intended to assist healthcare providers in all aspects of patient care, including, but not limited to, diagnosis, treatment, and follow-up. The system-wide goal of this guideline is to improve the patient’s health and well-being by providing evidence-based guidance to providers who are taking care of patients on or being considered for LOT. The expected outcome of successful implementation of this guideline is to:

- Assess the patient’s condition, provide education, and determine the best treatment methods in collaboration with the patient and a multidisciplinary care team
- Optimize the patient’s health outcomes and function and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care
II. How to Use This Clinical Practice Guideline

This guideline can be used in a variety of ways. It can be used by general clinicians or specialists to study and consider the latest information on opioid therapy (OT) and how and whether to incorporate that information or recommendations into their practice. It can be used to provide specific information to guide a patient encounter, such as looking up the dosing of a medication used less frequently or the meaning of the urine drug testing (UDT) result. The section on tapering and its accompanying appendix can be used to assist in the development of a framework for guiding an individualized, informed discussion when tapering is being considered. Patients can examine the guideline to educate themselves and better understand their care. A health care system can use the CPG to assure that its clinicians and patients have the resources available to compassionately, effectively, and safely evaluate and deliver LOT in a timely, culturally sensitive manner. The guideline can also be used to suggest specific education for identified gaps.

This guideline is not intended as a standard of care and should not be used as such. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advances and patterns evolve. Today there is variation among state regulations, and this guideline does not cover the variety of ever-changing state regulations that may be pertinent. The ultimate judgement regarding a particular clinical procedure or treatment course must be made by the individual clinician, in light of the patient’s clinical presentation, patient preferences, and the available diagnostic and treatment options. As noted previously, the guideline can assist care providers, but the use of a CPG must always be considered as a recommendation, within the context of a provider’s clinical judgment and patient values and preferences, in the care for an individual patient.
III. Recommendations

The following recommendations were made using a systematic approach considering four domains as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach as detailed in the section on Methods and Appendix E. These domains include: confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient or provider values and preferences, and other implications, as appropriate (e.g., resource use, equity, acceptability).

Given the relevance of all four domains in grading recommendations, the Work Group encountered multiple instances in which confidence in the quality of the evidence was low or very low, while there was marked imbalance of benefits and harms, as well as certain other important considerations arising from the domains of values and preferences and/or other implications. In particular, the harms due to the potential for severe adverse events associated with opioids, particularly overdose and OUD, often far outweigh the potential benefits. As such, in accounting for all four domains, these factors contributed to Strong recommendations in multiple instances.

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Strength*</th>
<th>Category†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>a) We recommend against initiation of long-term opioid therapy for chronic pain.</td>
<td>a) Strong against</td>
<td>Reviewed, New-replaced</td>
</tr>
<tr>
<td></td>
<td>b) We recommend alternatives to opioid therapy such as self-management strategies and other non-pharmacological treatments.</td>
<td>b) Strong for</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c) When pharmacologic therapies are used, we recommend non-opioids over opioids.</td>
<td>c) Strong for</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>If prescribing opioid therapy for patients with chronic pain, we recommend a short duration. Note: Consideration of opioid therapy beyond 90 days requires re-evaluation and discussion with patient of risks and benefits.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
</tr>
<tr>
<td>3.</td>
<td>For patients currently on long-term opioid therapy, we recommend ongoing risk mitigation strategies (see Recommendations 7-9), assessment for opioid use disorder, and consideration for tapering when risks exceed benefits (see Recommendation 14).</td>
<td>Strong for</td>
<td>Reviewed, New-replaced</td>
</tr>
<tr>
<td>4.</td>
<td>a) We recommend against long-term opioid therapy for pain in patients with untreated substance use disorder.</td>
<td>a) Strong against</td>
<td>Reviewed, Amended</td>
</tr>
<tr>
<td></td>
<td>b) For patients currently on long-term opioid therapy with evidence of untreated substance use disorder, we recommend close monitoring, including engagement in substance use disorder treatment, and discontinuation of opioid therapy for pain with appropriate tapering (see Recommendation 14 and Recommendation 17).</td>
<td>b) Strong for</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>We recommend against the concurrent use of benzodiazepines and opioids. Note: For patients currently on long-term opioid therapy and benzodiazepines, consider tapering one or both when risks exceed benefits and obtaining specialty consultation as appropriate (see Recommendation 14 and the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders).</td>
<td>Strong against</td>
<td>Reviewed, New-added</td>
</tr>
</tbody>
</table>
### Recommendation

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Strength*</th>
<th>Category†</th>
</tr>
</thead>
</table>
| 6. | a) We recommend against long-term opioid therapy for patients less than 30 years of age secondary to higher risk of opioid use disorder and overdose.  
    b) For patients less than 30 years of age currently on long-term opioid therapy, we recommend close monitoring and consideration for tapering when risks exceed benefits (see Recommendation 14 and Recommendation 17). | a) Strong against  
    b) Strong for | Reviewed, New-replaced |

### Risk Mitigation

7. We recommend implementing risk mitigation strategies upon initiation of long-term opioid therapy, starting with an informed consent conversation covering the risks and benefits of opioid therapy as well as alternative therapies. The strategies and their frequency should be commensurate with risk factors and include:
   - Ongoing, random urine drug testing (including appropriate confirmatory testing)
   - Checking state prescription drug monitoring programs
   - Monitoring for overdose potential and suicidality
   - Providing overdose education
   - Prescribing of naloxone rescue and accompanying education

   Strong for Reviewed, New-replaced

8. We recommend assessing suicide risk when considering initiating or continuing long-term opioid therapy and intervening when necessary.

   Strong for Reviewed, Amended

9. We recommend evaluating benefits of continued opioid therapy and risk for opioid-related adverse events at least every three months.

   Strong for Reviewed, New-replaced

### Type, Dose, Follow-up, and Taper of Opioids

10. If prescribing opioids, we recommend prescribing the lowest dose of opioids as indicated by patient-specific risks and benefits.
    Note: There is no absolutely safe dose of opioids.

    Strong for Reviewed, New-replaced

11. As opioid dosage and risk increase, we recommend more frequent monitoring for adverse events including opioid use disorder and overdose.
    Note:  
    - Risks for opioid use disorder start at any dose and increase in a dose dependent manner.  
    - Risks for overdose and death significantly increase at a range of 20-50 mg morphine equivalent daily dose.

    Strong for Reviewed, New-replaced

12. We recommend against opioid doses over 90 mg morphine equivalent daily dose for treating chronic pain.
    Note: For patients who are currently prescribed doses over 90 mg morphine equivalent daily dose, evaluate for tapering to reduced dose or to discontinuation (see Recommendations 14 and 15).

    Strong against Reviewed, New-replaced

13. We recommend against prescribing long-acting opioids for acute pain, as an as-needed medication, or on initiation of long-term opioid therapy.

    Strong against Reviewed, New-replaced

14. We recommend tapering to reduced dose or to discontinuation of long-term opioid therapy when risks of long-term opioid therapy outweigh benefits.
    Note: Abrupt discontinuation should be avoided unless required for immediate safety concerns.

    Strong for Reviewed, New-added
<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Strength*</th>
<th>Category†</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.</td>
<td>We recommend individualizing opioid tapering based on risk assessment and patient needs and characteristics.</td>
<td>Strong for</td>
<td>Reviewed, New-added</td>
</tr>
<tr>
<td></td>
<td>Note: There is insufficient evidence to recommend for or against specific tapering strategies and schedules.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td>We recommend interdisciplinary care that addresses pain, substance use disorders, and/or mental health problems for patients presenting with high risk and/or aberrant behavior.</td>
<td>Strong for</td>
<td>Reviewed, New-replaced</td>
</tr>
<tr>
<td>17.</td>
<td>We recommend offering medication assisted treatment for opioid use disorder to patients with chronic pain and opioid use disorder.</td>
<td>Strong for</td>
<td>Reviewed, New-replaced</td>
</tr>
<tr>
<td></td>
<td>Note: See the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders.</td>
<td></td>
<td></td>
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</tbody>
</table>

**Opioid Therapy for Acute Pain**

| 18. | a) We recommend alternatives to opioids for mild-to-moderate acute pain.                                                                                                                                        | a) Strong for | Reviewed, New-added |
|     | b) We suggest use of multimodal pain care including non-opioid medications as indicated when opioids are used for acute pain.                                                                               | b) Weak for   |                  |
|     | c) If take-home opioids are prescribed, we recommend that immediate-release opioids are used at the lowest effective dose with opioid therapy reassessment no later than 3-5 days to determine if adjustments or continuing opioid therapy is indicated. | c) Strong for |                  |
|     | Note: Patient education about opioid risks and alternatives to opioid therapy should be offered.                                                                                                             |              |                  |

*For additional information, please refer to the section on Grading Recommendations.
†For additional information, please refer to the section on Recommendation Categorization and Appendix H.
IV. Algorithm

This CPG follows an algorithm that is designed to facilitate understanding of the clinical pathway and decision making process used in management of LOT. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format may promote more efficient diagnostic and therapeutic decision making and has the potential to change patterns of resource use. Although the Work Group recognizes that not all clinical practices are linear, the simplified linear approach depicted through the algorithm and its format allows the provider to assess the critical information needed at the major decision points in the clinical process. It includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

For each guideline, the corresponding clinical algorithm is depicted by a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[2]

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Rounded rectangle" /></td>
<td>Rounded rectangles represent a clinical state or condition.</td>
</tr>
<tr>
<td><img src="image" alt="Hexagon" /></td>
<td>Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No.</td>
</tr>
<tr>
<td><img src="image" alt="Rectangle" /></td>
<td>Rectangles represent an action in the process of care.</td>
</tr>
</tbody>
</table>
A. Module A: Determination of Appropriateness for Opioid Therapy

Note: Non-pharmacologic and non-opioid pharmacologic therapies are preferred for chronic pain.

Sidebar A: Components of Biopsychosocial Assessment
- Pain assessment including history, physical exam, comorbidities, previous treatment and medications, duration of symptoms, onset and triggers, location/radiation, previous episodes, intensity and impact, patient perception of symptoms
- Patient functional goals
- Impact of pain on family, work, life
- Review of previous diagnostic studies
- Additional consultations and referrals
- Coexisting illness and treatments and effect on pain
- Significant psychological, social, or behavioral factors that may affect treatment
- Family history of chronic pain
- Collateral of family involvement
- Patient beliefs/knowledge of:
  - The cause of their pain
  - Their treatment preferences
  - The perceived efficacy of various treatment options

For patients already on OT, include assessment of psychological factors (e.g., beliefs, expectations, fears) related to continuing vs. tapering OT.

Sidebar B: Examples of Absolute Contraindications to Initiating Opioid Therapy for Chronic Pain
- True life-threatening allergy to opioids
- Active SUD
- Elevated suicide risk (see VA/DoD Suicide CPG)
- Concomitant use of benzodiazepines

Sidebar C: Consideration Checklist for LOT for Chronic Pain
- Risks do not outweigh potential modest benefits
- Patient is experiencing severe chronic pain that interferes with function and has failed to adequately respond to indicated non-opioid and non-opioid therapeutic interventions
- Patient is willing to continue to engage in comprehensive treatment plan including non-opioid treatments and implementation of learned active strategies that meets his or her needs to be successful with plan of care
- Clear and measurable treatment goals are established
- Patient is able to access adequate follow-up for OT (see Recommendations 7-9)
- PDMP and UDT are concordant with expectations
- Review of recent medical records is concordant with diagnosis and risk assessment
- Patient is fully informed and consents to the therapy

Abbreviations: LOT: long-term opioid therapy; OT: opioid therapy; PDMP: Prescription Drug Monitoring Program; SUD: substance use disorders; UDT: urine drug test; VA/DoD Suicide CPG: VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide
Module B: Treatment with Opioid Therapy

1. Candidate for trial of OT with consent (in conjunction with comprehensive pain care plan)

2. Initiate OT using the following approach:
   - Short duration (e.g., 1 week initial prescription; no more than 3 months total)
   - Use lowest effective dose, recognizing that no dose is completely safe
   - A strategy of escalating dose to achieve benefit increases risk and has not been shown to improve function
   - Dose escalation above 20-50 mg MEDD has not been shown to improve function and increases risk
   - Long-acting opioids should not be prescribed for opioid-naive individuals (see Recommendation 13 and Appendix D)
   - Consider alternatives to methadone and transdermal fentanyl (see Recommendation 13 and Appendix D)
   - Assessment of improvement in pain and functional status and adverse effects
   - Offer OEND

3. Is patient medically or psychiatrically unstable?
   - No

4. Admit/provide medical and psychiatric treatment to stabilize as indicated

5. Is there a clinically meaningful improvement in function in the absence of significant risk factors?
   - No

6. Taper to discontinuation (consult Module C if needed)
   - Exit algorithm
   - Manage with non-opioid modalities

7. Review and optimize comprehensive pain care plan (e.g., non-opioid treatments, self-management strategies)

8. Follow-up frequently based on patient risk factors (e.g., 1-4 weeks with any dose change; up to every 3 months without dose change if clinically and functionally stable);
   - Assess:
     - Function, risks, and benefits of OT
     - Progress toward functional treatment goals
     - Adverse effects
     - Adherence to treatment plan
     - Complications or co-occurring conditions (e.g., medical, mental health, and/or SUD)
   - Complete risk mitigation strategies (see Sidebar A)
   - Review and optimize comprehensive pain care plan

9. Are factors that increase risks of OT present (e.g., non-adherence, co-occurring conditions, behaviors suggesting OUD, indications for referral)?
   - No

10. Consider one or more of the following:
    - Shortening prescribing interval
    - Intensifying risk mitigation strategies
    - Increasing intensity of monitoring
    - Referring to interdisciplinary care
    - Consulting with or referring to specialty care

11. Are there indications to discontinue or taper? (see Sidebar B)
    - Yes

12. Reassess in 1-3 months or more frequently as determined by patient risk factors (see Sidebar C)
    - No

13. Taper to reduced dose or taper to discontinuation; proceed to Module C

Sidebar A: Necessary Risk Mitigation Strategies
- OEND
- UDT
- PDMP
- Face-to-face follow-up with frequency determined by risk

Sidebar B: Indications for Tapering and Discontinuation
- Risks of OT outweigh benefits
- Lack of clinically meaningful improvement in function
- Concomitant use of medications that increase risk of overdose
- Co-occurring medical or mental health conditions that increase risk
- Concerns about OUD or other SUD
- Patient non-compliance with opioid safety measures and opioid risk mitigation strategies
- Patient non-participation in a comprehensive pain care plan
- Prescribed dose higher than the maximal recommended dose (which increases risk of adverse events)
- Pain condition not effectively treated with opioids (e.g., back pain with normal MRI; fibromyalgia)
- Medical or mental health comorbidities that increase risk
- Improvement in the underlying pain condition being treated
- Unmanageable side effects
- Patient preference
- Diversion

Sidebar C: Factors That May Indicate Need for More Frequent Follow-up
- Non-adherence to comprehensive pain care plan (e.g., attendance at appointments)
- Unexpected UDT and PDMP results
- Non-adherence to opioid prescription (e.g., using more than prescribed and/or running out early)
- Higher risk medication characteristics (e.g., high-dose opioids, combination of opioids and benzodiazepines)
- Patients with mental health, medical, or SUD comorbidities that increase risk for adverse outcomes

Abbreviations: MEDD: morphine equivalent daily dose; mg: milligram(s); MRI: magnetic resonance imaging; OEND: Overdose Education and Naloxone Distribution; OT: opioid therapy; OUD: opioid use disorder; PDMP: Prescription Drug Monitoring Program; SUD: substance use disorders; UDT: urine drug test
C. Module C: Tapering or Discontinuation of Opioid Therapy

1. Indication to taper to reduced dose or taper to discontinuation
2. Repeat comprehensive biopsychosocial assessment (see Module A, Sidebar A)
3. Does the patient demonstrate signs or symptoms of SUD? (see VA/DoD SUD CPG)
   - Yes: Is patient willing to engage in SUD therapy?
   - No: Is there evidence of diversion?
5. Access specialized SUD care with monitoring and follow-up appropriate for the patient’s needs (e.g., MAT, treatment for comorbidities)
6. Is there evidence of diversion?
   - No: Is there high risk or dangerous behavior (e.g., overdose event, accidents, threatening provider)?
8. Address safety and misuse
   - Yes: Access immediate discontinuation of opioid therapy
   - No: Address concerns that may negatively impact taper (e.g., inability for adequate follow-up, inability to provide adequate treatment for co-occurring medical and mental health conditions and SUD)
7. Immediately discontinue opioid therapy
10. Develop individualized tapering treatment plan (including pace of tapering, setting of care) based on patient and treatment characteristics (see Sidebar A and Recommendations 14 and 15)
11. Follow-up 1 week to 1 month after each change in dosage and after discontinuation considering patient and treatment characteristics
   - Consider the following at each interaction with patient:
     - Educate on self-management and risks of DT
     - Optimize whole person approach to pain care
     - Optimize treatment of co-occurring mental health conditions
     - Optimize non-opioid pain treatment modalities
     - Reassess for OUD and readiness for OUD treatment as indicated

Sidebar A: Tapering Treatment
- When safety allows, a gradual taper rate (5-20% reduction every 4 weeks) allows time for neurobiological, psychological, and behavioral adaptations.
- When there are concerns regarding risks of tapering (e.g., unmasked OUD, exacerbation of underlying mental health conditions) consider interdisciplinary services that may include mental health, SUD, primary care, and specialty pain care.
- Address concerns that may negatively impact taper (e.g., inability for adequate follow-up, inability to provide adequate treatment for co-occurring medical and mental health conditions and SUD)

Patient and Treatment Characteristics to Consider when Determining Tapering Strategy
- Opioid dose
- Duration of therapy
- Type of opioid formulation
- Psychiatric, medical, and SUD comorbidities
- Other patient risk factors (e.g., non-adherence, high-risk medication-related behavior, strength of social support, coping)

12. Are one of the following present?
   - Patient resistance to taper
   - High risk or dangerous behaviors
   - Increase in patient distress
13. Repeat comprehensive biopsychosocial assessment (see Module A, Sidebar A)
14. Is an SUD identified?
15. Proceed to Module C, Box 4
16. Are either of the following identified?
   - Use of opioids to modulate emotions (i.e., “chemical coping”)
   - Untreated or undertreated psychiatric disorder
17. Engage patient in appropriate behavioral and/or psychiatric treatment, ideally in an interdisciplinary setting
   - Consider reduced rate of taper or pause in taper for patients actively engaged in skills training
18. Is patient fearful and/or anxious about taper and ability to function on lower dose or without opioids?
19. Provide additional education about whole person pain care and LOT and reassurance that the patient will not be abandoned
   - Consider more frequent follow-up using the expanded care team (registered nurse, clinical pharmacist, health coach, mental health provider)
   - Consider reduced rate of taper or pause in taper for patients actively engaged in skills training
   - Reassess for OUD throughout the taper
20. Is there concern for diversion?
21. Proceed to Module C, Box 11

Abbreviations: LOT: long-term opioid therapy; MAT: medication assisted treatment; OT: opioid therapy; OUD: opioid use disorder; SUD: substance use disorders; VA/DoD SUD CPG: VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders
D. Module D: Patients Currently on Opioid Therapy

1. Patient currently on OT

2. Are there factors that would require immediate attention and possible discontinuation of OT due to unacceptable risk? (see Sidebar A)
   - No
   - Yes

3. Admit/provide treatment to stabilize, including opioid tapering or SUD treatment as indicated

4. Obtain biopsychosocial assessment (see Module A, Sidebar A)
   - No
   - Yes

5. Are the following available for review? Prior medical records including current prescriber, prior and current UDT, PDMP
   - Address factors related to incomplete data prior to prescribing

6. Review data and re-assess risks and benefits of continuing OT
   - Consider strength and number of risk factors (see Sidebar B)
   - Yes
   - No

7. Do risks outweigh benefits of continuing OT?
   - Yes
   - No

8. Proceed to Module C

9. Educate/re-educate on the following (see Sidebar C for talking points):
   - Non-opioid management
   - Self-management to improve function and quality of life
   - Realistic expectations and limitations of medical treatment options
   - Preferred treatment methods are non-pharmacotherapy and non-opioid pharmacotherapy
   - New information on risks and lack of benefits of long-term OT

10. Are any of the following present?
    - Yes
    - No

    - Prescribed opioid dose >90 mg M ED D
    - Combined sedating medication that increases risk of adverse events (e.g., benzodiazepines)
    - Patient non-participation in a comprehensive pain care plan
    - Other indications for tapering (see Module B, Sidebar B)

11. Re-assess and optimize preferred non-opioid treatments for chronic pain (e.g., physical and psychological treatments) recognizing that patient is willing to continue to engage in comprehensive treatment plan including non-opioid treatments

12. Is the patient experiencing clear functional improvement with minimal risk?

13. Continue OT using the following approach:
    - Shortest duration
    - Use lowest effective dose (recognizing that no dose is completely safe and overdose risk increases at doses >20-50 mg M E D D)
    - Continual assessment of improvement in pain and functional status and adverse effects

Abbreviations: M E D D: morphine equivalent daily dose; mg: milligram(s); OT: opioid therapy; OUD: opioid use disorder; PDMP: Prescription Drug Monitoring Programs; SUD: substance use disorders; UDT: urine drug test; VA/DoD Suicide CPG: VA/DoD Clinical Practice Guideline for the Assessment and Management of Patients at Risk for Suicide
V. Background

A. Opioid Epidemic

Chronic pain is a national public health problem as outlined in the 2011 study by the National Academy of Medicine (previously the Institute of Medicine [IOM]). At least 100 million Americans suffer from some form of chronic pain. Until recently, the treatment of chronic pain with opioids was increasing at an alarming rate. The increase in prescriptions of these medications has been accompanied by an epidemic of opioid-related adverse events.

From 2000 through 2010, the proportion of pain visits during which opioid and non-opioid pharmacologic therapies were prescribed increased from 11.3% to 19.6% and from 26% to 29%, respectively. In 2012, for every 100 persons in the United States (U.S.), 82.5 opioid prescriptions and 37.6 benzodiazepine prescriptions were written by healthcare providers. In the emergency department, at least 17% of discharges included prescriptions for opioids.

There has been limited research on the effectiveness of LOT for non-end-of-life pain. At the same time, there is mounting evidence of the ill effects of LOT, including increased mortality, OUD, overdose, sexual dysfunction, fractures, myocardial infarction, constipation, and sleep-disordered breathing. Despite increasing awareness of the known harms of opioids, 259 million opioid prescriptions were still written in 2012.

The increase in opioid prescribing is matched by a parallel increase in morbidity, mortality, opioid-related overdose death rates, and substance use disorders (SUD) treatment admissions from 1999 to 2008. In 2009, drug overdose became the leading cause of injury-related death in the U.S., surpassing deaths from traffic accidents. In 2014, 1.9 million Americans were affected by an OUD related to non-medical use of prescription pain relievers, and in the same year, 18,893 individuals died as a result of a prescription drug overdose. There has been a four-fold increase in the absolute number of deaths associated with use of opioids since 2000, and a 14% increase between 2013 and 2014 alone. In a survey of patients prescribed opioids for chronic non-cancer pain (CNCP) and their family members, 34% of patients reported that they thought they were “addicted” or “dependent” on opioid pain medication, 34% said that they used the medication for “fun” or to “get high,” while 22% used the medication to relieve day-to-day stress.

Concurrent with the increase in prescription opioid use, the rate of heroin overdose deaths increased nearly four-fold between 2000 and 2013. According to a survey of patients entering SUD treatment for heroin use, the prescription opioid epidemic has resulted in a marked shift in how and which opioids are abused. In the 1960s, 80% of people entering treatment for heroin use started using heroin as their first opioid, while in the 2000s, 75% of people entering treatment for heroin use started using prescription opioids as their first opioid. This increase in the use of opioids, as well as associated morbidity,
mortality, and other adverse outcomes, has called attention to the need for a paradigm shift in pain and in the way it is treated. Consult the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders (VA/DoD SUD CPG)\(^1\) for further information.

**B. Paradigm Shift in Pain and Its Treatment**

The U.S. is in the midst of a cultural transformation in the way pain is viewed and treated. The biomedical model of pain care, in which the pain experience is reduced to a pain generator and pain treatment is aimed at fixing or numbing pain with medications, interventions, or surgery, dominated the 1990s and the first decade of the 2000s. As the cost, potential harm, and limited effectiveness of this approach to chronic pain was becoming apparent, the National Academy of Medicine issued a call for the transformation of pain care to a biopsychosocial, multimodal, interdisciplinary model.\[^3\]

A paradigm shift in the use of OT for chronic non-terminal pain has paralleled this transformation in pain care. Prior to the 1980s, OT was rarely used outside of severe acute injury or post-surgical pain, primarily due to concern for tolerance, physical dependence, and addiction. As the hospice and palliative care movement began defining end-of-life care in the U.S. during the 1980s and emphasizing the importance of pain relief, OT increasingly became a mainstay for cancer and end-of-life pain. Efforts to destigmatize the use of prescription opioids for chronic non-terminal pain encompassed primary care providers and the public. The efforts led to an unprecedented increase in opioid prescribing for chronic non-terminal pain. Chronic pain management became synonymous with LOT in the 1990s and the first decade of the 2000s with significant numbers of patients in pain clinics receiving LOT.\[^21\] Despite the absence of long-term safety or efficacy data, OT for chronic non-terminal pain became a mainstay of therapy. However, as observational and epidemiologic data of harm from LOT accumulated, a much more cautious approach to OT for chronic non-terminal pain has emerged in the decade of the 2010s.

The accumulation of evidence of harms and the absence of evidence of long-term benefits has warranted a newly cautious approach to LOT that prioritizes safety. This approach coupled with the evidence of both the safety and efficacy for non-pharmacologic and non-opioid pharmacologic pain therapies has led to the current transformation in the way in which pain is viewed and treated. The biopsychosocial model of pain recognizes pain as a complex multidimensional experience that requires multimodal and integrated care approaches. Within this context, non-pharmacologic treatments and non-opioid medications are the preferred treatments for chronic non-terminal pain. OT has a limited role, primarily in the treatment of severe acute pain, post-operative pain, and end-of-life pain.

**C. Prioritizing Safe Opioid Prescribing Practices and Use**

The increasing use of opioids, as well as the accompanying rise in morbidity and mortality associated with opioid use, has garnered increasing attention from federal and local officials as well as other policy makers.

\[^1\] See the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. Available at:
This public health issue, which has been labelled an epidemic,[22] became a focus of the President’s National Drug Control Strategy in 2010 and has since remained a focus. Two main goals introduced in the 2010 strategy included curtailing illicit drug consumption in America and improving the health and safety of the American people by reducing the consequences of drug abuse.[23] The 2015 strategy, and an accompanying presidential memorandum on preventing prescription drug abuse and heroin use, released in October 2015, encouraged the improvement of health and safety using evidence-based methods by calling for change in a number of key areas including preventing drug use in communities, seeking early intervention opportunities, and integrating SUD treatment and supporting recovery.[24, 25]

With the passage of the Patient Protection and Affordable Care Act (PPACA) in March 2010, the Interagency Pain Research Coordinating Committee was created to coordinate pain research efforts throughout federal government agencies. The Committee was tasked with summarizing advances in pain care research, identifying gaps in research, and developing recommendations regarding ways to minimize duplicative efforts, disseminate pain care information, and expand public/private research partnerships and collaborations. The Committee published the National Pain Strategy in March 2016 in response to the call from the National Academy of Medicine to increase awareness of pain as a significant public health issue in the U.S.[3] The strategy made recommendations in a number of areas including prevention and care, professional education and training, and population research. The plan is aimed at decreasing the prevalence of all types of pain (acute and chronic) in the U.S., as well as the disability and morbidity associated with pain.[26]

Government agencies, including the VA, DoD, and Substance Abuse and Mental Health Services Administration (SAMHSA), have also launched initiatives to improve the study and treatment of pain and adverse events associated with opioid analgesics such as OUD and overdose.[27] By August 2013, the VA deployed the Opioid Safety Initiative (OSI) requirements to all Veterans Integrated Service Networks (VISNs) with the aim of ensuring opioids are used in a safe, effective, and judicious manner. The goals of the OSI related to such topics as increased education, monitoring, use of safe and effective prescribing and management methods, tool development, collaboration, and use of alternative pain treatment. The OSI uses the Veterans Health Administration (VHA’s) electronic health record to identify patients who may be high-risk for adverse outcomes with use of opioids and providers whose prescribing practices do not reflect best evidence so that patient care can be improved. The OSI requirements include specific indicators (e.g., the number of unique pharmacy patients dispensed an opioid, the unique patients on LOT who have received UDT).[28] As part of the OSI, the VA launched the Opioid Overdose Education and Naloxone Distribution (OEND) program, which was implemented as a risk mitigation strategy aimed at reducing deaths from opioid overdose. The program components included education and training regarding the following topics: opioid overdose prevention, recognition, and rescue response; risk mitigation strategies; and issuing naloxone kits, which can be used as an antidote to opioid overdose.[29, 30]

Other initiatives are aimed at improving the safe use of opioids, including the OSI Toolkit and the patient guide Taking Opioids Responsibly for Your Safety and the Safety of Others: Patient Information Guide on Long-term Opioid Therapy for Chronic Pain. The OSI Toolkit was developed to provide clinicians with materials to inform clinical decision-making regarding opioid therapy and safe opioid prescribing.[31] The toolkit materials can be found at the following link:
Taking Opioids Responsibly for Your Safety and the Safety of Others: Patient Information Guide on Long-term Opioid Therapy for Chronic Pain is aimed at providing information to patients as well as their providers regarding the safe use of opioids. More information can be found at the following link: http://www.healthquality.va.gov/guidelines/Pain/cot/OpioidTherapyforChronicPainPatientTool20May2013print.pdf. To further promote safety and patient centered care, the VHA issued a policy in 2014 requiring standardized education and signature informed consent for all patients receiving LOT for non-cancer pain. [32]

The aforementioned presidential memorandum of October 2015 mandated that executive departments and agencies shall, to the extent permitted by law, provide training on the appropriate and effective prescribing of opioid medications to all employees who are health care professionals and who prescribe controlled substances as part of their federal responsibilities and duties. The DoD Opioid Prescriber Safety Training Program, launched accordingly, includes modules on pain management and opioid prescribing safety, the recent Centers for Disease Control and Prevention (CDC) guideline (see the below paragraph), and the identification of substance misuse and referral to specialized services. Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury is sponsoring the training and related management support. Training is available online at http://opstp.cds.pesgce.com/hub.php.

The CDC released its Guideline for Prescribing Opioids for Chronic Pain, directed toward primary care physicians, on March 15, 2016. [33] The aim of the guideline is to assist primary care providers in offering safe and effective treatment for patients with chronic pain in the outpatient setting (not including active cancer treatment, palliative care, or end-of-life care). It is also aimed at improving communication between providers and patients and decreasing adverse outcomes associated with LOT. The CDC guideline, similar to the VA/DoD OT CPG, covered topics including initiation and continuation of OT, management of OT, and risk assessment and use of risk mitigation strategies. It also used the GRADE system to assign a grade for the strength for each recommendation which includes assessment of the quality of the evidence and consideration of the balance of desirable and undesirable outcomes, patient values and preferences, and other considerations (e.g., resource use, equity) during recommendation development (see Grading Recommendations for more information on the use of GRADE in updating this CPG).

On July 22, 2016, the Comprehensive Addiction and Recovery Act (CARA) was enacted with the aim of addressing the epidemic of overdoses from prescription opioids and other prescription drugs and heroin. [34] While this act was primarily focused on opioid abuse treatment and prevention, it also gave specific instruction to the VA in regard to broad aspects of OT including consideration of the CDC guideline in revising the prior VA/DoD OT CPG and adopting it for the VA. There are, however, some important distinctions between the CDC guideline and the VA/DoD OT CPG.

The VA/DoD OT CPG was developed with a specific patient population in mind—Service Members, Veterans, and their families—that has unique characteristics and needs related to the military culture and communities to which they return. Throughout the VA/DoD OT CPG, attention is paid to the characteristics and needs of these patients, particularly regarding specific risk factors such as risk for suicide, SUD, and other medical and mental health co-occurring conditions that may complicate management of pain for these patients. Further, these recommendations were made keeping in mind the implications they would have within the VA/DoD healthcare settings, particularly regarding considerations such as resource use,
accessibility, and equity related to each recommendation. Finally, the recommendations were developed keeping in mind the urgent need for rigorous attention to the balance of risks and benefits for patients within the VA/DoD specifically.

There were also some differences in the methodology used between the development of the VA/DoD OT CPG and the CDC guideline. Along with a clinical evidence review, during which the evidence was evaluated using GRADE, the CDC guideline developers also considered the findings of a contextual evidence review. Further, the CDC Core Expert Group, which consisted of subject matter experts, representatives of primary care professional societies and state agencies, and an expert in guideline methodology, reviewed recommendations drafted by the CDC and evaluated how the evidence was used in the development of the recommendations, rather than developing the recommendations themselves (as was the VA/DoD OT Work Group’s role in development of the VA/DoD OT CPG). While experts provided feedback on the CDC recommendations and their development, the CDC determined the final recommendations. CDC also used a review process considering and incorporating feedback from federal partners (e.g., SAMHSA, VA, DoD), stakeholders (e.g., professional organizations, delivery systems, community organizations), and other constituents (e.g., clinicians, prospective patients). The CDC guideline development process included notice in the Federal Register for a public review and comment period as well as peer review. Thus, the recommendations made in the CDC guideline, although similar to those made in this CPG, were likely based on a slightly different evidence base and revised based on the feedback of individuals who were considering a larger group of potential patients relative to the VA/DoD.

Thus, while the VA/DoD OT Work Group was aware of the release of the CDC guideline and considered potential implications, the CDC guideline did not form the basis of the deliberations on the strength or direction of these recommendations. The Work Group followed the VA/DoD Guideline for Guidelines, a document that details the process by which VA/DoD guidelines will be developed, including the use of the GRADE methodology.[1] As required by Congress in CARA, the Work Group reviewed and considered the CDC guideline and its inclusion in the VA/DoD OT CPG.[34]

D. Taxonomy
Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage...Pain is always subjective...It is unquestionably a sensation in a part or parts of the body, but it is also always unpleasant and therefore also an emotional experience.”[3,35] All of these facets signify the complexity of pain as a condition by itself and how it relates to both the brain and the body.[36] Pain as a symptom is multifaceted and is described and characterized by many factors such as its quality (e.g., sharp versus dull), intensity, timing, location, and whether it is associated with position or movement.

Chronic pain is defined as pain lasting three months or more.[37] It is often associated with changes in the central nervous system (CNS) known as central sensitization.[38] Whereas acute and subacute pain are thought to involve primarily nociceptive processing areas in the CNS, chronic pain is thought to be associated with alterations in brain centers involved with emotions, reward, and executive function as well as central sensitization of nociceptive pathways across several CNS areas.[39-41]

There are many causes of chronic pain. Pain arising from persistent peripheral stimulation could be mechanical or chemical/inflammatory in nature typically leading to well-localized nociceptive mechanism
pain. Mechanical or inflammatory pain with a visceral origin may produce a less localized pain. Neuropathic pain due to injury or disease of the central or peripheral nervous system (e.g., spinal cord injury, diabetic neuropathy, radiculopathy) may lead to poorly localized symptoms such as diffuse pain, burning, numbness, or a feeling of skin sensitivity.

A comprehensive pain assessment includes a biopsychosocial interview and focused physical exam. Elements of the biopsychosocial pain interview include a pain-related history, assessment of pertinent medical and psychiatric comorbidities including personal and family history of SUD, functional status and functional goals, coping strategies, and a variety of psychosocial factors such as the patient’s beliefs and expectations about chronic pain and its treatment.[36] Patients with chronic pain may also experience worsened quality of life, mental health, immune system function, physical function, sleep, employment status, and impaired personal relationships.[3,42-44] Worsening of some of these factors (e.g., quality of life, change in employment status) seems to also be associated with pain severity and the presence of psychiatric comorbidities.[45,46] Patients with chronic pain report psychological complaints (e.g., depression, anxiety, poor self-efficacy, poor general emotional functioning) more often than patients without chronic pain.[47] Further, there can be social and psychological consequences such as decreased ability to successfully maintain relationship and career roles and increased depression, fear, and anxiety as a result of pain.[3,11]

E. Epidemiology and Impact

a. General Population

Chronic pain is among the most common, costly, and disabling chronic medical conditions in the U.S.[48-50] In the U.S., approximately 100 million adults experience chronic pain, and pain is associated with approximately 20% of ambulatory primary care and specialty visits.[3,4,11] As noted above (see Opioid Epidemic), since the late 1990s and early 2000s, the proportion of pain visits during which patients received opioids has increased significantly, as have opioid-related morbidity, mortality, overdose death, and SUD treatment admissions.[4,12,13] Approximately one in five patients with non-cancer pain or pain-related diagnoses is prescribed opioids in office-based settings.[4] According to the CDC, sales of prescription opioids U.S. quadrupled from 1999 and 2014.[12] The absolute number of deaths associated with use of opioids has increased four-fold since 2000, including by 14% from 2013 to 2014 alone.[17] Between 1999 and 2015, more than 183,000 people died from overdoses related to prescription opioids.[51] In one survey, approximately one-third of patients receiving OT for CNCP (or their family members) indicated thinking that they were “addicted” to or “dependent” on the medication or used the medication for “fun” or to “get high.”[18] From 2000 through 2013, the rate of heroin overdose deaths increased nearly four-fold.[19] In the 2000s, the majority of people entering treatment for heroin use used prescription opioids as their first opioid.[20]

b. VA/DoD Population

From fiscal years 2004 to 2012, the prevalence of opioid prescriptions among Veterans increased from 18.9% to 33.4%, an increase of 76.7%. The groups with the highest prevalence of opioid use were women and young adults (i.e., 18-34 years old).[52] In a sample of non-treatment-seeking members of the military who were interviewed within three months of returning from Afghanistan, 44% reported chronic pain and 15% reported using opioids—percentages much higher than in the general population.[53,54] Chronic pain
was also associated with poorer physical function, independent of comorbid mental health concerns in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans.[55]

In a study of Veterans with chronic pain who had been on opioids for at least 90 days, over 90% continued to use opioids one year later and nearly 80% continued to use opioids after completion of the 3.5 year follow-up period; while, in a study of civilian patients who had been on opioids for at least 90 days, approximately 65% remained on opioids through the 4.8 year follow-up period.[56,57] Rates of continuation in Veterans, based on this study, appeared to be related to age, marital status, race, geography, mental health comorbidity, and dosage. Compared to others, those who were age 50-65 years, were married, were a race other than African American, and who lived in a rural setting were more likely to continue using opioids. Veterans on higher doses of opioids were more likely to continue their use. Notably, those with mental health diagnoses were less likely to continue opioids, including those with schizophrenia and bipolar diagnoses.[56]

### F. Chronic Pain and Co-occurring Conditions

Individuals with conditions that result in or co-occur with chronic pain may have different needs or respond to treatment differently than individuals with chronic pain alone. Many different physical and psychological conditions have a pain component that can be difficult to distinguish from the underlying mechanism of illness. Furthermore, the treatment of co-occurring pain and other conditions may vary or require special considerations during their management. Readers are encouraged to consult other VA/DoD CPGs for further information (see VA/DoD Clinical Practice Guidelines website: [www.healthquality.va.gov](http://www.healthquality.va.gov)).

### G. Risk Factors for Adverse Outcomes of Opioid Therapy

The risk factors with the greatest impact for development of opioid-related adverse events are the duration and dose of opioid analgesic use. Beyond duration and dose of OT, many factors increase the risk of adverse outcomes and must be considered prior to initiating or continuing OT (Box 1).

Given the insufficient evidence of benefit for LOT, the clinician must carefully weigh harms and benefits and educate the patient as well as his or her family or caregiver prior to proceeding with treatment. As patient values and preferences may be impacted by other clinical considerations, some patients with one or more risk factors for adverse outcomes may differ with the clinician’s assessment that the risks of OT outweigh the potential for modest short-term benefits. Thus, it is important to consider patients’ values and concerns, address misconceptions, express empathy, and fully explain to patients with one or more risk factors that they may not benefit from, and may even be harmed by, treatment with OT.

Conditions that significantly increase the risk of adverse outcomes from LOT are listed below. Patients for whom LOT is initiated should be carefully monitored, and ongoing assessment of risk should be performed with vigilance for the development of additional risk factors and adverse outcomes (see Recommendations 7-9). Consider consultation with appropriate specialty care providers if there is uncertainty about whether benefits of OT, such as improved function (e.g., return-to-work), outweigh the risks.
Box 1: Selected Significant Risk Factors

- Duration and dose of OT
- Severe respiratory instability
- Sleep disordered breathing (e.g., sleep apnea)
- Acute psychiatric instability or intermediate to high acute suicide risk
  - Suicidality (see Recommendation 8; VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk for Suicide [VA/DoD Suicide CPG], available at: http://www.healthquality.va.gov/guidelines/MH/srb/)

- Mental disorders
  - Current or history of SUD (see VA/DoD SUD CPG, available at: http://www.healthquality.va.gov/guidelines/mh/sud/index.asp)
    - Untreated SUD confers additional risk (see Recommendation 4)
  - Depression or history of depression (see VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder [VA/DoD MDD CPG] as appropriate, available at: http://www.healthquality.va.gov/guidelines/MH/mdd/)
  - Generalized anxiety disorder
  - Borderline personality disorder
  - Antisocial personality disorder

- History of drug overdose
- Under 30 years of age (see Recommendation 6)
- Co-administration of a drug capable of inducing fatal drug-drug interactions (e.g., see Recommendation 5)
- QTc interval >450 milliseconds (ms) for using methadone
- Evidence for or history of diversion of controlled substances
- Intolerance, serious adverse effects, or a history of inadequate beneficial response to opioids
- Impaired bowel motility unresponsive to therapy
- Traumatic brain injury
- Pain conditions worsened by opioids (e.g., fibromyalgia, headache)
- True allergy to opioid agents (that cannot be resolved by switching agents)

a. Significant Risk Factors

- **Duration and dose of OT:** See Recommendation 2 for more guidance on duration of OT and Recommendations 10-12 for more guidance on dosing of OT.

- **Severe respiratory instability or sleep disordered breathing:** This would include any co-occurring condition that significantly affects respiratory rate or function such as chronic obstructive pulmonary disease (COPD), asthma, pneumonia, sleep apnea, or a neuromuscular condition (e.g., amyotrophic lateral sclerosis). Two large observational studies of patients with a history of COPD and sleep apnea who were prescribed opioids showed a weak but positive association with opioid-related toxicity/overdose and overdose-related death.[58,59]

- **Acute psychiatric instability or intermediate to high acute suicide risk:** Intermediate to high acute suicide risk, severe depression, unstable bipolar disorder, or unstable psychotic disorder precludes the safe use of self-administered LOT.[60] Im et al. (2015) (n=487,462) found that a diagnosis of a mood disorder was significantly associated with suicide attempts for the chronic use of short-acting and long-acting opioids compared with no diagnosis of a mood disorder.[61]
In a study of patients on opioids, Campbell et al. (2015) reported that those with bipolar disorder had 2.9 times the odds of a suicidal ideation within the past 12 months as well as 3.2 times the odds of a lifetime suicide attempt compared to those with no bipolar disorder.[62] See Recommendation 8 and the VA/DoD Suicide CPG for more information on suicidality. See the VA/DoD Clinical Practice Guideline for Management of Bipolar Disorder in Adults (VA/DoD BD CPG) for more information on bipolar disorder.3 Merrill and colleagues found that high dose chronic opioid therapy for pain was associated with depressed mood.[63] Treatment for chronic pain with movement, exercise and cognitive-behavioral therapy for pain may have benefit in treating depression, PTSD, and in reducing suicide risk.[64]

- Mental health disorders:
  - Current or history of SUD: For patients with untreated SUD, see Recommendation 4. For patients with diagnosed OUD, see Recommendation 17. Frequent requests for early refills or atypically large quantities required to control pain can signal an emerging SUD as well as diversion (see Evidence for or history of diversion of controlled substances). See the VA/DoD SUD CPG.4
  - Depression or history of depression: Zedler et al. (2014) reported that among patients being treated by the VHA system that received opioids, a history of depression was significantly associated with opioid-related toxicity/overdose compared to no history of depression.[58] LOT has been associated with worsening depressive symptoms.[63] See the VA/DoD MDD CPG.5
  - PTSD: Seal et al. (2012) (n=15,676) noted that among patients on OT, a prevalence of self-inflicted injuries was significantly higher among patients with a history of PTSD (with or without other mental health diagnoses) as compared to patients with other (or no) mental health diagnoses.[65] For more information, see the VA/DoD PTSD CPG.6

- History of drug overdose: A history of overdose is a red flag and providers should proceed with utmost caution when considering LOT for these patients.

- Under 30 years of age: See Recommendation 6.

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2 See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk of Suicide. Available at: http://www.healthquality.va.gov/guidelines/MH/srb/
3 See the VA/DoD Clinical Practice Guideline for Management of Bipolar Disorder in Adults. Available at: http://www.healthquality.va.gov/guidelines/MH/bd/
4 See the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. Available at: http://www.healthquality.va.gov/guidelines/mh/sud/index.asp.
5 See the VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder. Available at: http://www.healthquality.va.gov/guidelines/MH/mdd/
• **Co-administration of a drug capable of inducing fatal drug-drug interactions:** Providers should carefully rule out and avoid potential drug interactions prior to initiating LOT. For example, the following combinations are dangerous:[66]
  - Opioids with benzodiazepines (compared to patients with no prescription, the odds ratio [OR] and 95% confidence interval [CI] for drug-related death was OR: 14.92, 95% CI: 7.00-31.77 for patients who filled a prescription for opioids and benzodiazepines; OR: 3.40, 95% CI: 1.60-7.21 for patients who filled only an opioid prescription, and 7.21, 95% CI: 3.33-15.60 for patients who filled only a benzodiazepine prescription) (see Recommendation 5) [66,67]
  - Fentanyl with CYP3A4 inhibitors
  - Methadone with drugs that can prolong the QT interval (the heart rate’s corrected time interval from the start of the Q wave to the end of the T wave) (e.g., CYP450 2B6 inhibitors)

• **QTc interval >450 ms for using methadone:** Unlike most other commonly used opioids, methadone has unique pharmacodynamic properties that can prolong the QTc interval (the heart rate’s corrected time interval from the start of the Q wave to the end of the T wave) and precipitate torsades de pointes, a dangerous or fatal cardiac arrhythmia. Patients who may be at risk include those with other risk factors for QTc prolongation, current or prior electrocardiograms (ECGs) with a prolonged QTc >450 ms, or a history of syncope. Therefore, ECGs before and after initiating methadone are highly advised (see Methadone Dosing Guidance).

• **Evidence for or history of diversion of controlled substances:** The clinician should communicate to patients that drug diversion is a crime and constitutes an absolute contraindication to prescribing additional medications. Because suspicion is subjective and may be based on impression, bias, or prejudice, it is important that providers who suspect diversion base treatment plans on objective evidence. Suspicions may be confirmed by a negative mass spectrometry/liquid chromatography UDT for the substance being prescribed in the absence of withdrawal symptoms in someone who is receiving opioids. A negative UDT for the prescribed opioid could also by itself be a sign of diversion. Signs of diversion may also include frequent requests for early refills or atypically large quantities required to control pain. Routine UDT, however, may not reliably detect synthetic opioids (e.g., methadone, fentanyl, tramadol) or semi-synthetic opioids (e.g., oxycodone, hydrocodone, hydromorphone). When there is evidence that the patient is diverting opioids, discontinue opioids according to Recommendations 14 and 15 and assess for underlying OUD and/or psychiatric comorbidities. Consultation with a pain specialist, psychiatrist, or SUD specialist may be warranted. Also consider consultation with local risk management and/or counsel. For patients with OUD, keep in mind that sudden discontinuation of opioids due to suspected diversion may place them at high risk for illicit opioid use and resulting opioid overdose (see Recommendation 17).

• **Intolerance, serious adverse effects, or a history of inadequate beneficial response to opioids:** Serious harm may occur should patients be prescribed additional (or different) opioids if prior administration of opioids led to serious adverse effects or was not tolerated. It is also inadvisable to prescribe opioids to patients who already have had an adequate opioid trial (of
sufficient dose and duration to determine whether or not it will optimize benefit) without a positive response.

- **Impaired bowel motility unresponsive to therapy**: Opioids inhibit bowel peristalsis. Their use with patients with impaired bowel motility can increase the risk of severe constipation/impaction or possible obstruction.

- **Headache not responsive to other pain treatment modalities**: LOT is an ineffective treatment modality for patients with migraine headaches (with or without aura), tension-type headaches, occipital neuralgia, or myofascial pain and may result in worsening of the underlying headache condition through factors such as central sensitization and withdrawal.

- **Traumatic brain injury (TBI)**: Patients with a history of TBI who use chronic short-acting and long-acting opioids are more likely to attempt suicide.[61]

- **True allergy to opioid agents**: Morphine causes a release of histamine that frequently results in itching, but this does not constitute an allergic reaction. True allergy to opioid agents (e.g., anaphylaxis) is not common, but does occur. Generally, allergy to one opioid does not mean the patient is allergic to other opioids; many times, rotating to a different opioid may be effective. When an opioid allergy is present and OT is being considered, consultation with an allergist may be helpful.
VI. About this Clinical Practice Guideline

This OT CPG is in line with the efforts described above to improve our understanding and treatment of pain, as well as to mitigate the inappropriate prescribing and ill effects of opioids. It is intended for VA and DoD healthcare practitioners including physicians, nurse practitioners, physician assistants, physical and occupational therapists, psychologists, social workers, nurses, clinical pharmacists, chaplains, addiction counselors, and others involved in the care of Service Members and their beneficiaries, retirees and their beneficiaries, or Veterans on or being considered for LOT. In conjunction with other efforts already under way, this CPG is aimed at improving safe and appropriate prescribing and use of opioids to treat chronic pain.

As with other CPGs, there are limitations, including significant evidence gaps. Further, there is a need to develop effective strategies for guideline implementation and evaluation of the effect of guideline adherence on clinical outcomes. Thus, as stated in the qualifying statements at the beginning of the CPG, this CPG is not intended to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns evolve. This CPG is based on evidence available by December 2016 and is intended to provide a general guide to best practices. The guideline can assist healthcare providers, but the use of a CPG must always be considered as a recommendation, within the context of a provider’s clinical judgment and patient values and preferences, for the care of an individual patient.

A. Scope of this Clinical Practice Guideline

This OT CPG is designed to assist healthcare providers in managing or co-managing patients on or being considered for LOT. Specifically, this CPG is intended for adults, including Veterans as well as deployed and non-deployed Active Duty Service Members, their beneficiaries, and retirees and their beneficiaries, with chronic pain who are receiving care from the VA or DoD healthcare delivery systems. This CPG is not intended for and does not provide recommendations for the management of pain with LOT in children or adolescents, in patients with acute pain, or in patients receiving end-of-life care. As is so for any pharmacotherapy, any decision about prescribing opioids, or alternative medications for pain, for pregnant women should be made with due caution and cognizance of applicable U.S. Food and Drug Administration (FDA) labeling. Any patient in the VA or DoD healthcare system should be offered access to the interventions that are recommended in this guideline after taking into consideration the patient’s specific circumstances.

While these guidelines are broadly recommended, their implementation is intended to be patient-centered. Thus, treatment and care should take into account a patient’s needs and preferences. Good communication between healthcare professionals and the patient about the patient’s pain experience, treatment goals, and challenges is essential and should be guided by evidence-based information tailored to the patient’s needs. An empathetic and non-judgmental (versus a confrontational or adversarial) approach to communication with a patient is highly recommended in order to build trust and facilitate frank discussions relating to the social, economic, emotional, and cultural factors that influence patients’ perceptions, behaviors, and decision making.

The information that patients are given about treatment and care should be culturally appropriate and also available to people with limited literacy skills. It should also be accessible to people with additional
needs such as physical, sensory, or learning disabilities. Family involvement should be considered if appropriate.

The systematic review conducted for the update of this CPG encompassed interventional studies (primarily randomized controlled trials [RCTs]) published between March 2009 and December 2016 and targeted nine key questions (KQs) focusing on the means by which the delivery of healthcare could be optimized for patients on or being considered for LOT. Because a comprehensive review of the evidence related to LOT was not feasible, the nine selected KQs were prioritized from many possible KQs. Therefore, many of the 2010 OT CPG recommendations were considered for inclusion in the updated version of the guideline without an updated review of the evidence. The section on Recommendations delineates whether or not the current CPG recommendations were based on an updated evidence review. Appendix H delineates whether the 2010 OT CPG recommendations were considered for inclusion in the update based on an updated evidence review or based on the evidence included in the 2010 OT CPG. The section on Recommendation Categorization further describes the methodology used for the categorization.

B. Highlighted Features of this Clinical Practice Guideline

The 2017 version of the VA/DoD OT CPG is the second update to the original CPG. It provides practice recommendations for the care of populations with chronic pain already on or being considered for LOT. Although there are many other approaches to the treatment of chronic pain, the scope of this CPG is to focus on the use of opioids for chronic pain rather than being comprehensive about all treatment options. A particular strength of this CPG is the multidisciplinary stakeholder involvement from its inception, ensuring representation from the broad spectrum of clinicians engaged in the treatment and management of patients with chronic pain on or being considered for LOT.

The framework for recommendations in this CPG considered factors beyond the strength of the evidence, including balancing desired outcomes with potential harms of treatment, equity of resource availability, the potential for variation in patient values and preferences, and other considerations (see Methods for more information). Applicability of the evidence to VA/DoD populations was also taken into consideration. A structured algorithm (see Algorithm) accompanies the guideline to provide an overview of the recommendations in the context of the flow of patient care and clinician decision making and to assist with training providers. The algorithm may be used to help facilitate translation of guideline recommendations into effective practice.

C. Methods

The current document is an update to the 2010 VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. The methodology used in developing the 2017 CPG follows the VA/DoD Guideline for Guidelines, an internal document of the VA and DoD EBPGW. The VA/DoD Guideline for Guidelines can be downloaded from http://www.healthquality.va.gov/policy/index.asp. This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (“Champions”) and other subject matter experts from within the VA and DoD, known as the “Work Group,” and ultimately, the development and submission of an updated OT CPG. The VA Office of Quality, Safety and Value, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified two clinical leaders,
The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations and writing and publishing a guideline document to be used by providers within the VA and DoD healthcare systems. Specifically, the Champions and the Work Group were responsible for identifying the KQs – those considered most clinically relevant, important, and interesting with respect to the management of patients with chronic pain on or being considered for LOT. The Champions and the Work Group also provided direction on inclusion and exclusion criteria for the evidence review and assessed the level and quality of the evidence. The amount of new scientific evidence that had accumulated since the previous version of the CPG was taken into consideration in the identification of the KQs. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

The Lewin Team, including The Lewin Group, Duty First Consulting, ECRI Institute, and Sigma Health Consulting, LLC, was contracted by the VA and DoD to support the development of this CPG and conduct the evidence review. The first conference call was held in October 2015, with participation from the contracting officer’s representative (COR), leaders from the VA Office of Quality, Safety and Value and the DoD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review about the management of LOT. The group also identified a list of clinical specialties and areas of expertise that were important and relevant to the management of LOT, from which Work Group members were recruited. The specialties and clinical areas of interest included: Anesthesiology, Addictive Disorders and Addiction Medicine, Clinical Neurophysiology, Family Medicine, Geriatrics, Internal Medicine, Mental/Behavioral Health, Neurology, Nursing, Pain Management, Pain Medicine, Pain Psychology, Palliative Care, Pharmacy, Physical Medicine and Rehabilitation, Physical Therapy, Primary Care, Psychiatry, Psychology, and Social Work.

The guideline development process for the 2017 CPG update consisted of the following steps:

1. Formulating and prioritizing KQs (or evidence questions)
2. Conducting the systematic review of the literature
3. Convening a face-to-face meeting with the CPG Champions and Work Group
4. Drafting, revising, and submitting a final CPG about the management of LOT to the VA/DoD EBPWG

Appendix E provides a detailed description of each of these tasks.
b. Grading Recommendations

The Champions and Work Group used the GRADE system to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[68]

- Confidence in the quality of the evidence
- Balance of desirable and undesirable outcomes
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.,:
  - Resource use
  - Equity
  - Acceptability
  - Feasibility
  - Subgroup considerations

Using this system, the Champions and Work Group determined the direction (for or against) and relative strength (strong or weak) of each recommendation.[68] The direction indicates that the desirable effects of the recommendation outweigh the undesirable effects of the recommendation (for) or that the opposite is true (against). The strength indicates the Work Group’s level of confidence in the balance of desirable and undesirable effects of the recommendation among the intended patient population.[69] A strong recommendation indicates the Work Group is confident in this balance (e.g., that the desirable effects outweigh the undesirable effects). A weak recommendation indicates that the balance is still likely, but the Work Group’s confidence in the balance is lower than for a strong recommendation.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong For (or “We recommend offering this option ...”)
- Weak For (or “We suggest offering this option ...”)
- Weak Against (or “We suggest not offering this option ...”)
- Strong Against (or “We recommend against offering this option ...”)

The grade of each recommendation made in the 2017 OT CPG can be found in Recommendations. Additional information regarding the use of the GRADE system can be found in Grading Recommendations.

c. Reconciling 2010 Clinical Practice Guideline Recommendations

Evidence-based CPGs should be current, which typically requires revisions of previous guidelines based on new evidence or as scheduled, subject to time-based expirations.[70] For example, the United States Preventive Services Task Force (USPSTF) has a process for refining or otherwise updating its recommendations pertaining to preventive services.[71] Further, the inclusion criteria for the National Guideline Clearinghouse specify that a guideline must have been developed, reviewed, or revised within the past five years.
The 2017 OT CPG is an update of the 2010 CPG. Thus, the structure and content of the 2017 CPG is reflective of the previous version of the CPG, but modified where necessary to reflect new evidence and new clinical priorities.

The Work Group focused largely on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Work Group considered the current applicability of other recommendations that were included in the previous 2010 OT CPG without complete review of the relevant evidence, subject to evolving practice in today’s environment.

To indicate which recommendations were developed based on the updated review of the evidence versus recommendations that were carried forward from the 2010 version of the CPG, a set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE). These categories, along with their corresponding definitions, were used to account for the various ways in which older recommendations could have been updated. In brief, the categories took into account whether or not the evidence that related to a recommendation was systematically reviewed, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current patient care environment and inside the scope of the CPG. Additional information regarding these categories and their definitions can be found in the section on Recommendation Categorization. The categories for the recommendations included in the 2017 CPG can be found in the Recommendations section. The categorizations for each 2010 CPG recommendation can be found in Appendix H.

Between the development of the 2010 and 2017 versions of the OT CPG, VA/DoD adopted a new evidence rating system. The CPG Work Group recognized the need to accommodate this transition in evidence rating systems from the USPSTF system in the 2010 CPG to the GRADE system in the 2017 CPG. In order to report the strength of all recommendations using a consistent format (i.e., the GRADE system) the Work Group converted the USPSTF evidence grades accompanying the carryover recommendations from the 2010 guideline to the GRADE system. As such, the CPG Work Group considered the strength of the evidence cited for each recommendation in the 2010 OT CPG as well as harms and benefits, values and preferences, and other implications, where possible.

In cases where a 2010 OT CPG recommendation was covered by a 2017 KQ, peer-reviewed literature published since the 2010 OT CPG was considered along with the evidence base used for the 2010 CPG. Where new literature was considered in converting the strength of the recommendation from the USPSTF to the GRADE system, it is referenced in the discussion following the corresponding recommendation, as well as in Appendix G.

The CPG Work Group recognizes that, while there are practical reasons for incorporating findings from a previous systematic review, previous recommendations, or recent peer-reviewed publications into an updated CPG, doing so does not involve an original, comprehensive systematic review and, therefore, may introduce bias.
d. Peer Review Process

The CPG was developed through an iterative process in which the Work Group produced multiple drafts of
the CPG. The process for developing the initial draft is described in more detail in Drafting and Submitting
the Final Clinical Practice Guideline.

Once a near-final draft of the guideline was agreed upon by the Champions and Work Group, the draft was
sent out for peer review and comment. The draft was posted on a wiki website for a period of 14 business
days. The peer reviewers comprised individuals working within the VA and DoD health systems as well as
experts from relevant outside organizations designated by the Work Group. External organizations that
participated in the peer review included the following:

- American Academy of Addiction Psychiatry (AAAP)
- American Academy of Pain Medicine (AAPM)
- American Physical Therapy Association (APTA)
- American Society of Addiction Medicine (ASAM)
- University of Kentucky
- University of Minnesota

VA and DoD Leadership reached out to both the internal and external peer reviewers to solicit their
feedback on the CPG. Reviewers were provided a hyperlink to the wiki website where the draft CPG was
posted. For transparency, all reviewer feedback was posted in tabular form on the wiki site, along with the
name of the reviewer. All feedback from the peer reviewers was discussed and considered by the Work
Group. Modifications made throughout the CPG development process were made in accordance with the
evidence.

D. Implementation

This CPG, including its recommendations and algorithm, is designed to be adapted by healthcare providers
for the treatment of individual patients, bearing in mind patient-level considerations as well as local needs
and resources. The algorithm serves as a tool to prompt providers to consider key decision points in the
course of care.

Although this CPG represents the recommended practice on the date of its publication, medical practice is
evolving and this evolution requires continuous updating based on published information. New technology
and more research will improve patient care in the future. Identifying areas where evidence was lacking
for the 2017 CPG can help identify priority areas for future research. Future studies examining the results
of OT CPG implementation may lead to the development of new evidence particularly relevant to clinical
practice.

E. Summary of Patient Focus Group Methods and Findings

When forming guideline recommendations, consideration should be given to the values of those most
affected by the recommendations: patients. Patients bring perspectives, values, and preferences into their
healthcare experience, and more specifically their pain care experience, that can vary from those of
clinicians. These differences can affect decision making in various situations, and should thus be
highlighted and made explicit due to their potential to influence a recommendation’s implementation. [75, 76] Focus groups can be used as an efficient method to explore ideas and perspectives of a group of individuals with an a priori set of assumptions or hypotheses and collect qualitative data on a thoughtfully predetermined set of questions.

Therefore, as part of the effort to update this CPG, VA and DoD Leadership, along with the OT CPG Work Group, held a patient focus group on December 14, 2015, at the Washington DC VA Medical Center. One additional family caregiver was interviewed separately at a later date. The aim of the focus group and interview was to further the understanding of the perspectives of patients receiving OT within the VA and/or DoD healthcare systems. The focus group and interview explored patient perspectives on a set of topics related to management of OT in the VA and DoD healthcare systems, including knowledge of OT and other pain treatment options, delivery of care, and the impact of and challenges with OT and chronic pain.

It is important to note the focus group was a convenience sample and the Work Group recognizes the limitations inherent in the small sample size. Less than 10 people were included in the focus group consistent with the requirements of the federal Paperwork Reduction Act, 1980. The Work Group acknowledges that the sample of patients included in this focus group may not be representative of all VA and DoD patients on or being considered for OT for chronic pain. Further, time limitations for the focus group prevented exhaustive exploration of all topics related to pain care in the VA and DoD and the patients’ broader experiences with their care. Thus, the Work Group made decisions regarding the priority of topics to discuss at the focus group and interview. These limitations, as well as others, were considered as the information collected from the discussion was used for guideline development. Recruitment for participation in the focus group was managed by the Champions and VA and DoD Leadership, with assistance from coordinators at the facility at which the focus group took place.

The following concepts are ideas and suggestions about aspects of care that are important to patients and family caregivers and that emerged from the discussion. These concepts were needed and important parts of the participants’ care and added to the Work Group’s understanding of patient values and perspectives. Additional details regarding the patient focus group methods and findings can be found in Appendix F.

<table>
<thead>
<tr>
<th>OT CPG Focus Group Concepts</th>
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<tr>
<td>A. Using shared decision making, consider all treatment options and develop treatment plan based on the balance of risks, benefits, and patient-specific goals, values, and preferences</td>
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<tr>
<td>B. Modify treatment based on patient response, considering patient-specific goals, values, and preferences</td>
</tr>
<tr>
<td>C. Involve family caregivers in accordance with patient preferences and maintain open, trusting, and respectful relationship with patients and family caregivers</td>
</tr>
<tr>
<td>D. Educate patients regarding treatment plan, alternative treatment options, and monitoring</td>
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<tr>
<td>E. Within and between healthcare systems, work with appropriate providers to ensure continuity of high quality care</td>
</tr>
<tr>
<td>F. Organize treatment to encourage patient adherence and participation</td>
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<tr>
<td>G. Acknowledge and minimize effects of potential medical error and take action to prevent future medical error</td>
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F. Conflict of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest (COI) in
the past 24 months. Verbal affirmations of no COI were also used as necessary during meetings throughout the guideline development process. The project team was also subject to random web-based surveillance (e.g., ProPublica).

If a project team member reported a COI (actual or potential), measures were in place to mitigate the introduction of bias into the guideline development process. Identified COIs would be reported to the Office of Evidence Based Practice and disclosed to the CPG Work Group in tandem with their review of the evidence and development of recommendations. The Office of Evidence Based Practice and the OT CPG Work Group would then determine whether or not action, such as restricting participation and/or voting on sections related to the conflict or removal from the Work Group, was necessary. If deemed necessary, action would have been taken by the co-chairs and the Office of Evidence Based Practice, based on the level and extent of involvement, to mitigate the COI.

No OT CPG Work Group members reported relationships and/or affiliations which had the potential to introduce bias; thus, no further action was taken to mitigate COIs for this particular CPG.

G. Patient-centered Care

VA/DoD CPGs encourage clinicians to use a patient-centered care approach that is tailored to the patient’s capabilities, needs, goals, prior treatment experience, and preferences. Regardless of setting, all patients in the healthcare system should be offered access to evidence-based interventions appropriate to that patient. When properly executed, patient-centered care may decrease patient anxiety, increase trust in clinicians,[77] and improve treatment adherence.[78] Improved patient-clinician communication through patient-centered care can be used to convey openness to discuss any future concerns.

As part of the patient-centered care approach, clinicians should review the patient’s history including previous treatment approaches, their results, and any other outcomes with the patient. They should ask the patient about his or her willingness to accept a referral to an addiction or other behavioral health specialist when appropriate. Lastly, they should involve the patient in prioritizing problems to be addressed and in setting specific goals regardless of the selected setting or level of care. The below approach may be used in setting SMART (Specific, Measurable, Action Oriented, Realistic, Timed) goals for the patient (Table 1).
Table 1. Guide in Setting SMART Goals [79]

<table>
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<tr>
<th><strong>Specific</strong></th>
<th>A goal should be clear and concise. It is difficult to know when action toward a goal has been started and when it has been completed if it is not specific.</th>
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<tr>
<td><strong>Measurable</strong></td>
<td>A goal should be measurable so that Veterans can track their progress. Veterans need to have clear criteria for progress and completion when taking action on a goal. Keeping tabs on progress can be inspiring.</td>
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<tr>
<td><strong>Action Oriented</strong></td>
<td>A goal should include action. And that action should be in direct control of the Veteran.</td>
</tr>
<tr>
<td><strong>Realistic</strong></td>
<td>A goal should be largely within the reach of the Veterans. It is best to work on small lifestyle changes that are doable. Avoid the pitfalls of having Veterans see only the big picture and not the small steps.</td>
</tr>
<tr>
<td><strong>Timed</strong></td>
<td>A goal should be tied to a timetable for completing specific, measurable and realistic action.</td>
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H. Shared Decision Making

The shared decision making process for chronic pain treatment planning is based on the foundation of a patient-centered assessment of risks and benefits and a clinical synthesis performed by the provider (Figure 1). The patient-centered assessment incorporates a patient-centered interview, and exploration of patient values, goals, questions, concerns, and expectations. Next, the clinician performs a biopsychosocial assessment and determines clinically appropriate therapeutic options in which benefits are likely to outweigh risks. The process culminates in a shared decision making process to develop a patient-centered treatment plan by the patient selecting from the clinically appropriate treatment options generated in the first two steps.

Figure 1. Shared Decision Making for Chronic Pain Treatment and Long-Term Opioid Therapy

I. Stepped Care Model for Pain Management

The Stepped Care Model for Pain Management, developed by VA, has been implemented within both the VHA and Military Health System (MHS) with the aim of providing a continuum of effective, coordinated, and patient-centered treatment to patients with pain. With education, self-care, and whole-health approaches to wellness as the foundation, this model provides progressively more intensive biopsychosocial care within increasingly specialized settings as patients become more complex, have a greater degree of comorbidity, and present higher risk. Psychological, physical, complementary and
alternative, and medication therapies are often combined to create a multimodal pain care plan. The goals of the Stepped Care Model for Pain Management include functional rehabilitation, improvement in quality of life, and prevention of the pain becoming chronic and associated deterioration in function (Figure 2).

**Figure 2. Stepped Care Model for Pain Management***

*Adapted from the Interagency Pain Research Coordinating Committee’s National Pain Strategy (2016) [26]

Abbreviations: BPS: biopsychosocial; CAM: complementary and alternative medicine; CARF: Commission on Accreditation of Rehabilitation Facilities; MH-PC: Primary Care-Mental Health; OEF: Operation Enduring Freedom; OIF: Operation Iraqi Freedom; PACT: Patient Aligned Care Team; SUD: substance use disorders

### J. Transfer of Care

As the entire medical community is moving toward a greater understanding of the need for opioid safety, it is possible that a provider may receive, as a result of a transfer of care, a patient on a high-risk opioid regimen that raises concerns related to the provider’s and patient’s current understanding of opioid risks. Some universal approaches should be used in the management of care for the patient regardless of the location from which that patient is transferred.

- Clinicians should provide each new patient with a full evaluation, understanding that chronic pain is a complex process that requires a comprehensive assessment of the whole individual as well as their social circumstances. The general goals of the interview with the patient are to do more than just gather information. This process should build a therapeutic relationship as well as facilitate behavior change when necessary. It is important to understand the situation from
the patient’s perspective, elicit a pain-specific history to aid in establishing the correct pain diagnosis, identify patient-specific coping strategies, identify patient-specific pain interference with functioning, and identify important co-occurring conditions. The transferring provider should also communicate the patient’s medical history to the receiving provider to ensure it is taken into account along with the patient’s perspective. This can aid the clinician in synthesizing the full biopsychosocial story.

- Clinicians should review previous medical records to determine what diagnostic and therapeutic options have already been tried. In addition, previous medical records can help to determine the patient’s risk of a non-overdose opioid-related adverse event, overdose risk, and risk of having developed or developing OUD. It can also help to determine co-occurring conditions that will need to be evaluated and treated in order to put together a comprehensive approach to this patient’s pain.

- Clinicians should determine what the patient knows about current concerns related to OT and how comfortable he or she is with an approach that will be addressing opioid safety along with an integrated whole person approach to pain. Each patient may arrive from other providers with a different understanding of the current concerns related to OT, and educational gaps will need to be acknowledged and addressed.

- Clinicians should offer all new patients a physical exam to help to determine the cause of the pain as well as co-occurring conditions that may complicate pain symptoms and/or treatment.

- Clinicians should provide each patient an assessment that outlines the specifics related to opioid safety.
  - What is the diagnosis for which opioids are prescribed?
  - What non-opioid therapies have been trialed and/or is the patient currently using?
  - Are there co-occurring conditions or medication doses/combinations that would increase the risk of OT?

- Clinicians should use standard opioid risk mitigation strategies such as checking the Prescription Drug Monitoring Programs (PDMPs); making sure the patient has participated in shared-decision making about OT and signed and understands the opioid informed consent (see Appendix A); obtaining consent for and performing a UDT (see Appendix B); and offering OEND. See Recommendation 7 for more information on risk mitigation.

One frequently asked question is how to proceed when a patient requests to transfer an opioid prescription that the receiving provider has determined to be too risky to continue. For patients transferred from within the VA and/or DoD system, clinicians should employ risk stratified tapering strategies (see Recommendations 14 and 15). Clinicians should engage patients in shared decision making including consideration of the patient’s values, goals, concerns, and preferences prior to tapering. It is also important that clinicians assess for and treat OUD when present (see Recommendation 17).
For patients who are transferring from outside of the VA and/or DoD, there may be some unique issues to consider.

- Are complete medical records available that would inform treatment planning? Until full record review and communication with the previous prescriber are completed, there are significant risks of taking over opioid prescribing even if it is with intent to taper.

- Has the new plan of care been communicated to the previous prescriber and the patient? If it is felt that the regimen is too risky to take over the management with the resources available, then it is important to communicate this to the patient as well as the previous prescriber so that they can begin an exit plan for the patient as indicated. If the new provider feels comfortable taking over the OT, even if it is to start a taper, then this needs to be communicated to the previous prescriber as soon as possible to avoid duplication of prescriptions.

K. Clinical Decision Support Tools

There are electronic tools to facilitate clinical risk assessment and adherence to risk mitigation. Two tools currently used in the VA are the Opioid Therapy Risk Report (OTRR) and the Stratification Tool for Opioid Risk Mitigation (STORM). The OTRR allows VA providers to review clinical data related to opioid pain treatment within the electronic medical record (EMR), providing an efficient way of monitoring the data. The STORM tool incorporates co-occurring medical and mental health conditions, SUD, opioid dose, co-prescribed sedatives, and information about prior adverse events and generates estimates of patients’ risk or hypothetical risk when considering initiation of opioid therapy. It quantifies risk for poisoning or suicide-related events and for drug-related events, accidents, falls, and drug-induced conditions over a three-year window. Further, it provides suggestions as to what alternative treatments have not been tried and what risk mitigation strategies need to be applied. Evidence supporting their use is poor but they facilitate providers’ determination of current, past and potential therapies and strategies.
### VII. Guideline Work Group

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<th>Department of Veterans Affairs</th>
<th>Department of Defense</th>
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*Additional contributor contact information is available in Appendix I.*
VIII. Discussion of Recommendations

A. Initiation and Continuation of Opioids

Recommendation

1. a) We recommend against initiation of long-term opioid therapy for chronic pain. (Strong against)
   b) We recommend alternatives to opioid therapy such as self-management strategies and other non-pharmacological treatments. (Strong for)
   c) When pharmacologic therapies are used, we recommend non-opioids over opioids. (Strong for)
   (Reviewed, New-replaced)

Discussion

As outlined in this CPG, there is a rapidly growing understanding of the significant harms of LOT even at doses lower than 50 mg oral morphine equivalent daily dose [MEDD], including but not limited to overdose and OUD. At the same time there is a lack of high quality evidence that LOT improves pain, function, and/or quality of life. The literature review conducted for this CPG identified no studies evaluating the effectiveness of LOT for outcomes lasting longer than 16 weeks. Given the lack of evidence showing sustained functional benefit of LOT and moderate evidence outlining harms, non-opioid treatments are preferred for chronic pain. Patient values, goals, concerns, and preferences must be factored into clinical decision making on a case-by-case basis. When considering the initiation or continuation of LOT, it is important to consider whether LOT will result in clinically meaningful improvements in function such as readiness to return to work/duty and/or measurable improvement in other areas of function, such that the benefits outweigh the potential harms.

While there is currently no evidence in the literature documenting the benefit of LOT that demonstrates improvement in pain and function, we recognize that in a rare subset of individuals a decision to initiate LOT may be considered (e.g., for intermittent severe exacerbations of chronic painful conditions). If a decision is made to initiate LOT, a careful assessment of benefits and risks should be made to ensure that the benefits are expected to outweigh the well-documented risks. In addition, prior to this consideration, a multimodal treatment plan should be integrated into the patient’s care. Once opioid therapy is initiated, all opioid risk mitigation strategies outlined in this guideline (see Recommendation 7) should be put into place.

In 2011, in response to the recognition of pain and its management as a public health problem, the National Academy of Medicine investigated and reported on the state of pain research, treatment, and education in the U.S. The report called for a cultural transformation in the way pain is viewed and treated.[3] Accordingly, the U.S. Department of Health and Human Services (HHS) National Pain Strategy (March 2016) recommends a biopsychosocial approach to pain care that is multimodal and interdisciplinary.[26] The underlying concepts of the biopsychosocial model of pain include the idea that pain perception and its effects on the patient’s function is mediated by multiple factors (e.g., mood, social support, prior experience, biomechanical factors), not just biology alone. With this overall change in construct, a biopsychosocial assessment and treatment plan should be tailored accordingly.

Psychological therapies (e.g., cognitive behavioral interventions such as Cognitive Behavioral Therapy [CBT], biofeedback) have been found to be effective for pain reduction in multiple pain conditions.[80-82]
Exercise treatments, including yoga, also have evidence of benefit for reducing pain intensity and disability when compared to usual care in the treatment of chronic pain conditions. Exercise and psychological therapies may each exert their influence through multiple mechanisms including but not limited to the reduction in fear-avoidance, reduction in catastrophizing, and/or enhancing mood. Similarly, multidisciplinary biopsychosocial rehabilitation (described as a combination of a physical intervention such as graded exercise and a psychological, social, or occupational intervention) has been shown to be more effective than usual care in improving pain and disability. These interventions are safe and have not been shown to increase morbidity or mortality.

In light of the low harms associated with exercise and psychological therapies when compared with LOT these treatments are preferred over LOT, and should be offered to all patients with chronic pain including those currently receiving LOT. There is insufficient evidence to recommend psychological over physical therapies or vice versa; the choice of which to try first should be individualized based on patient assessment and a shared decision making process (see Patient Focus Group Methods and Findings).

In addition to non-pharmacological therapies (e.g., exercise, CBT), appropriate mechanism and condition-specific non-opioid pharmacologic agents should be tried and optimized before consideration of opioid medications (e.g., gabapentin in neuropathic pain states). Potential contraindications and long-term risks of use should be considered for non-opioid pharmacologic agents as well, as these also can carry risk of harm, depending on the specific patient and chosen medication.

Patient access to physical, psychological, and pain rehabilitation modalities should be considered. In some cases access to care may be limited; all VA and DoD clinics may not have access to multidisciplinary pain services. Still, all avenues for obtaining these treatments (e.g. Internet based CBT) and all appropriate non-opioid medications should be exhausted before consideration of LOT.

Further studies may help determine earlier in the course of treatment which patients are most likely to benefit from a specific non-pharmacologic therapy (physical, psychological, and pain rehabilitation) or non-opioid pharmacologic therapies alone or as part of a multimodal approach.

**Recommendations**

2. If prescribing opioid therapy for patients with chronic pain, we recommend a short duration.
   (Strong for | Reviewed, New-replaced)
   
   Note: Consideration of opioid therapy beyond 90 days requires re-evaluation and discussion with patient of risks and benefits.

3. For patients currently on long-term opioid therapy, we recommend ongoing risk mitigation strategies (see Recommendations 7-9), assessment for opioid use disorder, and consideration for tapering when risks exceed benefits (see Recommendation 14).
   (Strong for | Reviewed, New-replaced)

**Discussion**

The support for these recommendations is two-fold: a paucity of research showing benefit for LOT and the strength of the evidence demonstrating the potential for life-threatening harm. Of utmost concern is the
heightened risk for developing OUD in patients who receive OT beyond 90 days (see Appendix C for Diagnostic and Statistical Manual of Mental Disorders [DSM] 5 diagnostic criteria for OUD).

Similar to other risk factors, continuing OT beyond 90 days’ duration should be weighed heavily in the risk-benefit calculus for LOT. Continuing OT for longer than 90 days is not an absolute contraindication to LOT. There may be some situations where the benefits of LOT clearly outweigh the risks. That must be determined through individual clinical assessment.

Moderate quality evidence demonstrates that the prevalence of OUD in patients with CNCP is related to duration of opioid use as well as dose (see Recommendations 7-9).[86-88] There are two studies of patients with CNCP which support the current recommendations. Edlund et al. (2014) conducted a large retrospective cohort study where they examined claims data from a health insurance database between 2000 and 2005 to examine factors predictive of developing OUD.[86] Days’ supply of opioids was categorized as none, acute duration (1-90 days), or chronic duration (91+ days). Average daily dose was defined as none, low (1-36 mg MEDD), medium (36-120 mg MEDD), or high (>120 mg MEDD). The OR of developing OUD ranged based on dose and duration (OR: 3.03, 95% CI: 2.32-3.95 for low dose, acute opioid prescription; OR: 14.92, 95% CI: 10.38-21.46 for low dose, chronic opioids prescriptions; OR: 3.10, 95% CI: 1.67-5.77 for high dose, acute opioid prescriptions; OR: 122.45, 95% CI: 72.79-205.99 for high dose, chronic opioid prescriptions). They found that even greater than opioid dose, duration of OT was the strongest predictor of developing OUD. Additionally, a study by Boscariino et al. (2011) examined medical records from a large healthcare system.[89] Through interviews with a random sample of patients on LOT, they examined factors associated with and the prevalence of OUD (using DSM IV and 5 criteria). These results showed that the prevalence of lifetime OUD for patients on LOT was 34.9% (based on DSM-5 criteria) and 35.5% (based on DSM-IV criteria).

The relationship between OUD and duration of therapy is magnified when patients have a history of previous opioid or non-opioid SUD. A cross-sectional cohort study found that provision of LOT (four prescriptions within a 12 month period) to CNCP patients who had a history of severe OUD resulted in increased odds of developing OUD (OR: 56.36, 95% CI: 32.49-97.76).[88]

Patients should be informed that progression from acute to long-term OT is associated with little evidence for sustained analgesic efficacy but a substantial increase in risk for OUD. Providers should discuss this information with patients at initiation of OT and continuously thereafter to ensure that the patient understands the associated risks and benefits of LOT. Fully informed, some patients may desire continuation of OT while others may decline its continued provision.

Research is necessary to more accurately determine how long it takes for OUD to occur and whether the nature of the pain is one of the factors that can influence either of this phenomena.
**Recommendation**

4. a) We recommend against long-term opioid therapy for pain in patients with untreated substance use disorder. *(Strong against)*
   
b) For patients currently on long-term opioid therapy with evidence of untreated substance use disorder, we recommend close monitoring, including engagement in substance use disorder treatment, and discontinuation of opioid therapy for pain with appropriate tapering (see Recommendation 14 and Recommendation 17). *(Strong for)* *(Reviewed, Amended)*

**Discussion**

Opioids carry a significant risk for OUD, overdose, and death, especially among patients with untreated SUD. The recommendation against LOT for patients with SUD is supported by five large studies (four retrospective case cohort studies and one case cohort study).[59,61,66,86,87] Individually, these studies are of moderate strength; however, the combined weight of their results is strongly supportive of this recommendation. Clinicians should note that this recommendation does not refer to patients whose sole SUD relates to tobacco misuse.

The Edlund et al. (2014) study of 568,640 commercial health plan patients (see Recommendation 2 and 3) found that those diagnosed with CNCP and an alcohol use or non-opioid drug use disorder had higher rates of OUD (OR: 3.22, 95% CI: 1.79-5.80 for patients with pre-index alcohol use disorder compared to no alcohol use disorder; OR: 8.26, 95% CI: 4.74-14.39 for patients with pre-index non-opioid drug use disorders compared to no non-opioid drug use disorders).[86] Moreover, Huffman et al. (2015) found that the presence of a lifetime history of SUD for patients with CNCP was associated with 28 times increased odds of therapeutic opioid addiction compared to patients with CNCP without a lifetime history of SUD (OR: 28.58, 95% CI: 10.86-75.27).[87]

The following three studies concern the serious risks of overdose and death. A study of 206,869 health maintenance organization patients who received opioid prescriptions and who had a diagnosis of an alcohol or drug use disorder were also found to have a significantly higher risk of overdose.[66] The VHA’s National Patient Care Database case cohort study of 154,684 patients also found that patients diagnosed with SUD and CNCP had a significantly elevated risk of overdose death (hazard ratio [HR]: 2.53, 95% CI: 1.99-3.22) compared to patients with no SUD diagnosis.[59] The third study used a VHA database to review the outcomes of patients who had been prescribed chronic short-acting or long-acting opioids.[61] This study found that patients who received chronic short-acting or long-acting opioids and who were diagnosed with SUD had an increased risk of suicide attempts compared to those without an SUD diagnosis (OR: 2.42, standard error [SE]: 0.035 for chronic short-acting for patients with drug use disorder; OR: 2.83, SE: 0.057 for chronic long-acting for patients with drug use disorder; OR: 1.99, SE: 0.033 for chronic short-acting for patients with alcohol use disorder; OR: 1.87, SE: 0.056 for chronic long-acting for patients with alcohol use disorder).

Some patients with SUD may disagree with the recommendation to use non-opioid modalities in lieu of LOT to treat their pain. However, the lack of evidence of efficacy of LOT and considerable evidence of significant harms of overdose, death from overdose, and increased risk of suicide outweigh any potential modest benefit of prescribing LOT in this population. See Recommendation 7 for additional information.
regarding UDT and risk mitigation. See the VA/DoD SUD CPG for guidance on management of SUD.\textsuperscript{7}

Given the increasing use of cannabis among patients with chronic pain and the lack of RCTs comparing outcomes of prescribing LOT versus other therapies for patients with and without cannabis use and cannabis use disorder, future research is needed to optimize care for these patients. Research is also needed to determine which subpopulations of patients with active SUD are at greatest risk of OUD, overdose, and death. Finally, further research is needed on the efficacy of alternative treatments for pain and ways to mitigate risks of opioid-related adverse events in patients with SUD and pain.

**Recommendation**

5. We recommend against the concurrent use of benzodiazepines and opioids.  
   *(Strong against | Reviewed, New-added)*

   Note: For patients currently on long-term opioid therapy and benzodiazepines, consider tapering one or both when risks exceed benefits and obtaining specialty consultation as appropriate (see Recommendation 14 and the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders).

**Discussion**

Harms may outweigh benefits for the concurrent use of benzodiazepines and LOT. There is moderate quality evidence that concurrent use of benzodiazepines with prescription opioids increases the risk of overdose and overdose death.\textsuperscript{[66]} In a retrospective cohort study, the adjusted odds ratio (AOR) for drug overdose was highest for individuals on LOT for chronic pain (without anxiety or PTSD) who also received concurrent long-term benzodiazepine therapy.\textsuperscript{[66]} In another retrospective study that involved over 200,000 participants (not included in the evidence review), Veterans receiving both opioids and benzodiazepines were at an increased risk of death from drug overdose.\textsuperscript{[90]} Furthermore, there is a lack of evidence in favor of long-term therapy with benzodiazepines and opioids for chronic pain.\textsuperscript{[91]}

There is a large variation in patient preference regarding the concurrent use of benzodiazepines and LOT. This is especially true for patients who are already accustomed to receiving both medications (see Patient Focus Group Methods and Findings). Concurrent benzodiazepine and LOT use is a serious risk factor for unintentional overdose death and should be weighed heavily in the risk-benefit evaluation for tapering versus continuing one or both agents. Once initiated, benzodiazepines can be challenging to discontinue due to symptoms related to benzodiazepine dependence, exacerbations of PTSD, and/or anxiety.\textsuperscript{[91]} Moreover, abrupt discontinuation of benzodiazepines should be avoided, as it can lead to serious adverse effects including seizures and death. Tapering benzodiazepines should be performed with caution and within a team environment when possible (see Recommendation 26 in the VA/DoD SUD CPG).\textsuperscript{7} Due to the difficulty of tapering or discontinuing benzodiazepines, particular caution should be used when considering

\textsuperscript{7} See the VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. Available at: http://www.healthquality.va.gov/guidelines/mh/sud/index.asp
initiating benzodiazepines for Veterans with PTSD who have co-occurring chronic pain. The VA/DoD PTSD CPG\(^8\) recommends against benzodiazepines for the prevention of PTSD and cautions against their use in treatment of PTSD. Benzodiazepines to treat acute anxiety symptoms after trauma are associated with a higher incidence of PTSD symptoms. For treatment of PTSD, there is evidence of lack of efficacy from small clinical trials and evidence of harm from observational studies of benzodiazepines for PTSD. Although anxiety may initially improve with benzodiazepines, the improvement is short-lived and may result in tolerance to increasing doses and eventual failure of the treatment. Even gradual benzodiazepine taper may result in exacerbation of severe PTSD symptoms. Concomitant use of benzodiazepines is considered a contraindication to initiation of OT.

In addition to benzodiazepines, the addition of other psychoactive medications to LOT must be made with caution. While the evidence for harm associated with the combination of opioids and Z-drugs (e.g., zolpidem, eszopiclone) is not as strong as the evidence for harm associated with the combination of opioids and benzodiazepines, we suggest not prescribing Z-drugs to patients who are on LOT, as moderate quality evidence demonstrates that the combination of zolpidem and opioids increases the AOR of overdose.[66] The evidence reviewed also identifies potential adverse outcomes (e.g., risk of overdose) with the combined use of antidepressants and opioids in patients who do not have depression.[66] This particular study did not differentiate between classes of antidepressants, limiting the ability of the Work Group to recommend for or against prescribing opioids and a specific class of antidepressants. As such, there is no recommendation in this guideline with respect to using specific classes of antidepressants and LOT.

**Recommendation**

6. a) We recommend against long-term opioid therapy for patients less than 30 years of age secondary to higher risk of opioid use disorder and overdose. *(Strong against)*
   b) For patients less than 30 years of age currently on long-term opioid therapy, we recommend close monitoring and consideration for tapering when risks exceed benefits (see Recommendation 14 and Recommendation 17). *(Strong for)* *(Reviewed, New-replaced)*

**Discussion**

All patients who take opioids chronically are at risk for OUD and overdose, but especially those who are younger than 30 years of age. Seven studies were identified that examined age as a predictor of OUD, respiratory/CNS depression, and/or overdose. Four of the seven studies were rated as fair quality evidence,[59,86,88,92] while three were rated as poor quality evidence.[58,62,87] Six of the seven studies demonstrated that age was inversely associated with the risk of OUD and overdose.[59,62,86-88,92] One
of the three low quality studies showed that older subjects had a higher HR of overdose.[58] The Work Group’s overall confidence in the quality of the evidence was moderate.

Similar to other risk factors, age <30 years should be weighed heavily in the risk-benefit determination for initiating LOT. Age <30 years is not an absolute contraindication to LOT. There may be some situations where the benefits of LOT clearly outweigh the risks of OUD and overdose. Hospitalized patients recovering from battlefield injuries, for example, are known to have less chronic pain, depression, and PTSD when their pain is aggressively managed starting soon after injury.[93] In those cases, LOT may be appropriate only if risk mitigation strategies are employed and patients are titrated off LOT as soon as it is appropriate (see Recommendations 14 and 15).

The added risk that younger patients using opioids face for OUD and overdose is great. Edlund et al. (2014) found that, compared to patients ≥65 years old, patients 18-30 years old carried 11 times the odds of OUD and overdose. Patients 31-40 years old carried 5 times the odds of OUD and overdose compared to those ≥65 years old.[86] Bohnert et al. (2011) found that, compared to subjects 18-29 years old, patients 30-39 years old had roughly half the risk of developing OUD or overdose (HR: 0.56, 95% CI: 0.27-1.17). Compared to the subjects 18-29 years old, patients ≥70 years old had a far less risk (nearly 1/17) of developing OUD or overdose (HR: 0.06, 95% CI: 0.02, 0.18).[59]

Younger patients are also at a higher risk of opioid misuse (as suggested by a UDT indicating high-risk medication-related behavior). Turner et al. (2014) showed that patients in the 45-64 year age group were significantly less likely to have an aberrant UDT (detection of a non-prescribed opioid, non-prescribed benzodiazepine, illicit drug, or tetrahydrocannabinol [THC]) in comparison to patients in the 20-44 age group.[94] Patients in the 45-64 and ≥65 age groups were significantly less likely than 20-44 year olds to have non-detection of a prescribed opioid as well (indicating possible diversion).[94]

An age of 30 years was chosen based on how age was categorized in the six studies that showed an inverse relationship between age and OUD or overdose. One of those six studies found that patients with OUD were younger than patients without OUD, but did not find a statistically significant relationship.[87] Two of those six studies examined age as a continuous predictor, and neither reported a specific age where the risk of OUD or overdose changed markedly.[62,92] One study examined age as a dichotomous (<65 and ≥65) predictor.[88] In the two remaining studies, the highest risk included ages ranging from 18 to 30 years.[59,86] As such, the Work Group chose 30 years of age as a clinically reasonable threshold.

Some may interpret the recommendation to limit opioid use by age as arbitrary and potentially discriminatory when taken out of context; however, there is good neurophysiologic rationale explaining the relationship between age and OUD and overdose. Studies in other areas (e.g., use of different substances) indicate that developing brains (age <30 years) are at increased risk of abnormalities and addiction when exposed to substance use early in life.[95-98]

Toward augmenting this evidence base, we recommend that future observational research examine age as a continuous predictor of adverse outcomes. Additionally, we recommend that future trials examine which risk mitigation strategies can reduce the additional risk of OUD and overdose in younger patients on LOT. Lastly, a deeper understanding of the mechanisms for addiction to opioids in young brains is needed.
B. Risk Mitigation

Recommendation

7. We recommend implementing risk mitigation strategies upon initiation of long-term opioid therapy, starting with an informed consent conversation covering the risks and benefits of opioid therapy as well as alternative therapies. The strategies and their frequency should be commensurate with risk factors and include:

- Ongoing, random urine drug testing (including appropriate confirmatory testing)
- Checking state prescription drug monitoring programs
- Monitoring for overdose potential and suicidality
- Providing overdose education
- Prescribing of naloxone rescue and accompanying education

(Strong for | Reviewed, New-replaced)

Discussion

Risk mitigation for LOT should begin before the opioids are prescribed, through an informed consent discussion, reviewing the patient’s history, checking state PDMPs, or instructing patients about using drug take back programs to dispose of unused medication. It should also occur concurrently with the therapy (e.g., ongoing UDT, OEND) and in response to adverse events (e.g., needle exchange programs for those who develop an intravenous drug use disorder). The 2010 OT CPG recommended use of an opioid pain care agreement, monitoring for appropriate opioid use, and, with patients’ consent, obtaining a UDT. A literature search was conducted dating back to the original 2010 recommendation to identify studies comparing the effectiveness of different risk mitigation strategies for patients on or being considered for LOT. One identified study was a systematic review of 11 studies looking at opioid treatment agreements (OTAs) and UDT strategies utilizing opioid misuse risk reduction as the main outcome measure.[99] The study revealed weak evidence to support the use of OTAs and UDT. A second study, a retrospective database study, demonstrated decreased risk of suicide attempts in various cohorts with frequent UDT, regular follow-up (including follow-up within four weeks for patients with new opioid prescription), and rehabilitative services are offered.[61] The confidence in the quality of the evidence was moderate for the outcome of attempted suicide risk. The third study was a retrospective cohort study that looked at the intervention of a clinical pharmacist guidance team versus control.[100] Outcome measures included adverse events, pain management, and quality of life. Details of the actual intervention were vague and did not necessarily include OTAs or UDT. Thus, the confidence in the quality of the evidence was very low.

The confidence in the quality of the evidence was moderate for UDT and frequent follow-up and was low for OTAs. The frequency of follow-up and monitoring should be based on patient level of risk as determined by an individual risk assessment.

There may be some variation in patient values and preferences. Certain patients may appreciate the use of risk mitigation strategies and others may not. Participants in the patient focus group expressed an understanding of why various risk mitigation strategies were used (see Patient Focus Group Methods and Findings).

Implementing more extensive risk mitigation strategies entails an investment of resources. Primary care providers may require more time with patients to allow for shared decision making and treatment
planning. More frequent follow-up of patients on LOT can affect access to care for all empaneled patients. VHA providers must also follow VHA policy regarding education and signature informed consent when providing LOT for patients with non-cancer pain.[101]

*Written Informed Consent and Opioid Treatment Agreements*

There is a paradigm shift occurring in approaches to ensuring and documenting patient and provider understanding and expectations regarding the risks and benefits of LOT. The 2010 OT CPG reflected prior practice of using opioid treatment (or pain care) agreements. OTAs have been described as coercive rather than therapeutic, lack respect for individual autonomy, can be a barrier to pain care, and may be harmful to the patient-provider relationship.[102-105]

Given the recognized risks of opioid therapy, an optimal approach to care should include a robust, signature informed consent process that is patient-centered and provides patients with information about known benefits and harms of OT and treatment alternatives. In 2014, VA established a requirement for signature informed consent, consistent with VA policy for other treatments or procedures with a significant risk of complications or morbidity. See Appendix A, *Taking Opioids Responsibly for Your Safety and the Safety of Others: Patient Information Guide on Long-term Opioid Therapy for Chronic Pain* (found at http://www.healthquality.va.gov/guidelines/Pain/cot/OpioidTheraphyforChronicPainPatientTool20May2013print.pdf), and 38 C.F.R. §17.32 (2012).

Patients may decline offered treatments (e.g., OT) and may also decline risk mitigation strategies (e.g., UDT, pill counts) that are recommended in the course of clinical care. However, providers should discuss this decision with the patient, including the likelihood that their decision may result in the risks of LOT outweighing its potential benefits. This would require a consideration of patient’s safety, and a clinical decision may be made not to initiate OT or to discontinue ongoing OT through tapering (see Recommendation 14 and Recommendation 17).

*State Prescription Drug Monitoring Programs*

State database queries for detection of multi-sourcing of controlled substances are used throughout the country. Data comparing states with an implemented state database program to states without one showed 1.55 fewer deaths per 100,000 people.[106] The CDC currently recommends at least quarterly checks of the state database system.[33]

*Urine Drug Testing and Confirmatory Testing*

As substance misuse in patients on LOT is more than 30% in some series,[107] UDT and confirmatory testing is used as an additional method of examining for patient substance misuse and adherence to the prescribed regimen. UDTs, used in the appropriate way, help to address safety, fairness, and trust with OT.

 Availability of accurate and timely confirmatory testing (e.g., gas chromatography-mass spectrometry [GCMS]) is critical due to the false positive and negative rates associated with UDTs.[53] Interpretation of a UDT and confirmatory results requires education and knowledge of the local procedures and clinical scenario. Local education and access to expert interpretation is necessary.

UDT results are helpful and can help identify active SUD or possible diversion. Accordingly, clinicians should
obtain UDT prior to initiating or continuing LOT and periodically thereafter. When a patient is referred for SUD treatment or is engaged in on-going treatment there should be close communication between the SUD and pain management providers. The ideal approach is an interdisciplinary format (see Recommendation 16).

For more information, see Appendix B on UDT and confirmatory testing.

**Prescribing of Naloxone Rescue and Accompanying Education**

Naloxone administration has been identified as a life saving measure following opioid overdose. A systematic review of 22 observational studies provided moderate quality evidence that take home naloxone programs are effective in improving overdose survival and decreasing mortality, with a low rate of adverse events.[108] One meta-analysis of nine studies determined that take home naloxone kits were used approximately nine times within the first three months of follow-up for every 100 individuals trained.[109] Further, studies have shown that naloxone administration has been efficacious whether given by medical personnel or lay people, with more than 26,000 reversals documented by the CDC from 1996-2014.[110,111] In addition, prescription of naloxone rescue and accompanying education has also been found to reduce opioid-related emergency department visits.[112] Distribution of naloxone for reversal is supported by SAMHSA, the American Medical Association (AMA), and other medical societies, and is facilitated through the VA via Pharmacy Benefits Management. Clinical efficacy has been established for its use on short-acting opioids, but not for its use on long-acting opioids such as methadone or exceptionally potent opioids.[108]

Synthetic opioids such as fentanyl analogs, potent opioid receptor agonists, are responsible for a recent rise in death rates. Fentanyl analogs that may be used to create counterfeit opioid analgesic pills can cause a toxidrome characterized by significant CNS and profound respiratory depression requiring multiple naloxone doses for reversal.[113]

**Patients at High Risk for Opioid Use Disorder**

Those patients receiving opioid analgesics who do not meet DSM-5 criteria for OUD may benefit from an alternative management strategy: close follow-up and CBT. Jamison et al. (2010) randomized patients at high-risk for OUD (as measured by standard rating scales) to receive either standard pain management or close follow-up with CBT for pain.[114] Both of these groups were compared to a low-risk, chronic pain control group receiving standard management. The authors report that, compared to a matched high-risk group receiving standard care, patients receiving additional monitoring and CBT exhibited significantly reduced illicit substance use over six months (percentage of patients with positive drug misuse index scores: 73.7% versus 26.3% versus 25.0%; p<0.01). At six months, there was no difference between the high-risk group receiving close follow-up and the low-risk group receiving standard therapy. Authors also reported that pain perception was less in the high-risk group receiving additional monitoring and behavior therapy; however, analysis of activity interference reporting reflected no significant difference between study groups.
Other Risk Mitigation Strategies

Take Back Programs

Returning unused opioid medications has been explored as a strategy to reduce the amount of opioids in the community, as it has been estimated that 70% of opioid prescriptions are left unused.\[115\] Accordingly, the National Drug Control Strategy advocates take back programs as an effective tool.\[24\] For example, in a 2013 medication take back event in a Michigan community, 3,633 containers containing 345 different prescription medications were collected in four hours. The top five most common medications collected were pain relievers.\[116\] System-wide efficacy of a nationwide program is unknown.\[117\]

Community-based Needle Exchange Programs or Syringe Service Programs

Nearly 80% of new users of injectable opioids had previously used prescription oral opioid pain medication.\[118,119\] Illicit use of injectable opioids is accompanied by an increased rate of human immunodeficiency virus (HIV) and hepatitis infection. Community-based needle exchange programs have been shown to be an effective risk mitigation strategy for reducing high-risk behaviors (e.g., sharing needles) and infectious disease transmission among injection drug users.\[120\] For those patients who develop OUD and progress to intravenous drug use, the first recommendation should be for medication-assisted treatment (MAT) for OUD (see Recommendation 17). For patients who decline MAT for OUD, clinicians should consider educating the patient regarding sterile injection techniques and community-based needle exchange programs, if programs are available. The 2015 outbreak of HIV/hepatitis in rural Indiana and subsequent successful implementation of a needle exchange program is an example of the threat to rural communities from non-prescription opioid use and the potential benefits of needle exchange programs for use as a risk mitigation strategy.\[121,122\]

Recommendation

8. We recommend assessing suicide risk when considering initiating or continuing long-term opioid therapy and intervening when necessary.

(Strong for | Reviewed, Amended)

Discussion

Opioid medications are potentially lethal and an assessment of current suicide risk should be made at every phase of treatment. The VA/DoD Suicide CPG\[9\] recommends restricting the availability of lethal means for patients considered to be at intermediate or high acute risk of suicide (determined by presence and severity of suicidal ideation, level of intention to act, existence of risk factors, limited or absent protective factors, etc.). Accordingly, suicidality is considered to be an important risk factor for OT (see Risk Factors for Adverse Outcomes of Opioid Therapy).

\[9\] See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk of Suicide. Available at: http://www.healthquality.va.gov/guidelines/MH/srb/
A number of studies suggest certain chronic pain conditions represent an independent risk factor for suicide.[123-130] A recent large retrospective cohort study also suggests an association with prescribed opioid dose and suicide risk among Veterans receiving OT for CNCP.[131] Suicide risk is not static, and many factors influence an individual’s risk of suicide at any given point in time, as noted in the VA/DoD Suicide CPG.10 Thus, ongoing assessment of suicide risk is important whether one is initiating, maintaining, or terminating LOT.

There is moderate quality evidence that intensification of monitoring helps mitigate the risk of suicide among patients on LOT. Im et al. (2015) found moderate quality evidence that, at the facility level, patients on LOT within facilities ordering more drug screens than the comparison group were associated with decreased risk of suicide attempt (chronic short-acting opioid group: OR: 0.2, 95% CI: 0.1-0.3; chronic long-acting opioid group: OR: 0.3, 95% CI: 0.2-0.6). In addition, patients on long-acting opioids within the facilities providing more follow-up after new prescriptions were associated with decreased risk of suicide attempt (OR: 0.2, 95% CI: 0.0-0.7).[61]

Some patients on LOT who suffer from chronic pain and co-occurring OUD, depression, and/or personality disorders may threaten suicide when providers recommend discontinuation of opioids. However, continuing LOT to “prevent suicide” in someone with chronic pain is not recommended as an appropriate response if suicide risk is high or increases. In such cases, it is essential to involve behavioral health to assess, monitor, and treat a patient who becomes destabilized as a result of a medically appropriate decision to taper or cease LOT.

Further research is needed to identify strategies for safely managing patients at elevated risk of suicide who demand opioid medications or become further destabilized during tapering.

**Recommendation**

9. We recommend evaluating benefits of continued opioid therapy and risk for opioid-related adverse events at least every three months.

(Strong for | Reviewed, New-replaced)

**Discussion**

Prior to initiating OT, an individualized assessment of potential opioid-related harms relative to realistic treatment goals must be completed. After initiating OT, frequent visits contribute to the appropriate use and adjustment of the planned therapy.

The Work Group recommends follow-up at least every three months or more frequently (see Recommendation 7 and Recommendation 11) due to the balance of benefits and harms associated with this recommendation. Although the 2010 OT CPG recommended follow-up every six months, this

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