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Scott Walker, Governor
Dave Ross, Secretary

CONTROLLED SUBSTANCES COMMITTEE
BOARD OF NURSING

Room 121A, 1400 East Washington Avenue, Madison WI
Contact: Sharon Henes (608) 266-2112
September 27, 2016

Notice: The following agenda describes the issues that the Committee plans to consider at the meeting. At the time of the meeting, items may be removed from the agenda. Please consult the meeting minutes for a description of the actions and deliberations of the Committee. ***A quorum of the Board may be present during the committee meeting.***

1:00 p.m.

AGENDA

CALL TO ORDER – ROLL CALL – OPEN SESSION

A. Approval of Agenda (1-2)

B. Controlled Substances Guidelines – Discussion and Consideration (3-356)

1) Wisconsin Medical Examining Board Opioid Prescribing Guidelines **(4-10)**
2) Center for Disease Control Prescribing Opioid for Chronic Pain Guidelines
   a. Fact Sheet **(11-12)**
   b. Guidelines **(13-64)**
   c. Errata **(65)**
3) American Association of Nurse Anesthetists (AANA) Chronic Pain Management Guidelines **(66-72)**
4) Alaska Medical Board Guidelines Prescribing Controlled Substances **(73-74)**
5) California Medical Board Guidelines for Prescribing Controlled Substances for Pain **(75-164)**
6) Michigan Medical Board Guidelines for Use of Controlled Substances for Treatment of Pain **(165-170)**
7) Oregon Opioid Prescribing Guidelines **(171-237)**
8) Pennsylvania Medical Society Guidelines for Use of Opioids to Treat Chronic Non-Cancer Pain **(238-241)**
9) American Nursing Association (ANA) Nursing's Role in Addressing Nation's Opioid Crisis **(242-243)**
10) AANA Extended Release and Long Acting Opioid REMS Comment Letter **(244-246)**
11) National Council on State Boards of Nursing (NCSBN) Remediation for Opioid Over-Prescribing by Advanced Practice Registered Nurses **(247-268)**
12) Tennessee Board of Nursing 2016 NCSBN Discipline Case Management Conference **(269-317)**

13) Food and Drug Administration (FDA) Blueprint for Prescriber Education for Extended Release and Long Acting Opioid Analgesics **(318-334)**
14) Iowa Healthcare Collaborative - Performance Improvement: the Opiate Use Challenge **(335-341)**
15) Opioid Prescribing: A Systematic Review and Critical Appraisal of Guideline for Chronic Pain **(342-356)**

C. Public Comments

ADJOURNMENT

State of Wisconsin
Department of Safety & Professional Services

AGENDA REQUEST FORM

1) Name and Title of Person Submitting the Request:	2) Date When Request Submitted:
Sharon Henes **Administrative Rules Coordinator**	**22 September 2016** Items will be considered late if submitted after 12:00 p.m. on the deadline date: ▪ 8 business days before the meeting

3) Name of Board, Committee, Council, Sections:

BON Controlled Substances Committee

4) Meeting Date:	5) Attachments:	6) How should the item be titled on the agenda page?
27 Sept 2016	☐ Yes ☐ No	**A. Approval of Agenda** **B. Controlled Substances Guidelines – Discussion and Consideration** **1. Wisconsin Medical Examining Board Opioid Prescribing Guideline** **2. Center for Disease Control Prescribing Opioid for Chronic Pain Guidelines** **a. Fact Sheet** **b. Guidelines** **c. Errata** **3. AANA Chronic Pain Management Guidelines** **4. Alaska Medical Board Guidelines Prescribing Controlled Substances** **5. California Medical Board Guidelines for Prescribing Controlled Substances for Pain** **6. Michigan Medical Board Guidelines for Use of Controlled Substances for Treatment of Pain** **7. Oregon Opioid Prescribing Guidelines** **8. Pennsylvania Medical Society Guidelines Use of Opioids to Treat Chronic Noncancer Pain** **9. ANA Nursing's Role in Addressing Nation's Opioid Crisis** **10. AANA Extended Release and Long Acting Opioid REMS Comment Letter** **11. NCSBN Remediation for Opioid Over-Prescribing by APRNs** **12. Tennessee BON 2016 NCSBN Discipline Case Management Conference** **13. FDA Blueprint for Prescriber Education for Extended Release and Long Acting Opioid Analgesics** **14. Iowa Healthcare Collaborative Performance Improvement the Opiate Use Challenge** **15. Opioid Prescribing A Systematic Review and Critical Appraisal of Guideline for Chronic Pain** **C. Public Comments** **D. Adjournment**

7) Place Item in:	8) Is an appearance before the Board being scheduled?	9) Name of Case Advisor(s), if required:
☒ Open Session ☐ Closed Session ☐ Both	☐ Yes (Fill out Board Appearance Request) ☐ No	

10) Describe the issue and action that should be addressed:

11) Authorization

Sharon Henes

Signature of person making this request — Date

Supervisor (if required) — Date

Executive Director signature (indicates approval to add post agenda deadline item to agenda) — Date

Revised 8/13

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Wisconsin Medical Examining Board Opioid Prescribing Guideline

Scope and purpose of the guideline: To help providers make informed decisions about acute and chronic pain treatment -pain lasting longer than three months or past the time of normal tissue healing. The guideline is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care. Although not specifically designed for pediatric pain, many of the principals upon which they are based could be applied there, as well.

Opioids pose a potential risk to all patients. The guideline encourages providers to implement best practices for responsible prescribing which includes prescribing the lowest effective dose for the shortest possible duration for post-operative care and acutely-injured patients.

1) Identify and treat the cause of the pain, use non-opioid therapies
Use non-pharmacologic therapies (such as yoga, exercise, cognitive behavioral therapy and complementary/alternative medical therapies) and non-opioid pharmacologic therapies (such as acetaminophen and anti-inflammatories) for acute and chronic pain. Don't use opioids routinely for chronic pain. When opioids are used, combine them with non-pharmacologic or non-opioid pharmacologic therapy, as appropriate, to provide greater benefits.

2) Start low and go slow
When opioids are used, prescribe the lowest possible effective dosage and start with immediate-release opioids instead of extended-release/long-acting opioids. Only provide the quantity needed for the expected duration of pain.

3) Close follow-up
Regularly monitor patients to make sure opioids are improving pain and function without causing harm. If benefits do not outweigh harms, optimize other therapies and work with patients to taper or discontinue opioids, if needed.

What's included in the guideline?
The guideline addresses patient-centered clinical practices including conducting thorough assessments, considering all possible treatments, treating the cause of the pain, closely monitoring risks, and safely discontinuing opioids. The three main focus areas in the guideline include:

1) Determining when to initiate or continue opioids
-Selection of non-pharmacologic therapy, non-opioid pharmacologic therapy, opioid therapy
-Establishment of treatment goals
-Discussion of risks and benefits of therapy with patients

2) Opioid selection, dosage, duration, follow-up and discontinuation
-Selection of immediate-release or extended-release and long-acting opioids
-Dosage considerations
-Duration of treatment
-Considerations for follow-up and discontinuation of opioid therapy

3) Assessing risk and addressing harms of opioid use
-Evaluation of risk factors for opioid-related harms and ways to mitigate/reduce patient risk
-Review of prescription drug monitoring program (PDMP) data
-Use of urine drug testing
-Considerations for co-prescribing benzodiazepines
-Arrangement of treatment for opioid use disorder

Prescription Opioid Guideline

1. Pain is a subjective experience and at present, physicians lack options to objectively quantify pain severity other than by patient reported measures including pain intensity. While accepting the patient's report of pain, the clinician must simultaneously decide if the magnitude of the pain complaint is commensurate with causative factors and if these have been adequately evaluated and addressed with non-opioid therapy.

2. In treating acute pain, if opioids are at all indicated, the lowest dose and fewest number of opioid pills needed should be prescribed. In most cases, less than 3 days' worth are necessary, and rarely more than 5 days' worth. Left-over pills in medicine cabinets are often the source for illicit opioid abuse in teens and young adults. When prescribing opioids, physicians should consider writing two separate prescriptions for smaller amounts of opioids with specific refill dates, rather than a single large prescription. Most patients do not fill the second prescription, thus limiting opioid excess in a patient's home and potential misuse.

3. A practitioner's first priority in treating a patient in pain is to identify the cause of the pain and, if possible, to treat it. While keeping the patient comfortable during this treatment is important, it is critical to address to the extent possible the underlying condition as the primary objective of care.

a. Patients unwilling to obtain definitive treatment for the condition causing their pain should be considered questionable candidates for opioids. If opioids are prescribed to such patients, documentation of clear clinical rationale should exist.

b. Opioids should not be prescribed unless there is a medical condition present which would reasonably be expected to cause pain severe enough to require an opioid. For conditions where this is questionable, use of other treatments instead of opioids should be strongly considered.

c. Consultation should be considered if diagnosis of and/or treatment for the condition causing the pain is outside of the scope of the prescribing practitioner.

4. Opioids should not necessarily be the first choice in treating acute or chronic pain.

a. Acute pain: Evidence for opioids is weak. Other treatments such as acetaminophen, anti-inflammatories, and non-pharmacologic treatments should be attempted prior to initiating opioid

therapy. Although opioids could be simultaneously prescribed if it is apparent from the patient's condition that he/she will need opioids in addition to these. Don't use opioids routinely for chronic pain. When opioids are used, combine them with non-pharmacologic or non-opioid pharmacologic therapy, as appropriate, to provide greater benefits.

b. Acute pain lasting beyond the expected duration: A complication of the acute pain issue (surgical complication, nonunion of fracture, etc.) should be ruled out. If complications are ruled out, a transition to non-opioid therapy (tricyclic antidepressant, serotonin/norepinephrine re-uptake inhibitor, anticonvulsant, etc.) should be attempted.

c. Chronic pain: Evidence for opioids is poor. Other treatments such as acetaminophen, anti-inflammatories, and non-pharmacologic treatments (such as yoga, exercise, cognitive behavioral therapy and complementary/alternative medical therapies) should be utilized. Multiple meta-analyses demonstrate that the benefits of opioids are slight, while annualized mortality rates dramatically increased. There are few if any treatments in medicine with this poor a risk/benefit ratio, and there should be adequate clinical indication to indicate why chronic opioid therapy was chosen in a given patient. **Note:** There is no high-quality evidence to support opioid therapy longer than 6 months in duration. Despite this fact, it is considered acceptable although not preferable to continue patients on treatment who have been on chronic opioid therapy prior to this Guideline's release and who have shown no evidence of aberrant behavior.

d. Patients unwilling to accept non-pharmacological and/or nonnarcotic treatments (or those providing questionably credible justifications for not using them) should not be considered candidates for opioid therapy.

5. Patients should not receive opioid prescriptions from multiple physicians. There should be a dedicated provider such as a primary care or pain specialist to provide all opioids used in treating any patient's chronic pain, with existing pain contracts being honored. Physicians should avoid prescribing controlled substances for patients who have run out of previously prescribed medication or have had previous prescriptions lost or stolen.

6. Physicians should avoid using intravenous or intramuscular opioid injections for patients with exacerbations of chronic non-cancer pain in the emergency department or urgent care setting.

7. Physicians are encouraged to review the patient's history of controlled substance prescriptions using the Wisconsin Prescription Drug Monitoring Program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. As of April, 2017, Wisconsin state law requires prescribers to review the PDMP before prescribing any controlled substance for greater than a three-day supply.

8. Pain from acute trauma or chronic degenerative diseases can oftentimes be managed without opioids prior to surgery. Surgical patients using opioids preoperatively have higher complications rates, require more narcotics postoperatively, and have lower satisfaction rates with poorer outcomes following surgery.

9. Prescribing of opioids is not encouraged in patients concurrently taking benzodiazepines or other respiratory depressants. Benzodiazepines triple the already high increases in annual mortality rates from opioids. If they are used concurrently, clear clinical rationale must exist.

10. The use of oxycodone is discouraged. There is no evidence to support that oxycodone is more effective than other oral opioids, while there are multiple studies indicating that oxycodone is more abused and has qualities that would promote addiction to a greater degree than other opioids. As a result, oxycodone should not be considered first-line and should be used only in patients who cannot tolerate other opioids and who have been evaluated for and found not to demonstrate increased risk of abuse.

11. Patients presenting for chronic pain treatment should have a thorough evaluation, which may include the following:

a. Medical history and physical examination targeted to the pain condition

b. Nature and intensity of the pain

c. Current and past treatments, with response to each treatment

d. Underlying or co-existing diseases or conditions, including those which could complicate treatment (i.e., renal disease, sleep apnea, COPD, etc.)

e. Effect of pain on physical and psychological functioning

f. Personal and family history of substance abuse

g. History of psychiatric disorders associated with opioid abuse (bipolar, ADD/ ADHD, sociopathic, borderline, untreated/severe depression)

h. Medical indication(s) for use of opioids.

12. Initiation of opioids for chronic pain should be considered on a trial basis. Prior to starting opioids, objective symptomatic and functional goals should be established with the patient. If after a reasonable trial these goals are not met, then opioids should be weaned or discontinued.

13. Practitioners should always consider the risk-benefit ratio when deciding whether to start or continue opioids. Risks and benefits should be discussed with patients prior to initiating chronic opioid therapy, and continue to be reassessed during that therapy. If evidence of increased risk develops, weaning or discontinuation of opioids should be considered. If evidence emerges that indicates that the opioids put a patient at the risk of imminent danger (overdose, addiction, etc.), or that they are being diverted, opioids should be discontinued and the patient should be treated for withdrawal, if needed.

a. Exceptions to this include patients with unstable angina and pregnant patients, especially in the 3rd trimester (withdrawal could precipitate pre-term labor).

b. Components of ongoing assessment of risk include:

i. Review of the Prescription Drug Monitoring Program (PDMP) information

ii. Periodic urine drug testing (including chromatography) – at least yearly in low risk cases, more frequently with evidence of increased risk

iii. Periodic pill counts – at least yearly in low risk cases, more frequently if evidence of increased risk

iiii. Violations of the opioid agreement

14. All patients on chronic opioid therapy should have informed consent consisting of:

a. Specifically detailing significant possible adverse effects of opioids, including (but not limited to) addiction, overdose, and death

b. Treatment agreement, documenting the behaviors required of the patient by the prescribing practitioner to ensure that they are remaining safe from these adverse effects

15. Initial dose titration for both acute and chronic pain should be with short-acting opioids. For chronic therapy, it would be appropriate once an effective dose is established to consider long-acting agents for a majority of the daily dose.

16. Opioids should be prescribed in the lowest effective dose. This includes prescribing the lowest effective dose for the shortest possible duration for post-operative care and acutely-injured patients. If daily doses for chronic pain reach 50 morphine milligram equivalents (MMEs), additional precautions should be implemented (see #13.b. above). Given that there is no evidence base to support efficacy of doses over 90 MMEs, with dramatically increased risks, dosing above this level is strongly discouraged, and appropriate documentation to support such dosing should be present on the chart.

17. The use of methadone is not encouraged unless the practitioner has extensive training or experience in its use. Individual responses to methadone vary widely; a given dose may have no effect on one patient while causing overdose in another. Metabolism also varies widely and is highly sensitive to multiple drug interactions, which can cause accumulation in the body and overdose. For a given analgesic effect, the respiratory depressant effect is much stronger compared to other opioids. Finally, methadone can have a potent effect on prolonging the QTc, predisposing susceptible patients to potentially fatal arrhythmias.

18. Prescribing of opioids is strongly discouraged for patients abusing illicit drugs. These patients are at extremely high risk for abuse, overdose, and death. If opioids are prescribed to such patients, a clear and compelling justification should be present.

19. During initial opioid titration, practitioners should re-evaluate patients every 1-4 weeks. During chronic therapy, patients should be seen at least every 3 months, more frequently if they demonstrate higher risk.

20. Practitioners should consider prescribing naloxone for home use in case of overdose for patients at higher risk, including:

a. History of overdose (a relative contraindication to chronic opioid therapy)

b. Opioid doses over 50 MMEs/day

c. Clinical depression

d. Evidence of increased risk by other measures (behaviors, family history, PDMP, UDS, risk questionnaires, etc.)

The recommended dose is 0.4 mg for IM or intranasal use, with a second dose available if the first is ineffective or wears off before EMS arrives. Family members can be prescribed naloxone for use with the patient.

21. All practitioners are expected to provide care for potential complications of the treatments they provide, including opioid use disorder. As a result, if a patient receiving opioids develops behaviors indicative of opioid use disorder, the practitioner should be able to assist the patient in obtaining addiction treatment, either by providing it directly (buprenorphine, naltrexone, etc. plus behavioral therapy) or referring them to an addiction treatment center which is willing to accept the patient. Simply discharging a patient from the provider's practice after prescribing the medication that led to the complication of opioid use disorder is not considered acceptable.

22. Discontinuing Opioid Therapy

A. If lack of efficacy of opioid therapy is determined, discontinuation of therapy should be performed.

1. Opioid weaning can be performed by reducing the MED by 10% weekly until 5-10mg MED remain at which time the opioid can be fully discontinued.

2. Prescription of clonidine 0.2 mg po BID or tizanidine 2mg po TID can be provided to patients complaining of opioid withdrawal related symptoms.

B. If evidence of increased risk develops, weaning or discontinuation of opioid should be considered.

1. Opioid weaning can be performed by reducing the MED by 25% weekly until 5-10mg MED remain at which time the opioid can be fully discontinued.

2. Prescription of clonidine 0.2 mg po BID or tizanidine 2mg po TID can be provided to patients complaining of opioid withdrawal related symptoms.

3. Physicians can consider weekly or bi-monthly follow-up during the weaning process.

C. If evidence emerges that indicates that the opioids put a patient at the risk of imminent danger (overdose, addiction, etc.), or that they are being diverted, opioids should be immediately discontinued and the patient should be treated for withdrawal, if needed.

1. Exceptions to abrupt opioid discontinuation include patients with unstable angina and pregnant patients. These patients should be weaned from the opioid medications in a gradual manner with close follow-up.

Resources

CDC Guideline for Prescribing Opioids for Chronic Pain--United States 2016. Dowell D1, Haegerich TM1, Chou R1., JAMA. 2016 Apr 19;315(15):1624-45. doi:10.1001/jama.2016.1464.

Chronic Opioid Clinical Management Guidelines for Wisconsin Worker's Compensation Patient Care. https://dwd.wisconsin.gov/wc/medical/pdf/CHRONIC%20OPIOID%20CLINICAL %20MANAGEMENT%20GUIDELINES%20.pdf

Within-subject comparison of the psychopharmacological profiles of oral oxycodone and oral morphine in non-drug-abusing volunteers. Zacny, James, & Lichtor, Stephanie. Psychpharmacology (2008) 196:105-116

Subjective, Psychomotor, and Physiological Effects Profile of Hydrocodone/Acetaminophen and Oxycodone/Acetaminophen Combination Products. Zachny, James, & Gutierrez, Sandra. Pain Medicine (2008) Vol 9, No 4: 433-443

Positive and Negative Subjective Effects of Extended-Release Oxymorphone versus Controlled-Release Oxycodone in Recreational Opioid Users. Schoedel, Kerri et. al. Journal of Opioid Management 7:3 May/June 2011. 179-192

Tapentadol Abuse Potential: A Postmarketing Evaluation Using a Sample of Individuals Evaluated for Substance Abuse Treatment. Stephen F. Butler, PhD et. al., Pain Medicine 2015; 16: 119–130

Methadone Safety: A Clinical Practice Guideline from the American Pain Society and College on Problems of Drug Dependence, in collaboration with the Heart Rhythm Society. Chou R1, et. al., J Pain. 2014 Apr;15(4):321-37

Emerging Issues in the Use of Methadone. SAMHSA Substance Abuse Treatment Advisory, Spring 2009, Volume 8, Issue 1, available at http://store.samhsa.gov/shin/content//SMA09-4368/SMA09-4368.pdf

Opioid Use, Misuse, and Abuse in Orthopedic Practice. American Academy of Orthopedic Surgeons, Information Statement 1045, October, 2015, available at http://www.aaos.org/ PositionStatements/Statement1045/?ssopc=1

Wisconsin Medical Society Opioid Prescribing Principles. https://www.wisconsinmedicalsociety.org/advocacy/boards-councils/society-initiatives/opioid-task-force/opioid-prescribing-principles/

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

IMPROVING PRACTICE THROUGH RECOMMENDATIONS

CDC's *Guideline for Prescribing Opioids for Chronic Pain* is intended to improve communication between providers and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder and overdose. The Guideline is not intended for patients who are in active cancer treatment, palliative care, or end-of-life care.

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

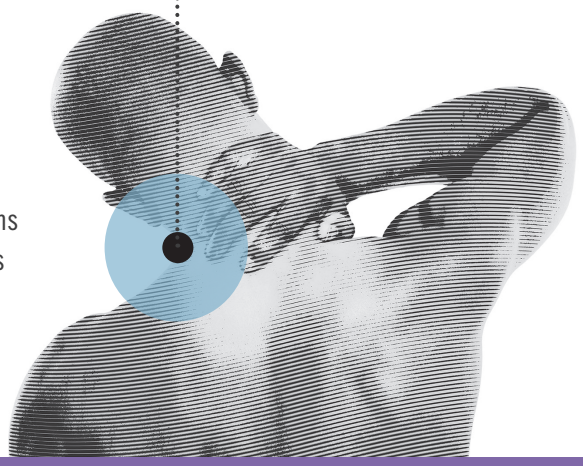
1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

CLINICAL REMINDERS

- **Opioids are not first-line or routine therapy for chronic pain**
- **Establish and measure goals for pain and function**
- **Discuss benefits and risks and availability of nonopioid therapies with patient**



U.S. Department of Health and Human Services
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LEARN MORE | www.cdc.gov/drugoverdose/prescribing/guideline.html

OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

CLINICAL REMINDERS

- **Use immediate-release opioids when starting**
- **Start low and go slow**
- **When opioids are needed for acute pain, prescribe no more than needed**
- **Do not prescribe ER/LA opioids for acute pain**
- **Follow-up and re-evaluate risk of harm; reduce dose or taper and discontinue if needed**

4 When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5 When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

6 Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

7 Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

ASSESSING RISK AND ADDRESSING HARMS OF OPIOID USE

8 Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.

9 Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

10 When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11 Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12 Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

CLINICAL REMINDERS

- **Evaluate risk factors for opioid-related harms**
- **Check PDMP for high dosages and prescriptions from other providers**
- **Use urine drug testing to identify prescribed substances and undisclosed use**
- **Avoid concurrent benzodiazepine and opioid prescribing**
- **Arrange treatment for opioid use disorder if needed**

Please note: An erratum has been published for this issue. To view the erratum, please click here.

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Recommendations and Reports / Vol. 65 / No. 1

March 18, 2016

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

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Disclosure of Relationship

The Core Expert Group (CEG) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Pam Archer discloses authorship of the Oklahoma Emergency Department and Urgent Care Clinic Opioid Prescribing Guidelines and the Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office Based Setting; Bonnie Burman discloses authorship of the Ohio Guidelines for Prescribing Opioids for the Treatment of Chronic, Non-Terminal Pain; Jane Ballantyne discloses that she has served as a paid consultant to Cohen Milstein Sellers & Toll, PLLC, and has special advisory committee responsibilities on the Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategies committee; Phillip Coffin discloses that in 2012 he provided expert testimony to the California State Assembly regarding a bill to expand naloxone access and reports that he is the principal investigator on a research study of methamphetamine dependence that receives donated injectable naltrexone from Alkermes, Inc.; Gary Franklin discloses authorship of the AMDG Interagency Guideline on Prescribing Opioids for Pain; Erin Krebs discloses that she represented the American College of Physicians at a 2014 Food and Drug Administration meeting on Abuse Deterrent Opioid Formulations; Lewis Nelson discloses his ad-hoc membership on the FDA Drug Safety and Risk Management Advisory Committee; Trupti Patel discloses authorship of the Arizona Opioid Prescribing Guidelines; Robert "Chuck" Rich discloses that he was an author of the 2013 American Academy of Family Physicians position paper on opioids and pain management; Joanna Starrels discloses that she received honoraria from the Betty Ford Institute; Thomas Tape discloses that he was an author of the 2013 American College of Physicians policy position paper on prescription drug abuse. CDC provided 100% of the funding for the supplemental evidence review tasks and meeting support. No foundation or industry support was accepted.

The Opioid Guideline Workgroup (OGW) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Anne Burns discloses that she participated in a congressional briefing sponsored by Reps. Carter and DeSaulnier on the pharmacist's role of furnishing Naloxone and that she participates on the National Advisory Board for the Prescription Drug Abuse and Heroin Summit. Chinazo Cunningham discloses that her husband is employed by Quest Diagnostics and Dr. Cunningham was recused from any discussion related to urine drug testing. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Erin Krebs discloses that she served on the CDC Opioid Prescribing Guideline CEG. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG. Greg Terman discloses that he serves as the President of the American Pain Society. Mark Wallace discloses that he served on a Kempharma advisory panel for an abuse-deterrent hydrocodone formulation to treat acute postoperative pain and Dr. Wallace was recused form any discussion related to abuse-deterrent drugs.

The NCIPC Board of Scientific Counselors (BSC) members disclose that they have no financial conflicts of interest. Two BSC members, Traci Green and Christina Porucznik, served on the Opioid Guideline Workgroup. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG.

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CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

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Summary

This guideline provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use. CDC developed the guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, and recommendations are made on the basis of a systematic review of the scientific evidence while considering benefits and harms, values and preferences, and resource allocation. CDC obtained input from experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee. It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (http://www.cdc.gov/drugoverdose/prescribingresources.html) with additional tools to guide clinicians in implementing the recommendations.

Introduction

Background

Opioids are commonly prescribed for pain. An estimated 20% of patients presenting to physician offices with noncancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription (*1*). In 2012, health care providers wrote 259 million prescriptions for opioid pain medication, enough for every adult in the United States to have a bottle of pills (*2*). Opioid prescriptions per capita increased 7.3% from 2007 to 2012, with opioid prescribing rates increasing more for family practice, general practice, and internal medicine compared with other specialties (*3*). Rates of opioid prescribing vary greatly across states in ways that cannot be explained by the underlying health status of the population, highlighting the lack of consensus among clinicians on how to use opioid pain medication (*2*).

Prevention, assessment, and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized, and patients, particularly members of racial and ethnic minority groups, women, the elderly, persons with cognitive impairment, and those with cancer and at the end of life, can be at risk for inadequate pain treatment (*4*). Patients can experience persistent pain that is not well controlled. There are clinical, psychological, and social consequences associated with chronic pain including limitations in complex activities, lost work productivity, reduced quality of life, and stigma, emphasizing the importance of appropriate and compassionate patient care (*4*). Patients should receive appropriate pain treatment based on a careful consideration of the benefits and risks of treatment options.

Chronic pain has been variably defined but is defined within this guideline as pain that typically lasts >3 months or past the time of normal tissue healing (*5*). Chronic pain can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause (*4*). Estimates of the prevalence of chronic pain vary, but it is clear that the number of persons experiencing chronic pain in the United States is substantial. The 1999–2002 National Health and Nutrition Examination Survey estimated that 14.6% of adults have current widespread or localized pain lasting at least 3 months (*6*). Based on a survey conducted during 2001–2003 (*7*), the overall prevalence of common, predominantly musculoskeletal pain conditions (e.g., arthritis, rheumatism, chronic back or neck problems, and frequent severe headaches) was estimated at 43% among adults in the

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United States, although minimum duration of symptoms was not specified. Most recently, analysis of data from the 2012 National Health Interview Study showed that 11.2% of adults report having daily pain (*8*). Clinicians should consider the full range of therapeutic options for the treatment of chronic pain. However, it is hard to estimate the number of persons who could potentially benefit from opioid pain medication long term. Evidence supports short-term efficacy of opioids for reducing pain and improving function in noncancer nociceptive and neuropathic pain in randomized clinical trials lasting primarily ≤12 weeks (*9*,*10*), and patients receiving opioid therapy for chronic pain report some pain relief when surveyed (*11*–*13*). However, few studies have been conducted to rigorously assess the long-term benefits of opioids for chronic pain (pain lasting >3 months) with outcomes examined at least 1 year later (*14*). On the basis of data available from health systems, researchers estimate that 9.6–11.5 million adults, or approximately 3%–4% of the adult U.S. population, were prescribed long-term opioid therapy in 2005 (*15*).

Opioid pain medication use presents serious risks, including overdose and opioid use disorder. From 1999 to 2014, more than 165,000 persons died from overdose related to opioid pain medication in the United States (*16*). In the past decade, while the death rates for the top leading causes of death such as heart disease and cancer have decreased substantially, the death rate associated with opioid pain medication has increased markedly (*17*). Sales of opioid pain medication have increased in parallel with opioid-related overdose deaths (*18*). The Drug Abuse Warning Network estimated that >420,000 emergency department visits were related to the misuse or abuse of narcotic pain relievers in 2011, the most recent year for which data are available (*19*). Although clinical criteria have varied over time, opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress. This disorder is manifested by specific criteria such as unsuccessful efforts to cut down or control use and use resulting in social problems and a failure to fulfill major role obligations at work, school, or home (*20*). This diagnosis has also been referred to as "abuse or dependence" and "addiction" in the literature, and is different from tolerance (diminished response to a drug with repeated use) and physical dependence (adaptation to a drug that produces symptoms of withdrawal when the drug is stopped), both of which can exist without a diagnosed disorder. In 2013, on the basis of DSM-IV diagnosis criteria, an estimated 1.9 million persons abused or were dependent on prescription opioid pain medication (*21*). Having a history of a prescription for an opioid pain medication increases the risk for overdose and opioid use disorder (*22*–*24*), highlighting the value of guidance on safer prescribing practices for clinicians. For example, a recent study of patients aged 15–64 years receiving opioids for chronic noncancer pain and followed for up to 13 years revealed that one in 550 patients died from opioid-related overdose at a median of 2.6 years from their first opioid prescription, and one in 32 patients who escalated to opioid dosages >200 morphine milligram equivalents (MME) died from opioid-related overdose (*25*).

This guideline provides recommendations for the prescribing of opioid pain medication by primary care clinicians for chronic pain (i.e., pain conditions that typically last >3 months or past the time of normal tissue healing) in outpatient settings outside of active cancer treatment, palliative care, and end-of-life care. Although the guideline does not focus broadly on pain management, appropriate use of long-term opioid therapy must be considered within the context of all pain management strategies (including nonopioid pain medications and nonpharmacologic treatments). CDC's recommendations are made on the basis of a systematic review of the best available evidence, along with input from experts, and further review and deliberation by a federally chartered advisory committee. The guideline is intended to ensure that clinicians and patients consider safer and more effective treatment, improve patient outcomes such as reduced pain and improved function, and reduce the number of persons who develop opioid use disorder, overdose, or experience other adverse events related to these drugs. Clinical decision making should be based on a relationship between the clinician and patient, and an understanding of the patient's clinical situation, functioning, and life context. The recommendations in the guideline are voluntary, rather than prescriptive standards. They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations. Clinicians should consider the circumstances and unique needs of each patient when providing care.

Rationale

Primary care clinicians report having concerns about opioid pain medication misuse, find managing patients with chronic pain stressful, express concern about patient addiction, and report insufficient training in prescribing opioids (*26*). Across specialties, physicians believe that opioid pain medication can be effective in controlling pain, that addiction is a common consequence of prolonged use, and that long-term opioid therapy often is overprescribed for patients with chronic noncancer pain (*27*). These attitudes and beliefs, combined with increasing trends in opioid-related overdose, underscore the need for better clinician guidance on opioid prescribing. Clinical practice guidelines focused on prescribing can improve clinician knowledge, change prescribing practices (*28*), and ultimately benefit patient health.

Professional organizations, states, and federal agencies (e.g., the American Pain Society/American Academy of Pain Medicine, 2009; the Washington Agency Medical Directors Group, 2015; and the U.S. Department of Veterans Affairs/Department of Defense, 2010) have developed guidelines for opioid prescribing (*29–31*). Existing guidelines share some common elements, including dosing thresholds, cautious titration, and risk mitigation strategies such as using risk assessment tools, treatment agreements, and urine drug testing. However, there is considerable variability in the specific recommendations (e.g., range of dosing thresholds of 90 MME/day to 200 MME/day), audience (e.g., primary care clinicians versus specialists), use of evidence (e.g., systematic review, grading of evidence and recommendations, and role of expert opinion), and rigor of methods for addressing conflict of interest (*32*). Most guidelines, especially those that are not based on evidence from scientific studies published in 2010 or later, also do not reflect the most recent scientific evidence about risks related to opioid dosage.

This CDC guideline offers clarity on recommendations based on the most recent scientific evidence, informed by expert opinion and stakeholder and public input. Scientific research has identified high-risk prescribing practices that have contributed to the overdose epidemic (e.g., high-dose prescribing, overlapping opioid and benzodiazepine prescriptions, and extended-release/long-acting [ER/LA] opioids for acute pain) (*24*,*33*,*34*). Using guidelines to address problematic prescribing has the potential to optimize care and improve patient safety based on evidence-based practice (*28*), as well as reverse the cycle of opioid pain medication misuse that contributes to the opioid overdose epidemic.

Scope and Audience

This guideline is intended for primary care clinicians (e.g., family physicians and internists) who are treating patients with chronic pain (i.e., pain lasting >3 months or past the time of normal tissue healing) in outpatient settings. Prescriptions by primary care clinicians account for nearly half of all dispensed opioid prescriptions, and the growth in prescribing rates among these clinicians has been above average (*3*). Primary care clinicians include physicians as well as nurse practitioners and physician assistants. Although the focus is on primary care clinicians, because clinicians work within team-based care, the recommendations refer to and promote integrated pain management and collaborative working relationships with other providers (e.g., behavioral health providers, pharmacists, and pain management specialists). Although the transition from use of opioid therapy for acute pain to use for chronic pain is hard to predict and identify, the guideline is intended to inform clinicians who are considering prescribing opioid pain medication for painful conditions that can or have become chronic.

This guideline is intended to apply to patients aged ≥18 years with chronic pain outside of palliative and end-of-life care. For this guideline, palliative care is defined in a manner consistent with that of the Institute of Medicine as care that provides relief from pain and other symptoms, supports quality of life, and is focused on patients with serious advanced illness. Palliative care can begin early in the course of treatment for any serious illness that requires excellent management of pain or other distressing symptoms (*35*). End-of-life care is defined as care for persons with a terminal illness or at high risk for dying in the near future in hospice care, hospitals, long-term care settings, or at home. Patients within the scope of this guideline include cancer survivors with chronic pain who have completed cancer treatment, are in clinical remission, and are under cancer surveillance only. The guideline is not intended for patients undergoing active cancer treatment, palliative care, or end-of-life care because of the unique therapeutic goals, ethical considerations, opportunities for medical supervision, and balance of risks and benefits with opioid therapy in such care.

The recommendations address the use of opioid pain medication in certain special populations (e.g., older adults and pregnant women) and in populations with conditions posing special risks (e.g., a history of substance use disorder). The recommendations do not address the use of opioid pain medication in children or adolescents aged <18 years. The available evidence concerning the benefits and harms of long-term opioid therapy in children and adolescents is limited, and few opioid medications provide information on the label regarding safety and effectiveness in pediatric patients. However, observational research shows significant increases in opioid prescriptions for pediatric populations from 2001 to 2010 (*36*), and a large proportion of adolescents are commonly prescribed opioid pain medications for conditions such as headache and sports injuries (e.g., in one study, 50% of adolescents presenting with headache received a prescription for an opioid pain medication [*37*,*38*]). Adolescents who misuse opioid pain medication often misuse medications from their own previous prescriptions (*39*), with an estimated 20% of adolescents with currently prescribed opioid medications reporting using them intentionally to get high or increase the effects of alcohol or other drugs (*40*). Use of prescribed opioid pain medication before high school graduation is associated with a 33% increase in the risk of later opioid misuse (*41*). Misuse of opioid pain medications in adolescence strongly predicts later onset of heroin use (*42*). Thus, risk of opioid medication use in pediatric populations is of great concern. Additional clinical trial and observational research is needed,

and encouraged, to inform development of future guidelines for this critical population.

The recommendations are not intended to provide guidance on use of opioids as part of medication-assisted treatment for opioid use disorder. Some of the recommendations might be relevant for acute care settings or other specialists, such as emergency physicians or dentists, but use in these settings or by other specialists is not the focus of this guideline. Readers are referred to other sources for prescribing recommendations within acute care settings and in dental practice, such as the American College of Emergency Physicians' guideline for prescribing of opioids in the emergency department (*43*); the American Society of Anesthesiologists' guideline for acute pain management in the perioperative setting (*44*); the Washington Agency Medical Directors' Group Interagency Guideline on Prescribing Opioids for Pain, Part II: Prescribing Opioids in the Acute and Subacute Phase (*30*); and the Pennsylvania Guidelines on the Use of Opioids in Dental Practice (*45*). In addition, given the challenges of managing the painful complications of sickle cell disease, readers are referred to the NIH National Heart, Lung, and Blood Institute's Evidence Based Management of Sickle Cell Disease Expert Panel Report for management of sickle cell disease (*46*).

Guideline Development Methods

Guideline Development Using the Grading of Recommendations Assessment, Development, and Evaluation Method

CDC developed this guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method (http://www.gradeworkinggroup.org). This method specifies the systematic review of scientific evidence and offers a transparent approach to grading quality of evidence and strength of recommendations. The method has been adapted by the CDC Advisory Committee on Immunization Practices (ACIP) (*47*). CDC has applied the ACIP translation of the GRADE framework in this guideline. Within the ACIP GRADE framework, the body of evidence is categorized in a hierarchy. This hierarchy reflects degree of confidence in the effect of a clinical action on health outcomes. The categories include type 1 evidence (randomized clinical trials or overwhelming evidence from observational studies), type 2 evidence (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 evidence (observational studies or randomized clinical trials with notable limitations), and type 4 evidence (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). Type of evidence is categorized by study design as well as limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and a constellation of plausible biases that could change observations of effects. Type 1 evidence indicates that one can be very confident that the true effect lies close to that of the estimate of the effect; type 2 evidence means that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; type 3 evidence means that confidence in the effect estimate is limited and the true effect might be substantially different from the estimate of the effect; and type 4 evidence indicates that one has very little confidence in the effect estimate, and the true effect is likely to be substantially different from the estimate of the effect (*47*,*48*). When no studies are present, evidence is considered to be insufficient. The ACIP GRADE framework places recommendations in two categories, Category A and Category B. Four major factors determine the category of the recommendation: the quality of evidence, the balance between desirable and undesirable effects, values and preferences, and resource allocation (cost). Category A recommendations apply to all persons in a specified group and indicate that most patients should receive the recommended course of action. Category B recommendations indicate that there should be individual decision making; different choices will be appropriate for different patients, so clinicians must help patients arrive at a decision consistent with patient values and preferences, and specific clinical situations (*47*). According to the GRADE methodology, a particular quality of evidence does not necessarily imply a particular strength of recommendation (*48–50*). Category A recommendations can be made based on type 3 or type 4 evidence when the advantages of a clinical action greatly outweigh the disadvantages based on a consideration of benefits and harms, values and preferences, and costs. Category B recommendations are made when the advantages and disadvantages of a clinical action are more balanced. GRADE methodology is discussed extensively elsewhere (*47*,*51*). The U.S. Preventive Services Task Force (USPSTF) follows different methods for developing and categorizing recommendations (http://www.uspreventiveservicestaskforce.org). USPSTF recommendations focus on preventive services and are categorized as A, B, C, D, and I. Under the Affordable Care Act, all "nongrandfathered" health plans (that is, those health plans not in existence prior to March 23, 2010 or those with significant changes to their coverage) and expanded Medicaid plans are required to cover

preventive services recommended by USPSTF with a category A or B rating with no cost sharing. The coverage requirements went into effect September 23, 2010. Similar requirements are in place for vaccinations recommended by ACIP, but do not exist for other recommendations made by CDC, including recommendations within this guideline.

A previously published systematic review sponsored by the Agency for Healthcare Research and Quality (AHRQ) on the effectiveness and risks of long-term opioid treatment of chronic pain (*14*,*52*) initially served to directly inform the recommendation statements. This systematic clinical evidence review addressed the effectiveness of long-term opioid therapy for outcomes related to pain, function, and quality of life; the comparative effectiveness of different methods for initiating and titrating opioids; the harms and adverse events associated with opioids; and the accuracy of risk-prediction instruments and effectiveness of risk mitigation strategies on outcomes related to overdose, addiction, abuse, or misuse. For the current guideline development, CDC conducted additional literature searches to update the evidence review to include more recently available publications and to answer an additional clinical question about the effect of opioid therapy for acute pain on long-term use. More details about the literature search strategies and GRADE methods applied are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026). CDC developed GRADE evidence tables to illustrate the quality of the evidence for each clinical question.

As identified in the AHRQ-sponsored clinical evidence review, the overall evidence base for the effectiveness and risks of long-term opioid therapy is low in quality per the GRADE criteria. Thus, contextual evidence is needed to provide information about the benefits and harms of nonpharmacologic and nonopioid pharmacologic therapy and the epidemiology of opioid pain medication overdose and inform the recommendations. Further, as elucidated by the GRADE Working Group, supplemental information on clinician and patient values and preferences and resource allocation can inform judgments of benefits and harms and be helpful for translating the evidence into recommendations. CDC conducted a contextual evidence review to supplement the clinical evidence review based on systematic searches of the literature. The review focused on the following four areas: effectiveness of nonpharmacologic and nonopioid pharmacologic treatments; benefits and harms related to opioid therapy (including additional studies not included in the clinical evidence review such as studies that evaluated outcomes at any duration or used observational study designs related to specific opioid pain medications, high-dose opioid therapy, co-prescription of opioids with other controlled substances, duration of opioid use, special populations, risk stratification/mitigation approaches, and effectiveness of treatments for addressing potential harms of opioid therapy); clinician and patient values and preferences; and resource allocation. CDC constructed narrative summaries of this contextual evidence and used the information to support the clinical recommendations. More details on methods for the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

On the basis of a review of the clinical and contextual evidence (review methods are described in more detail in subsequent sections of this report), CDC drafted recommendation statements focused on determining when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use. To help assure the draft guideline's integrity and credibility, CDC then began a multistep review process to obtain input from experts, stakeholders, and the public to help refine the recommendations.

Solicitation of Expert Opinion

CDC sought the input of experts to assist in reviewing the evidence and providing perspective on how CDC used the evidence to develop the draft recommendations. These experts, referred to as the "Core Expert Group" (CEG) included subject matter experts, representatives of primary care professional societies and state agencies, and an expert in guideline development methodology.* CDC identified subject matter experts with high scientific standing; appropriate academic and clinical training and relevant clinical experience; and proven scientific excellence in opioid prescribing, substance use disorder treatment, and pain management. CDC identified representatives from leading primary care professional organizations to represent the audience for this guideline. Finally, CDC identified state agency officials and representatives based on their experience with state guidelines for opioid prescribing that were developed with multiple agency stakeholders and informed by scientific literature and existing evidence-based guidelines.

Prior to their participation, CDC asked potential experts to reveal possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Experts could not serve if they had conflicts that might have a direct and predictable effect on the recommendations. CDC excluded experts who had a financial or promotional relationship with a company

* A list of the members appears at the end of this report. The recommendations and all statements included in this guideline are those of CDC and do not necessarily represent the official position of any persons or organizations providing comments on the draft guideline.

that makes a product that might be affected by the guideline. CDC reviewed potential nonfinancial conflicts carefully (e.g., intellectual property, travel, public statements or positions such as congressional testimony) to determine if the activities would have a direct and predictable effect on the recommendations. CDC determined the risk of these types of activities to be minimal for the identified experts. All experts completed a statement certifying that there was no potential or actual conflict of interest. Activities that did not pose a conflict (e.g., participation in Food and Drug Administration [FDA] activities or other guideline efforts) are disclosed.

CDC provided to each expert written summaries of the scientific evidence (both the clinical and contextual evidence reviews conducted for this guideline) and CDC's draft recommendation statements. Experts provided individual ratings for each draft recommendation statement based on the balance of benefits and harms, evidence strength, certainty of values and preferences, cost, recommendation strength, rationale, importance, clarity, and ease of implementation. CDC hosted an in-person meeting of the experts that was held on June 23–24, 2015, in Atlanta, Georgia, to seek their views on the evidence and draft recommendations and to better understand their premeeting ratings. CDC sought the experts' individual opinions at the meeting. Although there was widespread agreement on some of the recommendations, there was disagreement on others. Experts did not vote on the recommendations or seek to come to a consensus. Decisions about recommendations to be included in the guideline, and their rationale, were made by CDC. After revising the guideline, CDC sent written copies of it to each of the experts for review and asked for any additional comments; CDC reviewed these written comments and considered them when making further revisions to the draft guideline. The experts have not reviewed the final version of the guideline.

Federal Partner Engagement

Given the scope of this guideline and the interest of agencies across the federal government in appropriate pain management, opioid prescribing, and related outcomes, CDC invited its National Institute of Occupational Safety and Health and CDC's federal partners to observe the expert meeting, provide written comments on the full draft guideline after the meeting, and review the guideline through an agency clearance process; CDC reviewed comments and incorporated changes. Interagency collaboration will be critical for translating these recommendations into clinical practice. Federal partners included representatives from the Substance Abuse and Mental Health Services Administration, the National Institute on Drug Abuse, FDA, the U.S. Department of Veterans Affairs, the U.S. Department of Defense, the Office of the National Coordinator for Health Information Technology, the Centers for Medicare and Medicaid Services, the Health Resources and Services Administration, AHRQ, and the Office of National Drug Control Policy.

Stakeholder Comment

Given the importance of the guideline for a wide variety of stakeholders, CDC also invited review from a Stakeholder Review Group (SRG) to provide comment so that CDC could consider modifications that would improve the recommendations' specificity, applicability, and ease of implementation. The SRG included representatives from professional organizations that represent specialties that commonly prescribe opioids (e.g., pain medicine, physical medicine and rehabilitation), delivery systems within which opioid prescribing occurs (e.g., hospitals), and representation from community organizations with interests in pain management and opioid prescribing.* Representatives from each of the SRG organizations were provided a copy of the guideline for comment. Each of these representatives provided written comments. Once input was received from the full SRG, CDC reviewed all comments and carefully considered them when revising the draft guideline.

Constituent Engagement

To obtain initial perspectives from constituents on the recommendation statements, including clinicians and prospective patients, CDC convened a constituent engagement webinar and circulated information about the webinar in advance through announcements to partners. CDC hosted the webinar on September 16 and 17, 2015, provided information about the methodology for developing the guideline, and presented the key recommendations. A fact sheet was posted on the CDC Injury Center website (http://www.cdc.gov/injury) summarizing the guideline development process and clinical practice areas addressed in the guideline; instructions were included on how to submit comments via email. CDC received comments during and for 2 days following the first webinar. Over 1,200 constituent comments were received. Comments were reviewed and carefully considered when revising the draft guideline.

Peer Review

Per the final information quality bulletin for peer review (https://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf), peer review requirements applied to this guideline because it provides influential

scientific information that could have a clear and substantial impact on public- and private-sector decisions. Three experts independently reviewed the guideline to determine the reasonableness and strength of recommendations; the clarity with which scientific uncertainties were clearly identified; and the rationale, importance, clarity, and ease of implementation of the recommendations.* CDC selected peer reviewers based on expertise, diversity of scientific viewpoints, and independence from the guideline development process. CDC assessed and managed potential conflicts of interest using a process similar to the one as described for solicitation of expert opinion. No financial interests were identified in the disclosure and review process, and nonfinancial activities were determined to be of minimal risk; thus, no significant conflict of interest concerns were identified. CDC placed the names of peer reviewers on the CDC and the National Center for Injury Prevention and Control Peer Review Agenda websites that are used to provide information about the peer review of influential documents. CDC reviewed peer review comments and revised the draft guideline accordingly.

Public Comment

To obtain comments from the public on the full guideline, CDC published a notice in the *Federal Register* (80 FR 77351) announcing the availability of the guideline and the supporting clinical and contextual evidence reviews for public comment. The comment period closed January 13, 2016. CDC received more than 4,350 comments from the general public, including patients with chronic pain, clinicians, families who have lost loved ones to overdose, medical associations, professional organizations, academic institutions, state and local governments, and industry. CDC reviewed each of the comments and carefully considered them when revising the draft guideline.

Federal Advisory Committee Review and Recommendation

The National Center for Injury Prevention and Control (NCIPC) Board of Scientific Counselors (BSC) is a federal advisory committee that advises and makes recommendations to the Secretary of the Department of Health and Human Services, the Director of CDC, and the Director of NCIPC.* The BSC makes recommendations regarding policies, strategies, objectives, and priorities, and reviews progress toward injury and violence prevention. CDC sought the BSC's advice on the draft guideline. BSC members are special government employees appointed as CDC advisory committee members; as such, all members completed an OGE Form 450 to disclose relevant interests. BSC members also reported on their disclosures during meetings. Disclosures for the BSC are reported in the guideline.

To assist in guideline review, on December 14, 2015, via Federal Register notice, CDC announced the intent to form an Opioid Guideline Workgroup (OGW) to provide observations on the draft guideline to the BSC. CDC provided the BSC with the draft guideline as well as summaries of comments provided to CDC by stakeholders, constituents, and peer reviewers, and edits made to the draft guideline in response. During an open meeting held on January 7, 2016, the BSC recommended the formation of the OGW. The OGW included a balance of perspectives from audiences directly affected by the guideline, audiences that would be directly involved with implementing the recommendations, and audiences qualified to provide representation. The OGW comprised clinicians, subject matter experts, and a patient representative, with the following perspectives represented: primary care, pain medicine, public health, behavioral health, substance abuse treatment, pharmacy, patients, and research.* Additional sought-after attributes were appropriate academic and clinical training and relevant clinical experience; high scientific standing; and knowledge of the patient, clinician, and caregiver perspectives. In accordance with CDC policy, two BSC committee members also served as OGW members, with one serving as the OGW Chair. The professional credentials and interests of OGW members were carefully reviewed to identify possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Only OGW members whose interests were determined to be minimal were selected. When an activity was perceived as having the potential to affect a specific aspect of the recommendations, the activity was disclosed, and the OGW member was recused from discussions related to that specific aspect of the recommendations (e.g., urine drug testing and abuse-deterrent formulations). Disclosures for the OGW are reported. CDC and the OGW identified ad-hoc consultants to supplement the workgroup expertise, when needed, in the areas of pediatrics, occupational medicine, obstetrics and gynecology, medical ethics, addiction psychiatry, physical medicine and rehabilitation, guideline development methodology, and the perspective of a family member who lost a loved one to opioid use disorder or overdose.

The BSC charged the OGW with reviewing the quality of the clinical and contextual evidence reviews and reviewing each of the recommendation statements and accompanying rationales. For each recommendation statement, the OGW considered the quality of the evidence, the balance of benefits and risks, the values and preferences of clinicians and patients, the cost feasibility, and the category designation

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of the recommendation (A or B). The OGW also reviewed supplementary documents, including input provided by the CEG, SRG, peer reviewers, and the public. OGW members discussed the guideline accordingly during virtual meetings and drafted a summary report of members' observations, including points of agreement and disagreement, and delivered the report to the BSC.

NCIPC announced an open meeting of the NCIPC BSC in the Federal Register on January 11, 2015. The BSC met on January 28, 2016, to discuss the OGW report and deliberate on the draft guideline itself. Members of the public provided comments at this meeting. After discussing the OGW report, deliberating on specific issues about the draft guideline identified at the meeting, and hearing public comment, the BSC voted unanimously: to support the observations made by the OGW; that CDC adopt the guideline recommendations that, according to the workgroup's report, had unanimous or majority support; and that CDC further consider the guideline recommendations for which the group had mixed opinions. CDC carefully considered the OGW observations, public comments, and BSC recommendations, and revised the guideline in response.

Summary of the Clinical Evidence Review

Primary Clinical Questions

CDC conducted a clinical systematic review of the scientific evidence to identify the effectiveness, benefits, and harms of long-term opioid therapy for chronic pain, consistent with the GRADE approach (*47*,*48*). Long-term opioid therapy is defined as use of opioids on most days for >3 months. A previously published AHRQ-funded systematic review on the effectiveness and risks of long-term opioid therapy for chronic pain comprehensively addressed four clinical questions (*14*,*52*). CDC, with the assistance of a methodology expert, searched the literature to identify newly published studies on these four original questions. Because long-term opioid use might be affected by use of opioids for acute pain, CDC subsequently developed a fifth clinical question (last in the series below), and in collaboration with a methodologist conducted a systematic review of the scientific evidence to address it. In brief, five clinical questions were addressed:

- The effectiveness of long-term opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for long term (≥1 year) outcomes related to pain, function, and quality of life, and how effectiveness varies according to the type/cause of pain, patient demographics, and patient comorbidities (Key Question [KQ] 1).
- The risks of opioids versus placebo or no opioids on abuse, addiction, overdose, and other harms, and how harms vary according to the type/cause of pain, patient demographics, patient comorbidities, and dose (KQ2).
- The comparative effectiveness of opioid dosing strategies (different methods for initiating and titrating opioids; immediate-release versus ER/LA opioids; different ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled, continuous versus as-needed dosing; dose escalation versus dose maintenance; opioid rotation versus maintenance; different strategies for treating acute exacerbations of chronic pain; decreasing opioid doses or tapering off versus continuation; and different tapering protocols and strategies) (KQ3).
- The accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse; the effectiveness of risk mitigation strategies (use of risk prediction instruments); effectiveness of risk mitigation strategies including opioid management plans, patient education, urine drug testing, prescription drug monitoring program (PDMP) data, monitoring instruments, monitoring intervals, pill counts, and abuse-deterrent formulations for reducing risk for opioid overdose, addiction, abuse, or misuse; and the comparative effectiveness of treatment strategies for managing patients with addiction (KQ4).
- The effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain on long-term use (KQ5).

The review was focused on the effectiveness of long-term opioid therapy on long-term (>1 year) outcomes related to pain, function, and quality of life to ensure that findings are relevant to patients with chronic pain and long-term opioid prescribing. The effectiveness of short-term opioid therapy has already been established (*10*). However, opioids have unique effects such as tolerance and physical dependence that might influence assessments of benefit over time. These effects raise questions about whether findings on short-term effectiveness of opioid therapy can be extrapolated to estimate benefits of long-term therapy for chronic pain. Thus, it is important to consider studies that provide data on long-term benefit. For certain opioid-related harms (overdose, fractures, falls, motor vehicle crashes), observational studies were included with outcomes measured at shorter intervals because such outcomes can occur early during opioid therapy, and such harms are not captured well in short-term clinical trials. A detailed listing of the key questions is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Clinical Evidence Systematic Review Methods

Complete methods and data for the 2014 AHRQ report, upon which this updated systematic review is based, have been published previously (*14*,*52*). Study authors developed the protocol using a standardized process (*53*) with input from experts and the public and registered the protocol in the PROSPERO database (*54*). For the 2014 AHRQ report, a research librarian searched MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL for English-language articles published January 2008 through August 2014, using search terms for opioid therapy, specific opioids, chronic pain, and comparative study designs. Also included were relevant studies from an earlier review (*10*) in which searches were conducted without a date restriction, reference lists were reviewed, and ClinicalTrials.gov was searched. CDC updated the AHRQ literature search using the same search strategies as in the original review including studies published before April, 2015. Seven additional studies met inclusion criteria and were added to the review. CDC used the GRADE approach outlined in the ACIP Handbook for Developing Evidence-Based Recommendations (*47*) to rate the quality of evidence for the full body of evidence (evidence from the 2014 AHRQ review plus the update) for each clinical question. Evidence was categorized into the following types: type 1 (randomized clinical trials or overwhelming evidence from observational studies), type 2 (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 (observational studies, or randomized clinical trials with notable limitations), or type 4 (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). When no studies were present, evidence was considered to be insufficient. Per GRADE methods, type of evidence was categorized by study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects. Results were synthesized qualitatively, highlighting new evidence identified during the update process. Meta-analysis was not attempted due to the small numbers of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of the studies. More detailed information about data sources and searches, study selection, data extraction and quality assessment, data synthesis, and update search yield and new evidence for the current review is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Summary of Findings for Clinical Questions

The main findings of this updated review are consistent with the findings of the 2014 AHRQ report (*14*). In summary, evidence on long-term opioid therapy for chronic pain outside of end-of-life care remains limited, with insufficient evidence to determine long-term benefits versus no opioid therapy, though evidence suggests risk for serious harms that appears to be dose-dependent. These findings supplement findings from a previous review of the effectiveness of opioids for adults with chronic noncancer pain. In this previous review, based on randomized trials predominantly ≤12 weeks in duration, opioids were found to be moderately effective for pain relief, with small benefits for functional outcomes; although estimates vary, based on uncontrolled studies, a high percentage of patients discontinued long-term opioid use because of lack of efficacy and because of adverse events (*10*).

The GRADE evidence summary with type of evidence ratings for the five clinical questions for the current evidence review are outlined (Table 1). This summary is based on studies included in the AHRQ 2014 review (35 studies) plus additional studies identified in the updated search (seven studies). Additional details on findings from the original review are provided in the full 2014 AHRQ report (*14*,*52*). Full details on the clinical evidence review findings supporting this guideline are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Effectiveness

For KQ1, no study of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for chronic pain evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were ≤6 weeks in duration. Thus, the body of evidence for KQ1 is rated as insufficient (0 studies contributing) (*14*).

Harms

For KQ2, the body of evidence is rated as type 3 (12 studies contributing; 11 from the original review plus one new study). One fair-quality cohort study found that long-term opioid therapy is associated with increased risk for an opioid abuse or dependence diagnosis (as defined by ICD-9-CM codes) versus no opioid prescription (*22*). Rates of opioid abuse or dependence diagnosis ranged from 0.7% with lower-dose (≤36 MME) chronic therapy to 6.1% with higher-dose (≥120 MME) chronic therapy, versus 0.004% with no opioids prescribed. Ten fair-quality uncontrolled studies reported estimates of opioid abuse, addiction, and related outcomes (*55*–*65*). In primary care settings, prevalence of opioid dependence

(using DSM-IV criteria) ranged from 3% to 26% (*55*,*56*,*59*). In pain clinic settings, prevalence of addiction ranged from 2% to 14% (*57*,*58*,*60*,*61*,*63–65*).

Factors associated with increased risk for misuse included history of substance use disorder, younger age, major depression, and use of psychotropic medications (*55*,*62*). Two studies reported on the association between opioid use and risk for overdose (*66*,*67*). One large fair-quality retrospective cohort study found that recent opioid use was associated with increased risk for any overdose events and serious overdose events versus nonuse (*66*). It also found higher doses associated with increased risk. Relative to 1–19 MME/day, the adjusted hazard ratio (HR) for any overdose event (consisting of mostly nonfatal overdose) was 1.44 for 20 to 49 MME/day, 3.73 for 50–99 MME/day, and 8.87 for ≥100 MME/day. A similar pattern was observed for serious overdose. A good-quality population-based, nested case-control study also found a dose-dependent association with risk for overdose death (*67*). Relative to 1–19 MME/day, the adjusted odds ratio (OR) was 1.32 for 20–49 MME/day, 1.92 for 50–99 MME/day, 2.04 for 100–199 MME/day, and 2.88 for ≥200 MME/day.

Findings of increased fracture risk for current opioid use, versus nonuse, were mixed in two studies (*68*,*69*). Two studies found an association between opioid use and increased risk for cardiovascular events (*70*,*71*). Indirect evidence was found for endocrinologic harms (increased use of medications for erectile dysfunction or testosterone from one previously included study; laboratory-defined androgen deficiency from one newly reviewed study) (*72*,*73*). One study found that opioid dosages ≥20 MME/day were associated with increased odds of road trauma among drivers (*74*).

Opioid Dosing Strategies

For KQ3, the body of evidence is rated as type 4 (14 studies contributing; 12 from the original review plus two new studies). For initiation and titration of opioids, the 2014 AHRQ report found insufficient evidence from three fair-quality, open-label trials to determine comparative effectiveness of ER/LA versus immediate-release opioids for titrating patients to stable pain control (*75*,*76*). One new fair-quality cohort study of Veterans Affairs patients found initiation of therapy with an ER/LA opioid associated with greater risk for nonfatal overdose than initiation with an immediate-release opioid, with risk greatest in the first 2 weeks after initiation of treatment (*77*).

For comparative effectiveness and harms of ER/LA opioids, the 2014 AHRQ report included three randomized, head-to-head trials of various ER/LA opioids that found no clear differences in 1-year outcomes related to pain or function (*78–80*) but had methodological shortcomings. A fair-quality retrospective cohort study based on national Veterans Health Administration system pharmacy data found that methadone was associated with lower overall risk for all-cause mortality versus morphine (*81*), and a fair-quality retrospective cohort study based on Oregon Medicaid data found no statistically significant differences between methadone and long-acting morphine in risk for death or overdose symptoms (*82*). However, a new observational study (*83*) found methadone associated with increased risk for overdose versus sustained-release morphine among Tennessee Medicaid patients. The observed inconsistency in study findings suggests that risks of methadone might vary in different settings as a function of different monitoring and management protocols, though more research is needed to understand factors associated with safer methadone prescribing.

For dose escalation, the 2014 AHRQ report included one fair-quality randomized trial that found no differences between more liberal dose escalation and maintenance of current doses after 12 months in pain, function, all-cause withdrawals, or withdrawals due to opioid misuse (*84*). However, the difference in opioid dosages prescribed at the end of the trial was relatively small (mean 52 MME/day with more liberal dosing versus 40 MME/day). Evidence on other comparisons related to opioid dosing strategies (ER/LA versus immediate-release opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled continuous dosing versus as-needed dosing; or opioid rotation versus maintenance of current therapy; long-term effects of strategies for treating acute exacerbations of chronic pain) was not available or too limited to determine effects on long-term clinical outcomes. For example, evidence on the comparative effectiveness of opioid tapering or discontinuation versus maintenance, and of different opioid tapering strategies, was limited to small, poor-quality studies (*85–87*).

Risk Assessment and Mitigation

For KQ4, the body of evidence is rated as type 3 for the accuracy of risk assessment tools and insufficient for the effectiveness of use of risk assessment tools and mitigation strategies in reducing harms (six studies contributing; four from the original review plus two new studies). The 2014 AHRQ report included four studies (*88–91*) on the accuracy of risk assessment instruments, administered prior to opioid therapy initiation, for predicting opioid abuse or misuse. Results for the Opioid Risk Tool (ORT) (*89–91*) were extremely inconsistent; evidence for other risk assessment instruments was very sparse, and studies had serious methodological shortcomings. One additional fair-quality (*92*) and one poor-quality (*93*) study identified for this update compared the predictive accuracy of the ORT, the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), and the Brief Risk Interview.

For the ORT, sensitivity was 0.58 and 0.75 and specificity 0.54 and 0.86; for the SOAPP-R, sensitivity was 0.53 and 0.25 and specificity 0.62 and 0.73; and for the Brief Risk Interview, sensitivity was 0.73 and 0.83 and specificity 0.43 and 0.88. For the ORT, positive likelihood ratios ranged from noninformative (positive likelihood ratio close to 1) to moderately useful (positive likelihood ratio >5). The SOAPP-R was associated with noninformative likelihood ratios (estimates close to 1) in both studies.

No study evaluated the effectiveness of risk mitigation strategies (use of risk assessment instruments, opioid management plans, patient education, urine drug testing, use of PDMP data, use of monitoring instruments, more frequent monitoring intervals, pill counts, or use of abuse-deterrent formulations) for improving outcomes related to overdose, addiction, abuse, or misuse.

Effects of Opioid Therapy for Acute Pain on Long-Term Use

For KQ5, the body of evidence is rated as type 3 (two new studies contributing). Two fair-quality retrospective cohort studies found opioid therapy prescribed for acute pain associated with greater likelihood of long-term use. One study evaluated opioid-naïve patients who had undergone low-risk surgery, such as cataract surgery and varicose vein stripping (*94*). Use of opioids within 7 days of surgery was associated with increased risk for use at 1 year. The other study found that among patients with a workers' compensation claim for acute low back pain, compared to patients who did not receive opioids early after injury (defined as use within 15 days following onset of pain), patients who did receive early opioids had an increased likelihood of receiving five or more opioid prescriptions 30–730 days following onset that increased with greater early exposure. Versus no early opioid use, the adjusted OR was 2.08 (95% CI = 1.55–2.78) for 1–140 MME/day and increased to 6.14 (95% confidence interval [CI] = 4.92–7.66) for ≥450 MME/day (*95*).

Summary of the Contextual Evidence Review

Primary Areas of Focus

Contextual evidence is complementary information that assists in translating the clinical research findings into recommendations. CDC conducted contextual evidence reviews on four topics to supplement the clinical evidence review findings:

- Effectiveness of nonpharmacologic (e.g., cognitive behavioral therapy [CBT], exercise therapy, interventional treatments, and multimodal pain treatment) and nonopioid pharmacologic treatments (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, and anticonvulsants), including studies of any duration.
- Benefits and harms of opioid therapy (including additional studies not included in the clinical evidence review, such as studies that were not restricted to patients with chronic pain, evaluated outcomes at any duration, performed ecological analyses, or used observational study designs other than cohort and case-cohort control studies) related to specific opioids, high-dose therapy, co-prescription with other controlled substances, duration of use, special populations, and potential usefulness of risk stratification/mitigation approaches, in addition to effectiveness of treatments associated with addressing potential harms of opioid therapy (opioid use disorder).
- Clinician and patient values and preferences related to opioids and medication risks, benefits, and use.
- Resource allocation including costs and economic efficiency of opioid therapy and risk mitigation strategies.

CDC also reviewed clinical guidelines that were relevant to opioid prescribing and could inform or complement the CDC recommendations under development (e.g., guidelines on nonpharmacologic and nonopioid pharmacologic treatments and guidelines with recommendations related to specific clinician actions such as urine drug testing or opioid tapering protocols).

Contextual Evidence Review Methods

CDC conducted a contextual evidence review to assist in developing the recommendations by providing an assessment of the balance of benefits and harms, values and preferences, and cost, consistent with the GRADE approach. Given the public health urgency for developing opioid prescribing recommendations, a rapid review was required for the contextual evidence review for the current guideline. Rapid reviews are used when there is a need to streamline the systematic review process to obtain evidence quickly (*96*). Methods used to streamline the process include limiting searches by databases, years, and languages considered, and truncating quality assessment and data abstraction protocols. CDC conducted "rapid reviews" of the contextual evidence on nonpharmacologic and nonopioid pharmacologic treatments, benefits and harms, values and preferences, and resource allocation.

Detailed information about contextual evidence data sources and searches, inclusion criteria, study selection, and

data extraction and synthesis are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). In brief, CDC conducted systematic literature searches to identify original studies, systematic reviews, and clinical guidelines, depending on the topic being searched. CDC also solicited publication referrals from subject matter experts. Given the need for a rapid review process, grey literature (e.g., literature by academia, organizations, or government in the forms of reports, documents, or proceedings not published by commercial publishers) was not systematically searched. Database sources, including MEDLINE, PsycINFO, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews, varied by topic. Multiple reviewers scanned study abstracts identified through the database searches and extracted relevant studies for review. CDC constructed narrative summaries and tables based on relevant articles that met inclusion criteria, which are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Findings from the contextual reviews provide indirect evidence and should be interpreted accordingly. CDC did not formally rate the quality of evidence for the studies included in the contextual evidence review using the GRADE method. The studies that addressed benefits and harms, values and preferences, and resource allocation most often employed observational methods, used short follow-up periods, and evaluated selected samples. Therefore the strength of the evidence from these contextual review areas was considered to be low, comparable to type 3 or type 4 evidence. The quality of evidence for nonopioid pharmacologic and nonpharmacologic pain treatments was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines (e.g., for treatment of chronic neuropathic pain, low back pain, osteoarthritis, and fibromyalgia). Similarly, the quality of evidence on pharmacologic and psychosocial opioid use disorder treatment was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines.

Summary of Findings for Contextual Areas

Full narrative reviews and tables that summarize key findings from the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Effectiveness of Nonpharmacologic and Nonopioid Pharmacologic Treatments

Several nonpharmacologic and nonopioid pharmacologic treatments have been shown to be effective in managing chronic pain in studies ranging in duration from 2 weeks to 6 months. For example, CBT that trains patients in behavioral techniques and helps patients modify situational factors and cognitive processes that exacerbate pain has small positive effects on disability and catastrophic thinking (*97*). Exercise therapy can help reduce pain and improve function in chronic low back pain (*98*), improve function and reduce pain in osteoarthritis of the knee (*99*) and hip (*100*), and improve well-being, fibromyalgia symptoms, and physical function in fibromyalgia (*101*). Multimodal and multidisciplinary therapies (e.g., therapies that combine exercise and related therapies with psychologically based approaches) can help reduce pain and improve function more effectively than single modalities (*102*,*103*). Nonopioid pharmacologic approaches used for pain include analgesics such as acetaminophen, NSAIDs, and cyclooxygenase 2 (COX-2) inhibitors; selected anticonvulsants; and selected antidepressants (particularly tricyclics and serotonin and norepinephrine reuptake inhibitors [SNRIs]). Multiple guidelines recommend acetaminophen as first-line pharmacotherapy for osteoarthritis (*104*–*109*) or for low back pain (*110*) but note that it should be avoided in liver failure and that dosage should be reduced in patients with hepatic insufficiency or a history of alcohol abuse (*109*). Although guidelines also recommend NSAIDs as first-line treatment for osteoarthritis or low back pain (*106*,*110*), NSAIDs and COX-2 inhibitors do have risks, including gastrointestinal bleeding or perforation as well as renal and cardiovascular risks (*111*). FDA has recently strengthened existing label warnings that NSAIDs increase risks for heart attack and stroke, including that these risks might increase with longer use or at higher doses (*112*). Several guidelines agree that first- and second-line drugs for neuropathic pain include anticonvulsants (gabapentin or pregabalin), tricyclic antidepressants, and SNRIs (*113*–*116*). Interventional approaches such as epidural injection for certain conditions (e.g., lumbar radiculopathy) can provide short-term improvement in pain (*117*–*119*). Epidural injection has been associated with rare but serious adverse events, including loss of vision, stroke, paralysis, and death (*120*).

Benefits and Harms of Opioid Therapy

Balance between benefits and harms is a critical factor influencing the strength of clinical recommendations. In particular, CDC considered what is known from the epidemiology research about benefits and harms related to specific opioids and formulations, high dose therapy, co-prescription with other controlled substances, duration of use, special populations, and risk stratification and mitigation approaches. Additional information on benefits and harms of long-term opioid therapy from studies meeting rigorous selection criteria is provided in the clinical evidence review (e.g., see KQ2). CDC also considered the number of persons experiencing chronic pain, numbers potentially benefiting

from opioids, and numbers affected by opioid-related harms. A review of these data is presented in the background section of this document, with detailed information provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). Finally, CDC considered the effectiveness of treatments that addressed potential harms of opioid therapy (opioid use disorder).

Regarding specific opioids and formulations, as noted by FDA, there are serious risks of ER/LA opioids, and the indication for this class of medications is for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment in patients for whom other treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain (*121*). Time-scheduled opioid use was associated with substantially higher average daily opioid dosage than as-needed opioid use in one study (*122*). Methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for pain. Methadone has been found to account for as much as a third of opioid-related overdose deaths involving single or multiple drugs in states that participated in the Drug Abuse Warning Network, which was more than any opioid other than oxycodone, despite representing <2% of opioid prescriptions outside of opioid treatment programs in the United States; further, methadone was involved in twice as many single-drug deaths as any other prescription opioid (*123*).

Regarding high-dose therapy, several epidemiologic studies that were excluded from the clinical evidence review because patient samples were not restricted to patients with chronic pain also examined the association between opioid dosage and overdose risk (*23*,*24*,*124*–*126*). Consistent with the clinical evidence review, the contextual review found that opioid-related overdose risk is dose-dependent, with higher opioid dosages associated with increased overdose risk. Two of these studies (*23*,*24*), as well as the two studies in the clinical evidence review (*66*,*67*), evaluated similar MME/day dose ranges for association with overdose risk. In these four studies, compared with opioids prescribed at <20 MME/day, the odds of overdose among patients prescribed opioids for chronic nonmalignant pain were between 1.3 (*67*) and 1.9 (*24*) for dosages of 20 to <50 MME/day, between 1.9 (*67*) and 4.6 (*24*) for dosages of 50 to <100 MME/day, and between 2.0 (*67*) and 8.9 (*66*) for dosages of ≥100 MME/day. Compared with dosages of 1–<20 MME/day, absolute risk difference approximation for 50–<100 MME/day was 0.15% for fatal overdose (*24*) and 1.40% for any overdose (*66*), and for ≥100 MME/day was 0.25% for fatal overdose (*24*) and 4.04% for any overdose (*66*). A recent study of Veterans Health Administration patients with chronic pain found that patients who died of overdoses related to opioids were prescribed higher opioid dosages (mean: 98 MME/day; median: 60 MME/day) than controls (mean: 48 MME/day, median: 25 MME/day) (*127*). Finally, another recent study of overdose deaths among state residents with and without opioid prescriptions revealed that prescription opioid-related overdose mortality rates rose rapidly up to prescribed doses of 200 MME/day, after which the mortality rates continued to increase but grew more gradually (*128*). A listing of common opioid medications and their MME equivalents is provided (Table 2).

Regarding coprescription of opioids with benzodiazepines, epidemiologic studies suggest that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (*67*,*128*,*129*). In one of these studies (*67*), among decedents who received an opioid prescription, those whose deaths were related to opioids were more likely to have obtained opioids from multiple physicians and pharmacies than decedents whose deaths were not related to opioids.

Regarding duration of use, patients can experience tolerance and loss of effectiveness of opioids over time (*130*). Patients who do not experience clinically meaningful pain relief early in treatment (i.e., within 1 month) are unlikely to experience pain relief with longer-term use (*131*).

Regarding populations potentially at greater risk for harm, risk is greater for patients with sleep apnea or other causes of sleep-disordered breathing, patients with renal or hepatic insufficiency, older adults, pregnant women, patients with depression or other mental health conditions, and patients with alcohol or other substance use disorders. Interpretation of clinical data on the effects of opioids on sleep-disordered breathing is difficult because of the types of study designs and methods employed, and there is no clear consensus regarding association with risk for developing obstructive sleep apnea syndrome (*132*). However, opioid therapy can decrease respiratory drive, a high percentage of patients on long-term opioid therapy have been reported to have an abnormal apnea-hypopnea index (*133*), opioid therapy can worsen central sleep apnea in obstructive sleep apnea patients, and it can cause further desaturation in obstructive sleep apnea patients not on continuous positive airway pressure (CPAP) (*31*). Reduced renal or hepatic function can result in greater peak effect and longer duration of action and reduce the dose at which respiratory depression and overdose occurs (*134*). Age-related changes in patients aged ≥65 years, such as reduced renal function and medication clearance, even in the absence of renal disease (*135*), result in a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose. Older adults might also be at increased risk for falls and fractures related to opioids (*136*–*138*). Opioids used

in pregnancy can be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with birth defects, including neural tube defects (*139*,*140*), congenital heart defects (*140*), and gastroschisis (*140*); preterm delivery (*141*), poor fetal growth (*141*), and stillbirth (*141*). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome (*142*). Patients with mental health comorbidities and patients with histories of substance use disorders might be at higher risk than other patients for opioid use disorder (*62*,*143*,*144*). Recent analyses found that depressed patients were at higher risk for drug overdose than patients without depression, particularly at higher opioid dosages, although investigators were unable to distinguish unintentional overdose from suicide attempts (*145*). In case-control and case-cohort studies, substance abuse/dependence was more prevalent among patients experiencing overdose than among patients not experiencing overdose (12% versus 6% [*66*], 40% versus 10% [*24*], and 26% versus 9% [*23*]).

Regarding risk stratification approaches, limited evidence was found regarding benefits and harms. Potential benefits of PDMPs and urine drug testing include the ability to identify patients who might be at higher risk for opioid overdose or opioid use disorder, and help determine which patients will benefit from greater caution and increased monitoring or interventions when risk factors are present. For example, one study found that most fatal overdoses could be identified retrospectively on the basis of two pieces of information, multiple prescribers and high total daily opioid dosage, both important risk factors for overdose (*124*,*146*) that are available to prescribers in the PDMP (*124*). However, limited evaluation of PDMPs at the state level has revealed mixed effects on changes in prescribing and mortality outcomes (*28*). Potential harms of risk stratification include underestimation of risks of opioid therapy when screening tools are not adequately sensitive, as well as potential overestimation of risk, which could lead to inappropriate clinical decisions.

Regarding risk mitigation approaches, limited evidence was found regarding benefits and harms. Although no studies were found to examine prescribing of naloxone with opioid pain medication in primary care settings, naloxone distribution through community-based programs providing prevention services for substance users has been demonstrated to be associated with decreased risk for opioid overdose death at the community level (*147*).

Concerns have been raised that prescribing changes such as dose reduction might be associated with unintended negative consequences, such as patients seeking heroin or other illicitly obtained opioids (*148*) or interference with appropriate pain treatment (*149*). With the exception of a study noting an association between an abuse-deterrent formulation of OxyContin and heroin use, showing that some patients in qualitative interviews reported switching to another opioid, including heroin, for many reasons, including cost and availability as well as ease of use (*150*), CDC did not identify studies evaluating these potential outcomes.

Finally, regarding the effectiveness of opioid use disorder treatments, methadone and buprenorphine for opioid use disorder have been found to increase retention in treatment and to decrease illicit opioid use among patients with opioid use disorder involving heroin (*151*–*153*). Although findings are mixed, some studies suggest that effectiveness is enhanced when psychosocial treatments (e.g., contingency management, community reinforcement, psychotherapeutic counseling, and family therapy) are used in conjunction with medication-assisted therapy; for example, by reducing opioid misuse and increasing retention during maintenance therapy, and improving compliance after detoxification (*154*,*155*).

Clinician and Patient Values and Preferences

Clinician and patient values and preferences can inform how benefits and harms of long-term opioid therapy are weighted and estimate the effort and resources required to effectively provide implementation support. Many physicians lack confidence in their ability to prescribe opioids safely (*156*), to predict (*157*) or detect (*158*) prescription drug abuse, and to discuss abuse with their patients (*158*). Although clinicians have reported favorable beliefs and attitudes about improvements in pain and quality of life attributed to opioids (*159*), most consider prescription drug abuse to be a "moderate" or "big" problem in their community, and large proportions are "very" concerned about opioid addiction (55%) and death (48%) (*160*). Clinicians do not consistently use practices intended to decrease the risk for misuse, such as PDMPs (*161*,*162*), urine drug testing (*163*), and opioid treatment agreements (*164*). This is likely due in part to challenges related to registering for PDMP access and logging into the PDMP (which can interrupt normal clinical workflow if data are not integrated into electronic health record systems) (*165*), competing clinical demands, perceived inadequate time to discuss the rationale for urine drug testing and to order confirmatory testing, and feeling unprepared to interpret and address results (*166*).

Many patients do not have an opinion about "opioids" or know what this term means (*167*). Most are familiar with the term "narcotics." About a third associated "narcotics" with addiction or abuse, and about half feared "addiction" from long-term "narcotic" use (*168*). Most patients taking opioids experience side effects (73% of patients taking hydrocodone for noncancer pain [*11*], 96% of patients taking opioids for chronic pain [*12*]), and side effects, rather than pain relief,

have been found to explain most of the variation in patients' preferences related to taking opioids (*12*). For example, patients taking hydrocodone for noncancer pain commonly reported side effects including dizziness, headache, fatigue, drowsiness, nausea, vomiting, and constipation (*11*). Patients with chronic pain in focus groups emphasized effectiveness of goal setting for increasing motivation and functioning (*168*). Patients taking high dosages report reliance on opioids despite ambivalence about their benefits (*169*) and regardless of pain reduction, reported problems, concerns, side effects, or perceived helpfulness (*13*).

Resource Allocation

Resource allocation (cost) is an important consideration in understanding the feasibility of clinical recommendations. CDC searched for evidence on opioid therapy compared with other treatments; costs of misuse, abuse, and overdose from prescription opioids; and costs of specific risk mitigation strategies (e.g., urine drug testing). Yearly direct and indirect costs related to prescription opioids have been estimated (based on studies published since 2010) to be $53.4 billion for nonmedical use of prescription opioids (*170*); $55.7 billion for abuse, dependence (i.e., opioid use disorder), and misuse of prescription opioids (*171*); and $20.4 billion for direct and indirect costs related to opioid-related overdose alone (*172*). In 2012, total expenses for outpatient prescription opioids were estimated at $9.0 billion, an increase of 120% from 2002 (*173*). Although there are perceptions that opioid therapy for chronic pain is less expensive than more time-intensive nonpharmacologic management approaches, many pain treatments, including acetaminophen, NSAIDs, tricyclic antidepressants, and massage therapy, are associated with lower mean and median annual costs compared with opioid therapy (*174*). COX-2 inhibitors, SNRIs, anticonvulsants, topical analgesics, physical therapy, and CBT are also associated with lower median annual costs compared with opioid therapy (*174*). Limited information was found on costs of strategies to decrease risks associated with opioid therapy; however, urine drug testing, including screening and confirmatory tests, has been estimated to cost $211–$363 per test (*175*).

Recommendations

The recommendations are grouped into three areas for consideration:

- Determining when to initiate or continue opioids for chronic pain.
- Opioid selection, dosage, duration, follow-up, and discontinuation.
- Assessing risk and addressing harms of opioid use.

There are 12 recommendations (Box 1). Each recommendation is followed by a rationale for the recommendation, with considerations for implementation noted. In accordance with the ACIP GRADE process, CDC based the recommendations on consideration of the clinical evidence, contextual evidence (including benefits and harms, values and preferences, resource allocation), and expert opinion. For each recommendation statement, CDC notes the recommendation category (A or B) and the type of the evidence (1, 2, 3, or 4) supporting the statement (Box 2). Expert opinion is reflected within each of the recommendation rationales. While there was not an attempt to reach consensus among experts, experts from the Core Expert Group and from the Opioid Guideline Workgroup ("experts") expressed overall, general support for all recommendations. Where differences in expert opinion emerged for detailed actions within the clinical recommendations or for implementation considerations, CDC notes the differences of opinion in the supporting rationale statements.

Category A recommendations indicate that most patients should receive the recommended course of action; category B recommendations indicate that different choices will be appropriate for different patients, requiring clinicians to help patients arrive at a decision consistent with patient values and preferences and specific clinical situations. Consistent with the ACIP (*47*) and GRADE process (*48*), category A recommendations were made, even with type 3 and 4 evidence, when there was broad agreement that the advantages of a clinical action greatly outweighed the disadvantages based on a consideration of benefits and harms, values and preferences, and resource allocation. Category B recommendations were made when there was broad agreement that the advantages and disadvantages of a clinical action were more balanced, but advantages were significant enough to warrant a recommendation. All recommendations are category A recommendations, with the exception of recommendation 10, which is rated as category B. Recommendations were associated with a range of evidence types, from type 2 to type 4.

In summary, the categorization of recommendations was based on the following assessment:

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤6 weeks in duration).
- Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury).
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

BOX 1. CDC recommendations for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

* All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.

BOX 2. Interpretation of recommendation categories and evidence type

Recommendation Categories

Based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).

Category A recommendation: Applies to all persons; most patients should receive the recommended course of action.

Category B recommendation: Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

Evidence Type

Based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.

Type 2 evidence: Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies.

Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.

Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

Determining When to Initiate or Continue Opioids for Chronic Pain

1. **Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate (recommendation category: A, evidence type: 3).**

Patients with pain should receive treatment that provides the greatest benefits relative to risks. The contextual evidence review found that many nonpharmacologic therapies, including physical therapy, weight loss for knee osteoarthritis, psychological therapies such as CBT, and certain interventional procedures can ameliorate chronic pain. There is high-quality evidence that exercise therapy (a prominent modality in physical therapy) for hip (*100*) or knee (*99*) osteoarthritis reduces pain and improves function immediately after treatment and that the improvements are sustained for at least 2–6 months. Previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*). Exercise therapy also can help reduce pain and improve function in low back pain and can improve global well-being and physical function in fibromyalgia (*98*,*101*). Multimodal therapies and multidisciplinary biopsychosocial rehabilitation-combining approaches (e.g., psychological therapies with exercise) can reduce long-term pain and disability compared with usual care and compared with physical treatments (e.g., exercise) alone. Multimodal therapies are not always available or reimbursed by insurance and can be time-consuming and costly for patients. Interventional approaches such as arthrocentesis and intraarticular glucocorticoid injection for pain associated with rheumatoid arthritis (*117*) or osteoarthritis (*118*) and subacromial corticosteroid injection for rotator cuff disease (*119*) can provide short-term improvement in pain and function. Evidence is insufficient to determine the extent to which repeated glucocorticoid injection increases potential risks such as articular cartilage changes (in osteoarthritis) and sepsis (*118*). Serious adverse events are rare but have been reported with epidural injection (*120*).

Several nonopioid pharmacologic therapies (including acetaminophen, NSAIDs, and selected antidepressants and anticonvulsants) are effective for chronic pain. In particular, acetaminophen and NSAIDs can be useful for arthritis and low back pain. Selected anticonvulsants such as pregabalin and gabapentin can improve pain in diabetic neuropathy and post-herpetic neuralgia (contextual evidence review). Pregabalin, gabapentin, and carbamazepine are FDA-approved for treatment of certain neuropathic pain conditions, and pregabalin is FDA approved for fibromyalgia management. In patients with or without depression, tricyclic antidepressants and SNRIs provide effective analgesia for neuropathic pain conditions including diabetic neuropathy and post-herpetic neuralgia, often at lower dosages and with a shorter time to onset of effect than for treatment of depression (see contextual evidence review). Tricyclics and SNRIs can also relieve fibromyalgia symptoms. The SNRI duloxetine is FDA-approved for the treatment of diabetic neuropathy and fibromyalgia. Because patients with chronic pain often suffer from concurrent depression (*144*), and depression can exacerbate physical symptoms including pain (*177*), patients with co-occurring pain and depression are especially likely to benefit from antidepressant medication (see Recommendation 8). Nonopioid pharmacologic therapies

are not generally associated with substance use disorder, and the numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications (contextual evidence review). For example, acetaminophen, NSAIDs, and opioid pain medication were involved in 881, 228, and 16,651 pharmaceutical overdose deaths in the United States in 2010 (*178*). However, nonopioid pharmacologic therapies are associated with certain risks, particularly in older patients, pregnant patients, and patients with certain co-morbidities such as cardiovascular, renal, gastrointestinal, and liver disease (see contextual evidence review). For example, acetaminophen can be hepatotoxic at dosages of >3–4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease (*109*). NSAID use has been associated with gastritis, peptic ulcer disease, cardiovascular events (*111*,*112*), and fluid retention, and most NSAIDs (choline magnesium trilisate and selective COX-2 inhibitors are exceptions) interfere with platelet aggregation (*179*). Clinicians should review FDA-approved labeling including boxed warnings before initiating treatment with any pharmacologic therapy.

Although opioids can reduce pain during short-term use, the clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy (KQ1). While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant. Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury (KQ2). At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999 (see Contextual Evidence Review).

Integrated pain management requires coordination of medical, psychological, and social aspects of health care and includes primary care, mental health care, and specialist services when needed (*180*). Nonpharmacologic physical and psychological treatments such as exercise and CBT are approaches that encourage active patient participation in the care plan, address the effects of pain in the patient's life, and can result in sustained improvements in pain and function without apparent risks. Despite this, these therapies are not always or fully covered by insurance, and access and cost can be barriers for patients. For many patients, aspects of these approaches can be used even when there is limited access to specialty care. For example, previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*) and maintenance of activity for patients with low back pain (*110*). A randomized trial found no difference in reduced chronic low back pain intensity, frequency or disability between patients assigned to relatively low-cost group aerobics and individual physiotherapy or muscle reconditioning sessions (*181*). Low-cost options to integrate exercise include brisk walking in public spaces or use of public recreation facilities for group exercise. CBT addresses psychosocial contributors to pain and improves function (*97*). Primary care clinicians can integrate elements of a cognitive behavioral approach into their practice by encouraging patients to take an active role in the care plan, by supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise (*179*), or by providing education in relaxation techniques and coping strategies. In many locations, there are free or low-cost patient support, self-help, and educational community-based programs that can provide stress reduction and other mental health benefits. Patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, can be referred for formal therapy with a mental health specialist (e.g., psychologist, psychiatrist, clinical social worker). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, and convenience.

To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis. Detailed recommendations on diagnosis are provided in other guidelines (*110*,*179*), but evaluation should generally include a focused history, including history and characteristics of pain and potentially contributing factors (e.g., function, psychosocial stressors, sleep) and physical exam, with imaging or other diagnostic testing only if indicated (e.g., if severe or progressive neurologic deficits are present or if serious underlying conditions are suspected) (*110*,*179*). For complex pain syndromes, pain specialty consultation can be considered to assist with diagnosis as well as management. Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain; for example, improving glucose control to prevent progression of diabetic neuropathy; immune-modulating agents for rheumatoid arthritis; physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain; or surgical intervention to relieve mechanical/compressive pain (*179*). The underlying mechanism for most pain syndromes can be categorized as neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia), or nociceptive (e.g., osteoarthritis, muscular back pain). The diagnosis and pathophysiologic mechanism of pain have implications for symptomatic pain treatment with medication. For example, evidence is limited or insufficient

for improved pain or function with long-term use of opioids for several chronic pain conditions for which opioids are commonly prescribed, such as low back pain (*182*), headache (*183*), and fibromyalgia (*184*). Although NSAIDs can be used for exacerbations of nociceptive pain, other medications (e.g., tricyclics, selected anticonvulsants, or transdermal lidocaine) generally are recommended for neuropathic pain. In addition, improvement of neuropathic pain can begin weeks or longer after symptomatic treatment is initiated (*179*). Medications should be used only after assessment and determination that expected benefits outweigh risks given patient-specific factors. For example, clinicians should consider falls risk when selecting and dosing potentially sedating medications such as tricyclics, anticonvulsants, or opioids, and should weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults as well as patients with hypertension, renal insufficiency, or heart failure, or those with risk for peptic ulcer disease or cardiovascular disease. Some guidelines recommend topical NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) over oral NSAIDs in patients aged ≥75 years to minimize systemic effects (*176*).

Experts agreed that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue >3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care, given small to moderate short-term benefits, uncertain long-term benefits, and potential for serious harms; although evidence on long-term benefits of nonopioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower. This does not mean that patients should be required to sequentially "fail" nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy. Rather, expected benefits specific to the clinical context should be weighed against risks before initiating therapy. In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous nonpharmacologic and nonopioid pharmacologic therapies used. In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used. In addition, when opioid pain medication is used, it is more likely to be effective if integrated with nonpharmacologic therapy. Nonpharmacologic approaches such as exercise and CBT should be used to reduce pain and improve function in patients with chronic pain. Nonopioid pharmacologic therapy should be used when benefits outweigh risks and should be combined with nonpharmacologic therapy to reduce pain and improve function. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate, to provide greater benefits to patients in improving pain and function.

2. **Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. In addition, studies on currently available risk assessment instruments were sparse and showed inconsistent results (KQ4). The clinical evidence review for the current guideline considered studies with outcomes examined at ≥1 year that compared opioid use versus nonuse or placebo. Studies of opioid therapy for chronic pain that did not have a nonopioid control group have found that although many patients discontinue opioid therapy for chronic noncancer pain due to adverse effects or insufficient pain relief, there is weak evidence that patients who are able to continue opioid therapy for at least 6 months can experience clinically significant pain relief and insufficient evidence that function or quality of life improves (*185*). These findings suggest that it is very difficult for clinicians to predict whether benefits of opioids for chronic pain will outweigh risks of ongoing treatment for individual patients. Opioid therapy should not be initiated without consideration of an "exit strategy" to be used if the therapy is unsuccessful.

Experts agreed that before opioid therapy is initiated for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should determine how effectiveness will be evaluated and should establish treatment goals with patients. Because the line between acute pain and initial chronic pain is not always clear, it might be difficult for clinicians to determine when they are initiating opioids for chronic pain rather than treating acute pain. Pain lasting longer than 3 months or past the time of normal tissue healing (which could be substantially shorter than 3 months, depending on the condition) is generally no longer considered acute. However, establishing treatment goals with a patient who has already received opioid therapy for 3 months would defer this discussion well past the point of

initiation of opioid therapy for chronic pain. Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for ≥30 days are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for ≥30 days, clinicians should establish treatment goals with patients. Clinicians seeing new patients already receiving opioids should establish treatment goals for continued opioid therapy. Although the clinical evidence review did not find studies evaluating the effectiveness of written agreements or treatment plans (KQ4), clinicians and patients who set a plan in advance will clarify expectations regarding how opioids will be prescribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, opioids are no longer needed, or adverse events put the patient at risk) to improve patient safety.

Experts thought that goals should include improvement in both pain relief and function (and therefore in quality of life). However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (e.g., diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma). Experts noted that function can include emotional and social as well as physical dimensions. In addition, experts emphasized that mood has important interactions with pain and function. Experts agreed that clinicians may use validated instruments such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) to track patient outcomes. Clinically meaningful improvement has been defined as a 30% improvement in scores for both pain and function (*187*). Monitoring progress toward patient-centered functional goals (e.g., walking the dog or walking around the block, returning to part-time work, attending family sports or recreational activities) can also contribute to the assessment of functional improvement. Clinicians should use these goals in assessing benefits of opioid therapy for individual patients and in weighing benefits against risks of continued opioid therapy (see Recommendation 7, including recommended intervals for follow-up). Because depression, anxiety, and other psychological co-morbidities often coexist with and can interfere with resolution of pain, clinicians should use validated instruments to assess for these conditions (see Recommendation 8) and ensure that treatment for these conditions is optimized. If patients receiving opioid therapy for chronic pain do not experience meaningful improvements in both pain and function compared with prior to initiation of opioid therapy, clinicians should consider working with patients to taper and discontinue opioids (see Recommendation 7) and should use nonpharmacologic and nonopioid pharmacologic approaches to pain management (see Recommendation 1).

3. **Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (recommendation category: A, evidence type: 3).**

The clinical evidence review did not find studies evaluating effectiveness of patient education or opioid treatment plans as risk-mitigation strategies (KQ4). However, the contextual evidence review found that many patients lack information about opioids and identified concerns that some clinicians miss opportunities to effectively communicate about safety. Given the substantial evidence gaps on opioids, uncertain benefits of long-term use, and potential for serious harms, patient education and discussion before starting opioid therapy are critical so that patient preferences and values can be understood and used to inform clinical decisions. Experts agreed that essential elements to communicate to patients before starting and periodically during opioid therapy include realistic expected benefits, common and serious harms, and expectations for clinician and patient responsibilities to mitigate risks of opioid therapy.

Clinicians should involve patients in decisions about whether to start or continue opioid therapy. Given potentially serious risks of long-term opioid therapy, clinicians should ensure that patients are aware of potential benefits of, harms of, and alternatives to opioids before starting or continuing opioid therapy. Clinicians are encouraged to have open and honest discussions with patients to inform mutual decisions about whether to start or continue opioid therapy. Important considerations include the following:

- Be explicit and realistic about expected benefits of opioids, explaining that while opioids can reduce pain during short-term use, there is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely (clinical evidence review, KQ1).
- Emphasize improvement in function as a primary goal and that function can improve even when pain is still present.
- Advise patients about serious adverse effects of opioids, including potentially fatal respiratory depression and development of a potentially serious lifelong opioid use disorder that can cause distress and inability to fulfill major role obligations.
- Advise patients about common effects of opioids, such as constipation, dry mouth, nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids. To prevent constipation associated with opioid use, advise patients to increase

hydration and fiber intake and to maintain or increase physical activity. Stool softeners or laxatives might be needed.

- Discuss effects that opioids might have on ability to safely operate a vehicle, particularly when opioids are initiated, when dosages are increased, or when other central nervous system depressants, such as benzodiazepines or alcohol, are used concurrently.
- Discuss increased risks for opioid use disorder, respiratory depression, and death at higher dosages, along with the importance of taking only the amount of opioids prescribed, i.e., not taking more opioids or taking them more often.
- Review increased risks for respiratory depression when opioids are taken with benzodiazepines, other sedatives, alcohol, illicit drugs such as heroin, or other opioids.
- Discuss risks to household members and other individuals if opioids are intentionally or unintentionally shared with others for whom they are not prescribed, including the possibility that others might experience overdose at the same or at lower dosage than prescribed for the patient, and that young children are susceptible to unintentional ingestion. Discuss storage of opioids in a secure, preferably locked location and options for safe disposal of unused opioids (*188*).
- Discuss the importance of periodic reassessment to ensure that opioids are helping to meet patient goals and to allow opportunities for opioid discontinuation and consideration of additional nonpharmacologic or nonopioid pharmacologic treatment options if opioids are not effective or are harmful.
- Discuss planned use of precautions to reduce risks, including use of prescription drug monitoring program information (see Recommendation 9) and urine drug testing (see Recommendation 10). Consider including discussion of naloxone use for overdose reversal (see Recommendation 8).
- Consider whether cognitive limitations might interfere with management of opioid therapy (for older adults in particular) and, if so, determine whether a caregiver can responsibly co-manage medication therapy. Discuss the importance of reassessing safer medication use with both the patient and caregiver.

Given the possibility that benefits of opioid therapy might diminish or that risks might become more prominent over time, it is important that clinicians review expected benefits and risks of continued opioid therapy with patients periodically, at least every 3 months (see Recommendation 7).

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids (recommendation category: A, evidence type: 4).

ER/LA opioids include methadone, transdermal fentanyl, and extended-release versions of opioids such as oxycodone, oxymorphone, hydrocodone, and morphine. The clinical evidence review found a fair-quality study showing a higher risk for overdose among patients initiating treatment with ER/LA opioids than among those initiating treatment with immediate-release opioids (*77*). The clinical evidence review did not find evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of immediate-release opioids or that time-scheduled use of ER/LA opioids reduces risks for opioid misuse or addiction (KQ3).

In 2014, the FDA modified the labeling for ER/LA opioid pain medications, noting serious risks and recommending that ER/LA opioids be reserved for "management of pain severe enough to require daily, around-the-clock, long-term opioid treatment" when "alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain" and not used as "as needed" pain relievers (*121*). FDA has also noted that some ER/LA opioids are only appropriate for opioid-tolerant patients, defined as patients who have received certain dosages of opioids (e.g., 60 mg daily of oral morphine, 30 mg daily of oral oxycodone, or equianalgesic dosages of other opioids) for at least 1 week (*189*). Time-scheduled opioid use can be associated with greater total average daily opioid dosage compared with intermittent, as-needed opioid use (contextual evidence review). In addition, experts indicated that there was not enough evidence to determine the safety of using immediate-release opioids for breakthrough pain when ER/LA opioids are used for chronic pain outside of active cancer pain, palliative care, or end-of-life care, and that this practice might be associated with dose escalation.

Abuse-deterrent technologies have been employed to prevent manipulation intended to defeat extended-release properties of ER/LA opioids and to prevent opioid use by unintended routes of administration, such as injection of oral opioids. As indicated in FDA guidance for industry on evaluation and labeling of abuse-deterrent opioids (*190*), although abuse-deterrent technologies are expected to make manipulation of opioids more difficult or less rewarding, they do not prevent

opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by nonoral routes. The "abuse-deterrent" label does not indicate that there is no risk for abuse. No studies were found in the clinical evidence review assessing the effectiveness of abuse-deterrent technologies as a risk mitigation strategy for deterring or preventing abuse. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake. Experts agreed that recommendations could not be offered at this time related to use of abuse-deterrent formulations.

In comparing different ER/LA formulations, the clinical evidence review found inconsistent results for overdose risk with methadone versus other ER/LA opioids used for chronic pain (KQ3). The contextual evidence review found that methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for chronic pain. In addition, methadone is associated with cardiac arrhythmias along with QT prolongation on the electrocardiogram, and it has complicated pharmacokinetics and pharmacodynamics, including a long and variable half-life and peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect. Experts noted that the pharmacodynamics of methadone are subject to more inter-individual variability than other opioids. In regard to other ER/LA opioid formulations, experts noted that the absorption and pharmacodynamics of transdermal fentanyl are complex, with gradually increasing serum concentration during the first part of the 72-hour dosing interval, as well as variable absorption based on factors such as external heat. In addition, the dosing of transdermal fentanyl in mcg/hour, which is not typical for a drug used by outpatients, can be confusing. Experts thought that these complexities might increase the risk for fatal overdose when methadone or transdermal fentanyl is prescribed to a patient who has not used it previously or by clinicians who are not familiar with its effects.

Experts agreed that for patients not already receiving opioids, clinicians should not initiate opioid treatment with ER/LA opioids and should not prescribe ER/LA opioids for intermittent use. ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week. When changing to an ER/LA opioid for a patient previously receiving a different immediate-release opioid, clinicians should consult product labeling and reduce total daily dosage to account for incomplete opioid cross-tolerance. Clinicians should use additional caution with ER/LA opioids and consider a longer dosing interval when prescribing to patients with renal or hepatic dysfunction because decreased clearance of drugs among these patients can lead to accumulation of drugs to toxic levels and persistence in the body for longer durations. Although there might be situations in which clinicians need to prescribe immediate-release and ER/LA opioids together (e.g., transitioning patients from ER/LA opioids to immediate-release opioids by temporarily using lower dosages of both), in general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable, given potentially increased risk and diminishing returns of such an approach for chronic pain.

When an ER/LA opioid is prescribed, using one with predictable pharmacokinetics and pharmacodynamics is preferred to minimize unintentional overdose risk. In particular, unusual characteristics of methadone and of transdermal fentanyl make safe prescribing of these medications for pain especially challenging.

- Methadone should not be the first choice for an ER/LA opioid. Only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients, including risk assessment for QT prolongation and consideration of electrocardiographic monitoring, should consider prescribing methadone for pain. A clinical practice guideline that contains further guidance regarding methadone prescribing for pain has been published previously (*191*).
- Because dosing effects of transdermal fentanyl are often misunderstood by both clinicians and patients, only clinicians who are familiar with the dosing and absorption properties of transdermal fentanyl and are prepared to educate their patients about its use should consider prescribing it.

5. **When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day (recommendation category: A, evidence type: 3).**

Benefits of high-dose opioids for chronic pain are not established. The clinical evidence review found only one study (*84*) addressing effectiveness of dose titration for outcomes related to pain control, function, and quality of life (KQ3). This randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy and maintenance of current dosage. (These groups were prescribed average dosages of 52 and 40 MME/day, respectively, at the end of the trial.) At the same time, risks for serious harms

related to opioid therapy increase at higher opioid dosage. The clinical evidence review found that higher opioid dosages are associated with increased risks for motor vehicle injury, opioid use disorder, and overdose (KQ2). The clinical and contextual evidence reviews found that opioid overdose risk increases in a dose-response manner, that dosages of 50–<100 MME/day have been found to increase risks for opioid overdose by factors of 1.9 to 4.6 compared with dosages of 1–<20 MME/day, and that dosages ≥100 MME/day are associated with increased risks of overdose 2.0–8.9 times the risk at 1–<20 MME/day. In a national sample of Veterans Health Administration patients with chronic pain who were prescribed opioids, mean prescribed opioid dosage among patients who died from opioid overdose was 98 MME (median 60 MME) compared with mean prescribed opioid dosage of 48 MME (median 25 MME) among patients not experiencing fatal overdose (*127*).

The contextual evidence review found that although there is not a single dosage threshold below which overdose risk is eliminated, holding dosages <50 MME/day would likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages. Experts agreed that lower dosages of opioids reduce the risk for overdose, but that a single dosage threshold for safe opioid use could not be identified. Experts noted that daily opioid dosages close to or greater than 100 MME/day are associated with significant risks, that dosages <50 MME/day are safer than dosages of 50–100 MME/day, and that dosages <20 MME/day are safer than dosages of 20–50 MME/day. One expert thought that a specific dosage at which the benefit/risk ratio of opioid therapy decreases could not be identified. Most experts agreed that, in general, increasing dosages to 50 or more MME/day increases overdose risk without necessarily adding benefits for pain control or function and that clinicians should carefully reassess evidence of individual benefits and risks when considering increasing opioid dosages to ≥50 MME/day. Most experts also agreed that opioid dosages should not be increased to ≥90 MME/day without careful justification based on diagnosis and on individualized assessment of benefits and risks.

When opioids are used for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should start opioids at the lowest possible effective dosage (the lowest starting dosage on product labeling for patients not already taking opioids and according to product labeling guidance regarding tolerance for patients already taking opioids). Clinicians should use additional caution when initiating opioids for patients aged ≥65 years and for patients with renal or hepatic insufficiency because decreased clearance of drugs in these patients can result in accumulation of drugs to toxic levels. Clinicians should use caution when increasing opioid dosages and increase dosage by the smallest practical amount because overdose risk increases with increases in opioid dosage. Although there is limited evidence to recommend specific intervals for dosage titration, a previous guideline recommended waiting at least five half-lives before increasing dosage and waiting at least a week before increasing dosage of methadone to make sure that full effects of the previous dosage are evident (*31*). Clinicians should re-evaluate patients after increasing dosage for changes in pain, function, and risk for harm (see Recommendation 7). Before increasing total opioid dosage to ≥50 MME/day, clinicians should reassess whether opioid treatment is meeting the patient's treatment goals (see Recommendation 2). If a patient's opioid dosage for all sources of opioids combined reaches or exceeds 50 MME/day, clinicians should implement additional precautions, including increased frequency of follow-up (see Recommendation 7) and considering offering naloxone and overdose prevention education to both patients and the patients' household members (see Recommendation 8). Clinicians should avoid increasing opioid dosages to ≥90 MME/day or should carefully justify a decision to increase dosage to ≥90 MME/day based on individualized assessment of benefits and risks and weighing factors such as diagnosis, incremental benefits for pain and function relative to harms as dosages approach 90 MME/day, other treatments and effectiveness, and recommendations based on consultation with pain specialists. If patients do not experience improvement in pain and function at ≥90 MME/day, or if there are escalating dosage requirements, clinicians should discuss other approaches to pain management with the patient, consider working with patients to taper opioids to a lower dosage or to taper and discontinue opioids (see Recommendation 7), and consider consulting a pain specialist. Some states require clinicians to implement clinical protocols at specific dosage levels. For example, before increasing long-term opioid therapy dosage to >120 MME/day, clinicians in Washington state must obtain consultation from a pain specialist who agrees that this is indicated and appropriate (*30*). Clinicians should be aware of rules related to MME thresholds and associated clinical protocols established by their states.

Established patients already taking high dosages of opioids, as well as patients transferring from other clinicians, might consider the possibility of opioid dosage reduction to be anxiety-provoking, and tapering opioids can be especially challenging after years on high dosages because of physical and psychological dependence. However, these patients should be offered the opportunity to re-evaluate their continued use of opioids at high dosages in light of recent evidence regarding the association of opioid dosage and overdose risk. Clinicians should explain in a nonjudgmental manner to patients already taking high opioid dosages (≥90 MME/day) that there is

now an established body of scientific evidence showing that overdose risk is increased at higher opioid dosages. Clinicians should empathically review benefits and risks of continued high-dosage opioid therapy and should offer to work with the patient to taper opioids to safer dosages. For patients who agree to taper opioids to lower dosages, clinicians should collaborate with the patient on a tapering plan (see Recommendation 7). Experts noted that patients tapering opioids after taking them for years might require very slow opioid tapers as well as pauses in the taper to allow gradual accommodation to lower opioid dosages. Clinicians should remain alert to signs of anxiety, depression, and opioid use disorder (see Recommendations 8 and 12) that might be unmasked by an opioid taper and arrange for management of these co-morbidities. For patients agreeing to taper to lower opioid dosages as well as for those remaining on high opioid dosages, clinicians should establish goals with the patient for continued opioid therapy (see Recommendation 2), maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1), and consider consulting a pain specialist as needed to assist with pain management.

6. **Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed (recommendation category: A, evidence type: 4).**

The clinical evidence review found that opioid use for acute pain (i.e., pain with abrupt onset and caused by an injury or other process that is not ongoing) is associated with long-term opioid use, and that a greater amount of early opioid exposure is associated with greater risk for long-term use (KQ5). Several guidelines on opioid prescribing for acute pain from emergency departments (*192–194*) and other settings (*195*,*196*) have recommended prescribing ≤3 days of opioids in most cases, whereas others have recommended ≤7 days (*197*) or <14 days (*30*). Because physical dependence on opioids is an expected physiologic response in patients exposed to opioids for more than a few days (contextual evidence review), limiting days of opioids prescribed also should minimize the need to taper opioids to prevent distressing or unpleasant withdrawal symptoms. Experts noted that more than a few days of exposure to opioids significantly increases hazards, that each day of unnecessary opioid use increases likelihood of physical dependence without adding benefit, and that prescriptions with fewer days' supply will minimize the number of pills available for unintentional or intentional diversion.

Experts agreed that when opioids are needed for acute pain, clinicians should prescribe opioids at the lowest effective dose and for no longer than the expected duration of pain severe enough to require opioids to minimize unintentional initiation of long-term opioid use. The lowest effective dose can be determined using product labeling as a starting point with calibration as needed based on the severity of pain and on other clinical factors such as renal or hepatic insufficiency (see Recommendation 8). Experts thought, based on clinical experience regarding anticipated duration of pain severe enough to require an opioid, that in most cases of acute pain not related to surgery or trauma, a ≤3 days' supply of opioids will be sufficient. For example, in one study of the course of acute low back pain (not associated with malignancies, infections, spondylarthropathies, fractures, or neurological signs) in a primary care setting, there was a large decrease in pain until the fourth day after treatment with paracetamol, with smaller decreases thereafter (*198*). Some experts thought that because some types of acute pain might require more than 3 days of opioid treatment, it would be appropriate to recommend a range of ≤3–5 days or ≤3–7 days when opioids are needed. Some experts thought that a range including 7 days was too long given the expected course of severe acute pain for most acute pain syndromes seen in primary care.

Acute pain can often be managed without opioids. It is important to evaluate the patient for reversible causes of pain, for underlying etiologies with potentially serious sequelae, and to determine appropriate treatment. When the diagnosis and severity of nontraumatic, nonsurgical acute pain are reasonably assumed to warrant the use of opioids, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids, often 3 days or less, unless circumstances clearly warrant additional opioid therapy. More than 7 days will rarely be needed. Opioid treatment for post-surgical pain is outside the scope of this guideline but has been addressed elsewhere (*30*). Clinicians should not prescribe additional opioids to patients "just in case" pain continues longer than expected. Clinicians should re-evaluate the subset of patients who experience severe acute pain that continues longer than the expected duration to confirm or revise the initial diagnosis and to adjust management accordingly. Given longer half-lives and longer duration of effects (e.g., respiratory depression) with ER/LA opioids such as methadone, fentanyl patches, or extended release versions of opioids such as oxycodone, oxymorphone, or morphine, clinicians should not prescribe ER/LA opioids for the treatment of acute pain.

7. **Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (recommendation category: A, evidence type: 4).**

Although the clinical evidence review did not find studies evaluating the effectiveness of more frequent monitoring intervals (KQ4), it did find that continuing opioid therapy for 3 months substantially increases risk for opioid use disorder (KQ2); therefore, follow-up earlier than 3 months might be necessary to provide the greatest opportunity to prevent the development of opioid use disorder. In addition, risk for overdose associated with ER/LA opioids might be particularly high during the first 2 weeks of treatment (KQ3). The contextual evidence review found that patients who do not have pain relief with opioids at 1 month are unlikely to experience pain relief with opioids at 6 months. Although evidence is insufficient to determine at what point within the first 3 months of opioid therapy the risks for opioid use disorder increase, reassessment of pain and function within 1 month of initiating opioids provides an opportunity to minimize risks of long-term opioid use by discontinuing opioids among patients not receiving a clear benefit from these medications. Experts noted that risks for opioid overdose are greatest during the first 3–7 days after opioid initiation or increase in dosage, particularly when methadone or transdermal fentanyl are prescribed; that follow-up within 3 days is appropriate when initiating or increasing the dosage of methadone; and that follow-up within 1 week might be appropriate when initiating or increasing the dosage of other ER/LA opioids.

Clinicians should evaluate patients to assess benefits and harms of opioids within 1 to 4 weeks of starting long-term opioid therapy or of dose escalation. Clinicians should consider follow-up intervals within the lower end of this range when ER/LA opioids are started or increased or when total daily opioid dosage is ≥50 MME/day. Shorter follow-up intervals (within 3 days) should be strongly considered when starting or increasing the dosage of methadone. At follow up, clinicians should assess benefits in function, pain control, and quality of life using tools such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) and/or asking patients about progress toward functional goals that have meaning for them (see Recommendation 2). Clinicians should also ask patients about common adverse effects such as constipation and drowsiness (see Recommendation 3), as well as asking about and assessing for effects that might be early warning signs for more serious problems such as overdose (e.g., sedation or slurred speech) or opioid use disorder (e.g., craving, wanting to take opioids in greater quantities or more frequently than prescribed, or difficulty controlling use). Clinicians should ask patients about their preferences for continuing opioids, given their effects on pain and function relative to any adverse effects experienced.

Because of potential changes in the balance of benefits and risks of opioid therapy over time, clinicians should regularly reassess all patients receiving long-term opioid therapy, including patients who are new to the clinician but on long-term opioid therapy, at least every 3 months. At reassessment, clinicians should determine whether opioids continue to meet treatment goals, including sustained improvement in pain and function, whether the patient has experienced common or serious adverse events or early warning signs of serious adverse events, signs of opioid use disorder (e.g., difficulty controlling use, work or family problems related to opioid use), whether benefits of opioids continue to outweigh risks, and whether opioid dosage can be reduced or opioids can be discontinued. Ideally, these reassessments would take place in person and be conducted by the prescribing clinician. In practice contexts where virtual visits are part of standard care (e.g., in remote areas where distance or other issues make follow-up visits challenging), follow-up assessments that allow the clinician to communicate with and observe the patient through video and audio could be conducted, with in-person visits occurring at least once per year. Clinicians should re-evaluate patients who are exposed to greater risk of opioid use disorder or overdose (e.g., patients with depression or other mental health conditions, a history of substance use disorder, a history of overdose, taking ≥50 MME/day, or taking other central nervous system depressants with opioids) more frequently than every 3 months. If clinically meaningful improvements in pain and function are not sustained, if patients are taking high-risk regimens (e.g., dosages ≥50 MME/day or opioids combined with benzodiazepines) without evidence of benefit, if patients believe benefits no longer outweigh risks or if they request dosage reduction or discontinuation, or if patients experience overdose or other serious adverse events (e.g., an event leading to hospitalization or disability) or warning signs of serious adverse events, clinicians should work with patients to reduce opioid dosage or to discontinue opioids when possible. Clinicians should maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to assist with pain management.

Considerations for Tapering Opioids

Although the clinical evidence review did not find high-quality studies comparing the effectiveness of different tapering protocols for use when opioid dosage is reduced or opioids are discontinued (KQ3), tapers reducing weekly dosage by 10%–50% of the original dosage have been recommended by other clinical guidelines (*199*), and a rapid taper over 2–3 weeks has been recommended in the case of a severe adverse event such as overdose (*30*). Experts noted that tapers slower than 10% per week (e.g., 10% per month) also might be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g., for years). Opioid withdrawal during pregnancy has been associated with spontaneous abortion and premature labor.

When opioids are reduced or discontinued, a taper slow enough to minimize symptoms and signs of opioid withdrawal (e.g., drug craving, anxiety, insomnia, abdominal pain, vomiting, diarrhea, diaphoresis, mydriasis, tremor, tachycardia, or piloerection) should be used. A decrease of 10% of the original dose per week is a reasonable starting point; experts agreed that tapering plans may be individualized based on patient goals and concerns. Experts noted that at times, tapers might have to be paused and restarted again when the patient is ready and might have to be slowed once patients reach low dosages. Tapers may be considered successful as long as the patient is making progress. Once the smallest available dose is reached, the interval between doses can be extended. Opioids may be stopped when taken less frequently than once a day. More rapid tapers might be needed for patient safety under certain circumstances (e.g., for patients who have experienced overdose on their current dosage). Ultrarapid detoxification under anesthesia is associated with substantial risks, including death, and should not be used (*200*). Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal. Patients who are not taking opioids (including patients who are diverting all opioids they obtain) do not require tapers. Clinicians should discuss with patients undergoing tapering the increased risk for overdose on abrupt return to a previously prescribed higher dose. Primary care clinicians should collaborate with mental health providers and with other specialists as needed to optimize nonopioid pain management (see Recommendation 1), as well as psychosocial support for anxiety related to the taper. More detailed guidance on tapering, including management of withdrawal symptoms has been published previously (*30*,*201*). If a patient exhibits signs of opioid use disorder, clinicians should offer or arrange for treatment of opioid use disorder (see Recommendation 12) and consider offering naloxone for overdose prevention (see Recommendation 8).

Assessing Risk and Addressing Harms of Opioid Use

8. **Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on patient demographics or patient comorbidities (KQ2). However, based on the contextual evidence review and expert opinion, certain risk factors are likely to increase susceptibility to opioid-associated harms and warrant incorporation of additional strategies into the management plan to mitigate risk. Clinicians should assess these risk factors periodically, with frequency varying by risk factor and patient characteristics. For example, factors that vary more frequently over time, such as alcohol use, require more frequent follow up. In addition, clinicians should consider offering naloxone, re-evaluating patients more frequently (see Recommendation 7), and referring to pain and/or behavioral health specialists when factors that increase risk for harm, such as history of overdose, history of substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids, are present.

Patients with Sleep-Disordered Breathing, Including Sleep Apnea

Risk factors for sleep-disordered breathing include congestive heart failure, and obesity. Experts noted that careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with mild sleep-disordered breathing. Clinicians should avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose (contextual evidence review).

Pregnant Women

Opioids used in pregnancy might be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with stillbirth, poor fetal growth, pre-term delivery, and birth defects (contextual evidence review). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome. Clinicians and patients together should carefully weigh risks and benefits when making decisions

about whether to initiate opioid therapy for chronic pain during pregnancy. In addition, before initiating opioid therapy for chronic pain for reproductive-age women, clinicians should discuss family planning and how long-term opioid use might affect any future pregnancy. For pregnant women already receiving opioids, clinicians should access appropriate expertise if considering tapering opioids because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal (see Recommendation 7). For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine or methadone has been associated with improved maternal outcomes and should be offered (*202*) (see Recommendation 12). Clinicians caring for pregnant women receiving opioids for pain or receiving buprenorphine or methadone for opioid use disorder should arrange for delivery at a facility prepared to monitor, evaluate for, and treat neonatal opioid withdrawal syndrome. In instances when travel to such a facility would present an undue burden on the pregnant woman, it is appropriate to deliver locally, monitor and evaluate the newborn for neonatal opioid withdrawal syndrome, and transfer the newborn for additional treatment if needed. Neonatal toxicity and death have been reported in breast-feeding infants whose mothers are taking codeine (contextual evidence review); previous guidelines have recommended that codeine be avoided whenever possible among mothers who are breast feeding and, if used, should be limited to the lowest possible dose and to a 4-day supply (*203*).

Patients with Renal or Hepatic Insufficiency

Clinicians should use additional caution and increased monitoring (see Recommendation 7) to minimize risks of opioids prescribed for patients with renal or hepatic insufficiency, given their decreased ability to process and excrete drugs, susceptibility to accumulation of opioids, and reduced therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review; see Recommendations 4, 5, and 7).

Patients Aged ≥65 Years

Inadequate pain treatment among persons aged ≥65 years has been documented (*204*). Pain management for older patients can be challenging given increased risks of both nonopioid pharmacologic therapies (see Recommendation 1) and opioid therapy in this population. Given reduced renal function and medication clearance even in the absence of renal disease, patients aged ≥65 years might have increased susceptibility to accumulation of opioids and a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review). Some older adults suffer from cognitive impairment, which can increase risk for medication errors and make opioid-related confusion more dangerous. In addition, older adults are more likely than younger adults to experience co-morbid medical conditions and more likely to receive multiple medications, some of which might interact with opioids (such as benzodiazepines). Clinicians should use additional caution and increased monitoring (see Recommendations 4, 5, and 7) to minimize risks of opioids prescribed for patients aged ≥65 years. Experts suggested that clinicians educate older adults receiving opioids to avoid risky medication-related behaviors such as obtaining controlled medications from multiple prescribers and saving unused medications. Clinicians should also implement interventions to mitigate common risks of opioid therapy among older adults, such as exercise or bowel regimens to prevent constipation, risk assessment for falls, and patient monitoring for cognitive impairment.

Patients with Mental Health Conditions

Because psychological distress frequently interferes with improvement of pain and function in patients with chronic pain, using validated instruments such as the Generalized Anxiety Disorder (GAD)-7 and the Patient Health Questionnaire (PHQ)-9 or the PHQ-4 to assess for anxiety, post-traumatic stress disorder, and/or depression (*205*), might help clinicians improve overall pain treatment outcomes. Experts noted that clinicians should use additional caution and increased monitoring (see Recommendation 7) to lessen the increased risk for opioid use disorder among patients with mental health conditions (including depression, anxiety disorders, and PTSD), as well as increased risk for drug overdose among patients with depression. Previous guidelines have noted that opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk, and that clinicians should consider behavioral health specialist consultation for any patient with a history of suicide attempt or psychiatric disorder (*31*). In addition, patients with anxiety disorders and other mental health conditions are more likely to receive benzodiazepines, which can exacerbate opioid-induced respiratory depression and increase risk for overdose (see Recommendation 11). Clinicians should ensure that treatment for depression and other mental health conditions is optimized, consulting with behavioral health specialists when needed. Treatment for depression can improve pain symptoms as well as depression and might decrease overdose risk (contextual evidence review). For treatment of chronic pain in patients with depression, clinicians should strongly consider using tricyclic or SNRI antidepressants for analgesic as well as antidepressant effects if these medications are not otherwise contraindicated (see Recommendation 1).

Patients with Substance Use Disorder

Illicit drugs and alcohol are listed as contributory factors on a substantial proportion of death certificates for opioid-related overdose deaths (contextual evidence review). Previous guidelines have recommended screening or risk assessment tools to identify patients at higher risk for misuse or abuse of opioids. However, the clinical evidence review found that currently available risk-stratification tools (e.g., Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain Version 1, SOAPP-R, and Brief Risk Interview) show insufficient accuracy for classification of patients as at low or high risk for abuse or misuse (KQ4). Clinicians should always exercise caution when considering or prescribing opioids for any patient with chronic pain outside of active cancer, palliative, and end-of-life care and should not overestimate the ability of these tools to rule out risks from long-term opioid therapy.

Clinicians should ask patients about their drug and alcohol use. Single screening questions can be used (*206*). For example, the question "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" (with an answer of one or more considered positive) was found in a primary care setting to be 100% sensitive and 73.5% specific for the detection of a drug use disorder compared with a standardized diagnostic interview (*207*). Validated screening tools such as the Drug Abuse Screening Test (DAST) (*208*) and the Alcohol Use Disorders Identification Test (AUDIT) (*209*) can also be used. Clinicians should use PDMP data (see Recommendation 9) and drug testing (see Recommendation 10) as appropriate to assess for concurrent substance use that might place patients at higher risk for opioid use disorder and overdose. Clinicians should also provide specific counseling on increased risks for overdose when opioids are combined with other drugs or alcohol (see Recommendation 3) and ensure that patients receive effective treatment for substance use disorders when needed (see Recommendation 12).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on past or current substance use disorder (KQ2), although a history of substance use disorder was associated with misuse. Similarly, based on contextual evidence, patients with drug or alcohol use disorders are likely to experience greater risks for opioid use disorder and overdose than persons without these conditions. If clinicians consider opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care for patients with drug or alcohol use disorders, they should discuss increased risks for opioid use disorder and overdose with patients, carefully consider whether benefits of opioids outweigh increased risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed. Because pain management in patients with substance use disorder can be complex, clinicians should consider consulting substance use disorder specialists and pain specialists regarding pain management for persons with active or recent past history of substance abuse. Experts also noted that clinicians should communicate with patients' substance use disorder treatment providers if opioids are prescribed.

Patients with Prior Nonfatal Overdose

Although studies were not identified that directly addressed the risk for overdose among patients with prior nonfatal overdose who are prescribed opioids, based on clinical experience, experts thought that prior nonfatal overdose would substantially increase risk for future nonfatal or fatal opioid overdose. If patients experience nonfatal opioid overdose, clinicians should work with them to reduce opioid dosage and to discontinue opioids when possible (see Recommendation 7). If clinicians continue opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care in patients with prior opioid overdose, they should discuss increased risks for overdose with patients, carefully consider whether benefits of opioids outweigh substantial risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed.

Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present

Naloxone is an opioid antagonist that can reverse severe respiratory depression; its administration by lay persons, such as friends and family of persons who experience opioid overdose, can save lives. Naloxone precipitates acute withdrawal among patients physically dependent on opioids. Serious adverse effects, such as pulmonary edema, cardiovascular instability, and seizures, have been reported but are rare at doses consistent with labeled use for opioid overdose (*210*). The contextual evidence review did not find any studies on effectiveness of prescribing naloxone for overdose prevention among patients prescribed opioids for chronic pain. However, there is evidence for effectiveness of naloxone provision in preventing opioid-related overdose death at the community level through community-based distribution (e.g., through overdose education and naloxone distribution programs in community service agencies) to persons at risk for overdose

(mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

9. **Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).**

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve.

In addition, improved timeliness of PDMP data will improve their value in identifying patient risks.

If patients are found to have high opioid dosages, dangerous combinations of medications, or multiple controlled substance prescriptions written by different clinicians, several actions can be taken to augment clinicians' abilities to improve patient safety:

- Clinicians should discuss information from the PDMP with their patient and confirm that the patient is aware of the additional prescriptions. Occasionally, PDMP information can be incorrect (e.g., if the wrong name or birthdate has been entered, the patient uses a nickname or maiden name, or another person has used the patient's identity to obtain prescriptions).
- Clinicians should discuss safety concerns, including increased risk for respiratory depression and overdose, with patients found to be receiving opioids from more than one prescriber or receiving medications that increase risk when combined with opioids (e.g., benzodiazepines) and consider offering naloxone (see Recommendation 8).
- Clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. Clinicians should communicate with others managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care (see Recommendation 11).
- Clinicians should calculate the total MME/day for concurrent opioid prescriptions to help assess the patient's overdose risk (see Recommendation 5). If patients are found to be receiving high total daily dosages of opioids, clinicians should discuss their safety concerns with the patient, consider tapering to a safer dosage (see Recommendations 5 and 7), and consider offering naloxone (see Recommendation 8).
- Clinicians should discuss safety concerns with other clinicians who are prescribing controlled substances for their patient. Ideally clinicians should first discuss concerns with their patient and inform him or her that they plan to coordinate care with the patient's other prescribers to improve the patient's safety.
- Clinicians should consider the possibility of a substance use disorder and discuss concerns with their patient (see Recommendation 12).
- If clinicians suspect their patient might be sharing or selling opioids and not taking them, clinicians should consider urine drug testing to assist in determining whether opioids can be discontinued without causing withdrawal (see Recommendations 7 and 10). A negative drug test for prescribed opioids might indicate the patient is not taking prescribed opioids, although clinicians should consider other possible reasons for this test result (see Recommendation 10).

Experts agreed that clinicians should not dismiss patients from their practice on the basis of PDMP information. Doing so can adversely affect patient safety, could represent patient abandonment, and could result in missed opportunities to provide potentially lifesaving information (e.g., about risks of opioids and overdose prevention) and interventions (e.g., safer prescriptions, nonopioid pain treatment [see Recommendation 1], naloxone [see Recommendation 8], and effective treatment for substance use disorder [see Recommendation 12]).

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs (recommendation category: B, evidence type: 4).

Concurrent use of opioid pain medications with other opioid pain medications, benzodiazepines, or heroin can increase patients' risk for overdose. Urine drug tests can provide information about drug use that is not reported by the patient. In addition, urine drug tests can assist clinicians in identifying when patients are not taking opioids prescribed for them, which might in some cases indicate diversion or other clinically important issues such as difficulties with adverse effects. Urine drug tests do not provide accurate information about how much or what dose of opioids or other drugs a patient took. The clinical evidence review did not find studies evaluating the effectiveness of urine drug screening for risk mitigation during opioid prescribing for pain (KQ4). The contextual evidence review found that urine drug testing can provide useful information about patients assumed not to be using unreported drugs. Urine drug testing results can be subject to misinterpretation and might sometimes be associated with practices that might harm patients (e.g., stigmatization, inappropriate termination from care). Routine use of urine drug tests with standardized policies at the practice or clinic level might destigmatize their use. Although random drug testing also might destigmatize urine drug testing, experts thought that truly random testing was not feasible in clinical practice. Some clinics obtain a urine specimen at every visit, but only send it for testing on a random schedule. Experts noted that in addition to direct costs of urine drug testing, which often are not covered fully by insurance and can be a burden for patients, clinician time is needed to interpret, confirm, and communicate results.

Experts agreed that prior to starting opioids for chronic pain and periodically during opioid therapy, clinicians should

use urine drug testing to assess for prescribed opioids as well as other controlled substances and illicit drugs that increase risk for overdose when combined with opioids, including nonprescribed opioids, benzodiazepines, and heroin. There was some difference of opinion among experts as to whether this recommendation should apply to all patients, or whether this recommendation should entail individual decision making with different choices for different patients based on values, preferences, and clinical situations. While experts agreed that clinicians should use urine drug testing before initiating opioid therapy for chronic pain, they disagreed on how frequently urine drug testing should be conducted during long-term opioid therapy. Most experts agreed that urine drug testing at least annually for all patients was reasonable. Some experts noted that this interval might be too long in some cases and too short in others, and that the follow-up interval should be left to the discretion of the clinician. Previous guidelines have recommended more frequent urine drug testing in patients thought to be at higher risk for substance use disorder (*30*). However, experts thought that predicting risk prior to urine drug testing is challenging and that currently available tools do not allow clinicians to reliably identify patients who are at low risk for substance use disorder.

In most situations, initial urine drug testing can be performed with a relatively inexpensive immunoassay panel for commonly prescribed opioids and illicit drugs. Patients prescribed less commonly used opioids might require specific testing for those agents. The use of confirmatory testing adds substantial costs and should be based on the need to detect specific opioids that cannot be identified on standard immunoassays or on the presence of unexpected urine drug test results. Clinicians should be familiar with the drugs included in urine drug testing panels used in their practice and should understand how to interpret results for these drugs. For example, a positive "opiates" immunoassay detects morphine, which might reflect patient use of morphine, codeine, or heroin, but this immunoassay does not detect synthetic opioids (e.g., fentanyl or methadone) and might not detect semisynthetic opioids (e.g., oxycodone). However, many laboratories use an oxycodone immunoassay that detects oxycodone and oxymorphone. In some cases, positive results for specific opioids might reflect metabolites from opioids the patient is taking and might not mean the patient is taking the specific opioid for which the test was positive. For example, hydromorphone is a metabolite of hydrocodone, and oxymorphone is a metabolite of oxycodone. Detailed guidance on interpretation of urine drug test results, including which tests to order and expected results, drug detection time in urine, drug metabolism, and other considerations has been published previously (*30*). Clinicians should not test for substances for which results would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC). In addition, restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of urine drug testing, given the substantial costs associated with confirmatory testing methods. Before ordering urine drug testing, clinicians should have a plan for responding to unexpected results. Clinicians should explain to patients that urine drug testing is intended to improve their safety and should also explain expected results (e.g., presence of prescribed medication and absence of drugs, including illicit drugs, not reported by the patient). Clinicians should ask patients about use of prescribed and other drugs and ask whether there might be unexpected results. This will provide an opportunity for patients to provide information about changes in their use of prescribed opioids or other drugs. Clinicians should discuss unexpected results with the local laboratory or toxicologist and with the patient. Discussion with patients prior to specific confirmatory testing can sometimes yield a candid explanation of why a particular substance is present or absent and obviate the need for expensive confirmatory testing on that visit. For example, a patient might explain that the test is negative for prescribed opioids because she felt opioids were no longer helping and discontinued them. If unexpected results are not explained, a confirmatory test using a method selective enough to differentiate specific opioids and metabolites (e.g., gas or liquid chromatography/mass spectrometry) might be warranted to clarify the situation.

Clinicians should use unexpected results to improve patient safety (e.g., change in pain management strategy [see Recommendation 1], tapering or discontinuation of opioids [see Recommendation 7], more frequent re-evaluation [see Recommendation 7], offering naloxone [see Recommendation 8], or referral for treatment for substance use disorder [see Recommendation 12], all as appropriate). If tests for prescribed opioids are repeatedly negative, confirming that the patient is not taking the prescribed opioid, clinicians can discontinue the prescription without a taper. Clinicians should not dismiss patients from care based on a urine drug test result because this could constitute patient abandonment and could have adverse consequences for patient safety, potentially including the patient obtaining opioids from alternative sources and the clinician missing opportunities to facilitate treatment for substance use disorder.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently

whenever possible (recommendation category: A, evidence type: 3).

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. The clinical evidence review did not address risks of benzodiazepine co-prescription among patients prescribed opioids. However, the contextual evidence review found evidence in epidemiologic series of concurrent benzodiazepine use in large proportions of opioid-related overdose deaths, and a case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (*212*). Experts agreed that although there are circumstances when it might be appropriate to prescribe opioids to a patient receiving benzodiazepines (e.g., severe acute pain in a patient taking long-term, stable low-dose benzodiazepine therapy), clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (e.g., muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians (see Recommendation 9) and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. Because of greater risks of benzodiazepine withdrawal relative to opioid withdrawal, and because tapering opioids can be associated with anxiety, when patients receiving both benzodiazepines and opioids require tapering to reduce risk for fatal respiratory depression, it might be safer and more practical to taper opioids first (see Recommendation 7). Clinicians should taper benzodiazepines gradually if discontinued because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and, in rare cases, death (contextual evidence review). A commonly used tapering schedule that has been used safely and with moderate success is a reduction of the benzodiazepine dose by 25% every 1–2 weeks (*213*,*214*). CBT increases tapering success rates and might be particularly helpful for patients struggling with a benzodiazepine taper (*213*). If benzodiazepines prescribed for anxiety are tapered or discontinued, or if patients receiving opioids require treatment for anxiety, evidence-based psychotherapies (e.g., CBT) and/or specific anti-depressants or other nonbenzodiazepine medications approved for anxiety should be offered. Experts emphasized that clinicians should communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2).

Opioid use disorder (previously classified as opioid abuse or opioid dependence) is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two defined criteria occurring within a year (http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf) (*20*).

The clinical evidence review found prevalence of opioid dependence (using DSM-IV diagnosis criteria) in primary care settings among patients with chronic pain on opioid therapy to be 3%–26% (KQ2). As found in the contextual evidence review and supported by moderate quality evidence, opioid agonist or partial agonist treatment with methadone maintenance therapy or buprenorphine has been shown to be more effective in preventing relapse among patients with opioid use disorder (*151*–*153*). Some studies suggest that using behavioral therapies in combination with these treatments can reduce opioid misuse and increase retention during maintenance therapy and improve compliance after detoxification (*154*,*155*); behavioral therapies are also recommended by clinical practice guidelines (*215*). The cited studies primarily evaluated patients with a history of illicit opioid use, rather than prescription opioid use for chronic pain. Recent studies among patients with prescription opioid dependence (based on DSM-IV criteria) have found maintenance therapy with buprenorphine and buprenorphine-naloxone effective in preventing relapse (*216*,*217*). Treatment need in a community is often not met by capacity to provide buprenorphine or methadone maintenance therapy (*218*), and patient cost can be a barrier to buprenorphine treatment because insurance coverage of buprenorphine for opioid use disorder is often limited (*219*). Oral or long-acting injectable formulations of naltrexone can also be used as medication-assisted treatment for opioid use disorder in nonpregnant adults, particularly for highly motivated persons (*220*,*221*). Experts agreed that clinicians prescribing opioids should identify treatment resources for opioid use disorder in the community and should work together to ensure sufficient treatment capacity for opioid use disorder at the practice level.

If clinicians suspect opioid use disorder based on patient concerns or behaviors or on findings in prescription drug monitoring program data (see Recommendation 9) or from urine drug testing (see Recommendation 10), they should discuss their concern with their patient and provide an opportunity for the patient to disclose related concerns or problems. Clinicians should assess for the presence of opioid use disorder using DSM-5 criteria (*20*). Alternatively, clinicians can arrange for a substance use disorder treatment specialist to assess for the presence of opioid use disorder. For patients meeting criteria for opioid use disorder, clinicians should offer or arrange for patients to receive evidence-based treatment, usually medication-assisted treatment with buprenorphine or methadone maintenance therapy in combination with behavioral therapies. Oral or long-acting injectable naltrexone, a long-acting opioid antagonist, can also be used in non-pregnant adults. Naltrexone blocks the effects of opioids if they are used but requires adherence to daily oral therapy or monthly injections. For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine (without naloxone) or methadone has been associated with improved maternal outcomes and should be offered (see Recommendation 8). Clinicians should also consider offering naloxone for overdose prevention to patients with opioid use disorder (see Recommendation 8). For patients with problematic opioid use that does not meet criteria for opioid use disorder, experts noted that clinicians can offer to taper and discontinue opioids (see Recommendation 7). For patients who choose to but are unable to taper, clinicians may reassess for opioid use disorder and offer opioid agonist therapy if criteria are met.

Physicians not already certified to provide buprenorphine in an office-based setting can undergo training to receive a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA) that allows them to prescribe buprenorphine to treat patients with opioid use disorder. Physicians prescribing opioids in communities without sufficient treatment capacity for opioid use disorder should strongly consider obtaining this waiver. Information about qualifications and the process to obtain a waiver are available from SAMHSA (*222*). Clinicians do not need a waiver to offer naltrexone for opioid use disorder as part of their practice.

Additional guidance has been published previously (*215*) on induction, use, and monitoring of buprenorphine treatment (see Part 5) and naltrexone treatment (see Part 6) for opioid use disorder and on goals, components of, and types of effective psychosocial treatment that are recommended in conjunction with pharmacological treatment of opioid use disorder (see Part 7). Clinicians unable to provide treatment themselves should arrange for patients with opioid use disorder to receive care from a substance use disorder treatment specialist, such as an office-based buprenorphine or naltrexone treatment provider, or from an opioid treatment program certified by SAMHSA to provide supervised medication-assisted treatment for patients with opioid use disorder. Clinicians should assist patients in finding qualified treatment providers and should arrange for patients to follow up with these providers, as well as arranging for ongoing coordination of care. Clinicians should not dismiss patients from their practice because of a substance use disorder because this can adversely affect patient safety and could represent patient abandonment. Identification of substance use disorder represents an opportunity for a clinician to initiate potentially life-saving interventions, and it is important for the clinician to collaborate with the patient regarding their safety to increase the likelihood of successful treatment. In addition, although identification of an opioid use disorder can alter the expected benefits and risks of opioid therapy for pain, patients with co-occurring pain and substance use disorder require ongoing pain management that maximizes benefits relative to risks. Clinicians should continue to use nonpharmacologic and nonopioid pharmacologic pain treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to provide optimal pain management.

Resources to help with arranging for treatment include SAMHSA's buprenorphine physician locator (http://buprenorphine.samhsa.gov/bwns_locator); SAMHSA's Opioid Treatment Program Directory (http://dpt2.samhsa.gov/treatment/directory.aspx); SAMHSA's Provider Clinical Support System for Opioid Therapies (http://pcss-o.org), which offers extensive experience in the treatment of substance use disorders and specifically of opioid use disorder, as well as expertise on the interface of pain and opioid misuse; and SAMHSA's Provider's Clinical Support System for Medication-Assisted Treatment (http://pcssmat.org), which offers expert physician mentors to answer questions about assessment for and treatment of substance use disorders.

Conclusions and Future Directions

Clinical guidelines represent one strategy for improving prescribing practices and health outcomes. Efforts are required to disseminate the guideline and achieve widespread adoption and implementation of the recommendations in clinical settings. CDC will translate this guideline into user-friendly materials for distribution and use by health systems, medical professional societies, insurers, public health departments, health information technology developers, and clinicians and engage in dissemination efforts. CDC has provided a

checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025), additional resources such as fact sheets (http://www.cdc.gov/drugoverdose/prescribing/resources.html), and will provide a mobile application to guide clinicians in implementing the recommendations. CDC will also work with partners to support clinician education on pain management options, opioid therapy, and risk mitigation strategies (e.g., urine drug testing). Activities such as development of clinical decision support in electronic health records to assist clinicians' treatment decisions at the point of care; identification of mechanisms that insurers and pharmacy benefit plan managers can use to promote safer prescribing within plans; and development of clinical quality improvement measures and initiatives to improve prescribing and patient care within health systems have promise for increasing guideline adoption and improving practice. In addition, policy initiatives that address barriers to implementation of the guidelines, such as increasing accessibility of PDMP data within and across states, e-prescribing, and availability of clinicians who can offer medication-assisted treatment for opioid use disorder, are strategies to consider to enhance implementation of the recommended practices. CDC will work with federal partners and payers to evaluate strategies such as payment reform and health care delivery models that could improve patient health and safety. For example, strategies might include strengthened coverage for nonpharmacologic treatments, appropriate urine drug testing, and medication-assisted treatment; reimbursable time for patient counseling; and payment models that improve access to interdisciplinary, coordinated care.

As highlighted in the forthcoming report on the National Pain Strategy, an overarching federal effort that outlines a comprehensive population-level health strategy for addressing pain as a public health problem, clinical guidelines complement other strategies aimed at preventing illnesses and injuries that lead to pain. A draft of the National Pain Strategy has been published previously (*180*). These strategies include strengthening the evidence base for pain prevention and treatment strategies, reducing disparities in pain treatment, improving service delivery and reimbursement, supporting professional education and training, and providing public education. It is important that overall improvements be made in developing the workforce to address pain management in general, in addition to opioid prescribing specifically. This guideline also complements other federal efforts focused on addressing the opioid overdose epidemic including prescriber training and education, improving access to treatment for opioid use disorder, safe storage and disposal programs, utilization management mechanisms, naloxone distribution programs, law enforcement and supply reduction efforts, prescription drug monitoring program improvements, and support for community coalitions and state prevention programs.

This guideline provides recommendations that are based on the best available evidence that was interpreted and informed by expert opinion. The clinical scientific evidence informing the recommendations is low in quality. To inform future guideline development, more research is necessary to fill in critical evidence gaps. The evidence reviews forming the basis of this guideline clearly illustrate that there is much yet to be learned about the effectiveness, safety, and economic efficiency of long-term opioid therapy. As highlighted by an expert panel in a recent workshop sponsored by the National Institutes of Health on the role of opioid pain medications in the treatment of chronic pain, "evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain" (*223*). The National Institutes of Health panel recommended that research is needed to improve our understanding of which types of pain, specific diseases, and patients are most likely to be associated with benefit and harm from opioid pain medications; evaluate multidisciplinary pain interventions; estimate cost-benefit; develop and validate tools for identification of patient risk and outcomes; assess the effectiveness and harms of opioid pain medications with alternative study designs; and investigate risk identification and mitigation strategies and their effects on patient and public health outcomes. It is also important to obtain data to inform the cost feasibility and cost-effectiveness of recommended actions, such as use of nonpharmacologic therapy and urine drug testing. Research that contributes to safer and more effective pain treatment can be implemented across public health entities and federal agencies (*4*). Additional research can inform the development of future guidelines for special populations that could not be adequately addressed in this guideline, such as children and adolescents, where evidence and guidance is needed but currently lacking. CDC is committed to working with partners to identify the highest priority research areas to build the evidence base. Yet, given that chronic pain is recognized as a significant public health problem, the risks associated with long-term opioid therapy, the availability of effective nonpharmacological and nonopioid pharmacologic treatment options for pain, and the potential for improvement in the quality of health care with the implementation of recommended practices, a guideline for prescribing is warranted with the evidence that is currently available. The balance between the benefits and the risks of long-term opioid therapy for chronic pain based on both clinical and contextual evidence is strong enough to support the issuance of category A recommendations in most cases.

CDC will revisit this guideline as new evidence becomes available to determine when evidence gaps have been sufficiently closed to warrant an update of the guideline. Until this research is conducted, clinical practice guidelines will have to be based on the best available evidence and expert opinion. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC is committed to evaluating the guideline to identify the impact of the recommendations on clinician and patient outcomes, both intended and unintended, and revising the recommendations in future updates when warranted.

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TABLE 1. Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness and comparative effectiveness (KQ1)							
Effectiveness of long-term opioid therapy versus placebo or no opioid therapy for long-term (≥1 year) outcomes							
Pain, function, and quality of life	None	—[†]	—	—	Insufficient	—	No evidence
Harms and adverse events (KQ2)							
Risks of opioids versus placebo or no opioids on opioid abuse, addiction, and related outcomes; overdose; and other harms							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found long-term use of prescribed opioids associated with an increased risk of abuse or dependence diagnosis versus no opioid use (adjusted OR ranged from 14.9 to 122.5, depending on dose).
Abuse or addiction	10 uncontrolled studies (n = 3,780)	Very serious limitations	Very serious inconsistency	No imprecision	4	None identified	In primary care settings, prevalence of opioid abuse ranged from 0.6% to 8% and prevalence of dependence from 3% to 26%. In pain clinic settings, prevalence of misuse ranged from 8% to 16% and addiction from 2% to 14%. Prevalence of aberrant drug-related behaviors ranged from 6% to 37%.
Overdose	1 cohort study (n = 9,940)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Current opioid use associated with increased risk of any overdose events (adjusted HR 5.2, 95% CI = 2.1–12) and serious overdose events (adjusted HR 8.4, 95% CI = 2.5–28) versus current nonuse.
Fractures	1 cohort study (n = 2,341) and 1 case–control study (n = 21,739 case patients)	Serious limitations	No inconsistency	No imprecision	3	None identified	Opioid use associated with increased risk of fracture in 1 cohort study (adjusted HR 1.28, 95% CI = 0.99–1.64) and 1 case-control study (adjusted OR 1.27, 95% CI = 1.21–1.33).
Myocardial infarction	1 cohort study (n = 426,124) and 1 case–control study (n = 11,693 case patients)	No limitations	No inconsistency	No imprecision	3	None identified	Current opioid use associated with increased risk of myocardial infarction versus nonuse (adjusted OR 1.28, 95% CI = 1.19–1.37 and incidence rate ratio 2.66, 95% CI = 2.30–3.08).
Endocrinologic harms	1 cross-sectional study (n = 11,327)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Long-term opioid use associated with increased risk for use of medications for erectile dysfunction or testosterone replacement versus nonuse (adjusted OR 1.5, 95% CI = 1.1–1.9).
How do harms vary depending on the opioid dose used?							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found higher doses of long-term opioid therapy associated with increased risk of opioid abuse or dependence than lower doses. Compared to no opioid prescription, the adjusted odds ratios were 15 (95% CI = 10–21) for 1 to 36 MME/day, 29 (95 % CI = 20–41) for 36 to120 MME/day, and 122 (95 % CI = 73–205) for ≥120 MME/day.
Overdose	1 cohort study (n = 9,940) and 1 case–control study (n = 593 case patients in primary analysis)	Serious limitations	No inconsistency	No imprecision	3	Magnitude of effect, dose response relationship	Versus 1 to <20 MME/day, one cohort study found an adjusted HR for an overdose event of 1.44 (95% CI = 0.57–3.62) for 20 to <50 MME/day that increased to 8.87 (95% CI = 3.99–19.72) at ≥100 MME/day; one case-control study found an adjusted OR for an opioid-related death of 1.32 (95% CI = 0.94–1.84) for 20 to 49 MME/day that increased to 2.88 (95% CI = 1.79–4.63) at ≥200 MME/day.
Fractures	1 cohort study (n = 2,341)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Risk of fracture increased from an adjusted HR of 1.20 (95% CI = 0.92–1.56) at 1 to <20 MME/day to 2.00 (95% CI = 1.24–3.24) at ≥50 MME/day; the trend was of borderline statistical significance.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Myocardial infarction	1 cohort study (n = 426,124)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Relative to a cumulative dose of 0 to 1,350 MME during a 90-day period, the incidence rate ratio for myocardial infarction for 1350 to <2700 MME was 1.21 (95% CI = 1.02–1.45), for 2,700 to <8,100 MME was 1.42 (95% CI = 1.21–1.67), for 8,100 to <18,000 MME was 1.89 (95% CI = 1.54–2.33), and for ≥18,000 MME was 1.73 (95% CI = 1.32–2.26).
Motor vehicle crash injuries	1 case–control study (n = 5,300 case patients)	No limitations	Unknown (1 study)	No imprecision	3	None identified	No association between opioid dose and risk of motor vehicle crash injuries even though opioid doses >20 MME/day were associated with increased odds of road trauma among drivers.
Endocrinologic harms	1 cross-sectional study (n = 11,327) New for update: 1 additional cross-sectional study (n=1,585)	Serious limitations	Consistent	No imprecision	3	None identified	Relative to 0 to <20 MME/day, the adjusted OR for ≥120 MME/day for use of medications for erectile dysfunction or testosterone replacement was 1.6 (95% CI = 1.0–2.4). One new cross-sectional study found higher-dose long-term opioid therapy associated with increased risk of androgen deficiency among men receiving immediate-release opioids (adjusted OR per 10 MME/day 1.16, 95% CI = 1.09–1.23), but the dose response was very weak among men receiving ER/LA opioids.
Dosing strategies (KQ3)							
Comparative effectiveness of different methods for initiating opioid therapy and titrating doses							
Pain	3 randomized trials (n = 93)	Serious limitations	Serious inconsistency	Very serious imprecision	4	None identified	Trials on effects of titration with immediate-release versus ER/LA opioids reported inconsistent results and had additional differences between treatment arms in dosing protocols (titrated versus fixed dosing) and doses of opioids used.
Overdose	New for update: 1 cohort study (n = 840,606)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One new cross-sectional study found initiation of therapy with an ER/LA opioid associated with increased risk of overdose versus initiation with an immediate-release opioid (adjusted HR 2.33, 95% CI = 1.26–4.32).
Comparative effectiveness of different ER/LA opioids							
Pain and function	3 randomized trials (n = 1,850)	Serious limitations	No inconsistency	No imprecision	3	None identified	No differences
All-cause mortality	1 cohort study (n = 108,492) New for update: 1 cohort study (n = 38,756)	Serious limitations	Serious inconsistency	No imprecision	4	None identified	One cohort study found methadone to be associated with lower all-cause mortality risk than sustained-release morphine in a propensity-adjusted analysis (adjusted HR 0.56, 95% CI = 0.51–0.62) and one cohort study among Tennessee Medicaid patients found methadone to be associated with higher risk of all-cause mortality than sustained-release morphine (adjusted HR 1.46, 95% CI = 1.17–1.73).
Abuse and related outcomes	1 cohort study (n = 5,684)	Serious limitations	Unknown (1 study)	Serious imprecision	4	None identified	One cohort study found some differences between ER/LA opioids in rates of adverse outcomes related to abuse, but outcomes were nonspecific for opioid-related adverse events, precluding reliable conclusions.
ER/LA versus immediate-release opioids							
Endocrinologic harms	New for update: 1 cross-sectional study (n = 1,585)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One cross-sectional study found ER/LA opioids associated with increased risk of androgen deficiency versus immediate-release opioids (adjusted OR 3.39, 95% CI = 2.39–4.77).

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Dose escalation versus dose maintenance or use of dose thresholds							
Pain, function, or withdrawal due to opioid misuse	1 randomized trial (n = 140)	Serious limitations	Unknown (1 study)	Very serious imprecision	3	None identified	No difference between more liberal dose escalation versus maintenance of current doses in pain, function, or risk of withdrawal due to opioid misuse, but there was limited separation in opioid doses between groups (52 versus 40 MME/day at the end of the trial).
Immediate-release versus ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled and continuous versus as-needed dosing of opioids; or opioid rotation versus maintenance of current therapy							
Pain, function, quality of life, and outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of decreasing or tapering opioid doses versus continuation of opioid therapy							
Pain and function	1 randomized trial (n = 10)	Very serious limitations	Unknown (1 study)	Very serious imprecision	4	None identified	Abrupt cessation of morphine was associated with increased pain and decreased function compared with continuation of morphine.
Comparative effectiveness of different tapering protocols and strategies							
Opioid abstinence	2 nonrandomized trials (n = 150)	Very serious limitations	No inconsistency	Very serious imprecision	4	None identified	No clear differences between different methods for opioid discontinuation or tapering in likelihood of opioid abstinence after 3–6 months
Risk assessment and risk mitigation strategies (KQ4)							
Diagnostic accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse among patients with chronic pain being considered for long-term opioid therapy							
Opioid risk tool	3 studies of diagnostic accuracy (n = 496) New for update: 2 studies of diagnostic accuracy (n = 320)	Serious limitations	Very serious inconsistency	Serious imprecision	4	None identified	Based on a cutoff score of >4 (or unspecified), five studies (two fair-quality, three poor-quality) reported sensitivity that ranged from 0.20 to 0.99 and specificity that ranged from 0.16 to 0.88.
Screener and Opioid Assessment for Patients with Pain, Version 1	2 studies of diagnostic accuracy (n = 203)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of ≥8, sensitivity was 0.68 and specificity was 0.38 in one study, for a positive likelihood ratio of 1.11 and a negative likelihood ratio of 0.83. Based on a cutoff score of >6, sensitivity was 0.73 in one study.
Screener and Opioid Assessment for Patients with Pain-Revised	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of >3 or unspecified, sensitivity was 0.25 and 0.53 and specificity was 0.62 and 0.73 in two studies, for likelihood ratios close to 1.
Brief Risk Interview	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a "high risk" assessment, sensitivity was 0.73 and 0.83 and specificity was 0.43 and 0.88 in two studies, for positive likelihood ratios of 1.28 and 7.18 and negative likelihood ratios of 0.63 and 0.19.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Comparative effectiveness of treatment strategies for managing patients with addiction to prescription opioids							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of opioid therapy for acute pain on long-term use (KQ5)							
Long-term opioid use	New for update: 2 cohort studies (n = 399,852)	Serious limitations	No inconsistency	No imprecision	3	None identified	One study found use of opioids within 7 days of low-risk surgery associated with increased likelihood of opioid use at 1 year (adjusted OR 1.44, 95% CI = 1.39–1.50), and one study found use of opioids within 15 days of onset of low back pain among workers with a compensation claim associated with increased risk of late opioid use (adjusted OR 2.08, 95% CI = 1.55–2.78 for 1 to 140 MME/day and OR 6.14, 95% CI = 4.92–7.66 for ≥450 MME/day).

Abbreviations: CI = confidence interval; ER/LA = extended release/long-acting; HR = hazard ratio; MME = morphine milligram equivalents; OR = odds ratio.
* Ratings were made per GRADE quality assessment criteria; "no limitations" indicates that limitations assessed through the GRADE method were not identified.
† Not applicable as no evidence was available for rating.

TABLE 2. Morphine milligram equivalent (MME) doses for commonly prescribed opioids

Opioid	Conversion factor*
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1–20 mg/day	4
21–40 mg/day	8
41–60 mg/day	10
≥61–80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Tapentadol†	0.4

Source: Adapted from Von Korff M, Saunders K, Ray GT, et al. Clin J Pain 2008;24:521–7 and Washington State Interagency Guideline on Prescribing Opioids for Pain (http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf).

* Multiply the dose for each opioid by the conversion factor to determine the dose in MMEs. For example, tablets containing hydrocodone 5 mg and acetaminophen 300 mg taken four times a day would contain a total of 20 mg of hydrocodone daily, equivalent to 20 MME daily; extended-release tablets containing oxycodone 10mg and taken twice a day would contain a total of 20mg of oxycodone daily, equivalent to 30 MME daily. The following cautions should be noted: 1) All doses are in mg/day except for fentanyl, which is mcg/hr. 2) Equianalgesic dose conversions are only estimates and cannot account for individual variability in genetics and pharmacokinetics. 3) Do not use the calculated dose in MMEs to determine the doses to use when converting opioid to another; when converting opioids the new opioid is typically dosed at substantially lower than the calculated MME dose to avoid accidental overdose due to incomplete cross-tolerance and individual variability in opioid pharmacokinetics. 4) Use particular caution with methadone dose conversions because the conversion factor increases at higher doses. 5) Use particular caution with fentanyl since it is dosed in mcg/hr instead of mg/day, and its absorption is affected by heat and other factors.

† Tapentadol is a mu receptor agonist and norepinephrine reuptake inhibitor. MMEs are based on degree of mu-receptor agonist activity, but it is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely mu receptor agonists.

Please note: An erratum has been published for this issue. To view the erratum, please click here.

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Errata

Vol. 65, No. RR-1

In the report, "CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016," three errors occurred. On page 1, the last sentence of the Summary should read, "CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (**http://www.cdc.gov/drugoverdose/prescribing/resources.html**) with additional tools to guide clinicians in implementing the recommendations." On page 8, the first sentence of the first full paragraph should read, "NCIPC announced an open meeting of the NCIPC BSC in the Federal Register on January 11, **2016**." On page 49, in the fourth line of the Stakeholder Review Group, the affiliation for Gerald "Jerry" F. Joseph should read, "American College of **Obstetricians and Gynecologists**."

Vol. 65, No. 9

In the report, "Notes from the Field: Lymphocytic Choriomeningitis Virus Meningoencephalitis from a Household Rodent Infestation — Minnesota, 2015," on page 248, the first sentence of the fourth paragraph should read, "The family was referred for integrated pest management services through **the St. Paul-Ramsey County Department of Public Health, with assistance from the Minnesota Department of Health Healthy Homes grant program**."

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Chronic Pain Management Guidelines

Introduction

The International Association for the Study of Pain defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."[1] Pain is a multifactorial process that has both objective and subjective components. Additionally, the Institute of Medicine estimates that 100 million Americans suffer from chronic pain.[2]

Chronic pain is complex and can manifest in many ways.[3] Pain is a continuum; inappropriately treated acute pain can transition to chronic pain.[4,5] Chronic pain may result from injury, nerve damage, or various disease states, or it can be idiopathic. Additionally, chronic pain may have a psychological component leading to anxiety, depression, or somatization disorders. Chronic pain is differentiated from acute pain by its persistence, physiological maintenance mechanisms, and its potential impact on an individual's functioning and quality of life.[6] Inadequate treatment of pain, either under treatment or over treatment, can lead to negative health effects, a decreased quality of life, or adverse events. Finally, the goal of chronic pain management is to use a patient-centered approach to treat the patient's pain and improve the patient's well-being, functionality, and quality of life.

Purpose

The purpose of these guidelines is to promote safe and effective chronic pain management. The *Standards for Nurse Anesthesia Practice* are the foundation for chronic pain management practice.[7] The *Chronic Pain Management Guidelines* are intended to promote high-quality care and do not assure specific outcomes. These guidelines were developed using an evidence-based literature review process, AANA pain management scope of practice membership survey, ongoing consultation with the AANA Practice Committee and the Pain Management Work Team, which is composed of Certified Registered Nurse Anesthetist (CRNA) pain management experts, and an open comment survey of a sample of AANA members.

CRNA Scope of Practice

CRNAs practice in accordance with their professional scope of practice, federal and state law, and facility policy to provide chronic pain management services.[8]

As advanced practice registered nurses, CRNAs are uniquely skilled to deliver pain treatment in a compassionate and holistic manner. By virtue of education and individual clinical experience and competency, a CRNA may practice chronic pain management utilizing a variety of therapeutic, physiological, pharmacological, interventional, and psychological modalities in the management and treatment of pain. As part of their educational preparation, CRNAs are required to learn and demonstrate competence in the management of pain, a critical component in the delivery of anesthesia care. The Council on Accreditation of Nurse Anesthesia Educational Programs (COA) standards require that nurse anesthesia programs provide content in anatomy, physiology, pathophysiology, pharmacology, and pain management, and require that nurse anesthesia students obtain clinical experiences in regional anesthetic techniques (i.e., spinal, epidural, and peripheral).[9]

As the understanding of the patient's pain experience, its corresponding transmission processes, and pain treatment modalities have evolved, the role of healthcare professionals in treating pain has seen a similar evolution. As new knowledge is discovered and new treatment modalities and technologies emerge, these advancements will logically translate into clinical practice with the goal of improving patient outcomes.

CRNA Chronic Pain Management Practice Models

The guidelines below outline the broad process for the management of chronic pain. Chronic pain management services are provided by CRNAs in a variety of practice models based on patient, provider, and facility needs. CRNAs may be members of a multidisciplinary pain management team, receive referrals from other clinicians, or serve as the sole providers of chronic pain management services. CRNAs provide patient-centered chronic pain treatments, working toward the common goal of decreasing the patient's pain and improving the patient's quality of life and functionality.

When working in collaboration with a patient's primary care provider or other referring clinician, CRNAs may share certain responsibilities of chronic pain management. The CRNA reviews and may add relevant findings to information provided by a referring clinician (e.g., history and physical, diagnostic results, etc.) in order to safely administer chronic pain management services. CRNAs are responsible and accountable for judgments made and actions taken in their professional practice.[10]

Chronic Pain Management Guidelines

1. **Patient Evaluation**
   a. **Patient History and Physical**
   Complete a patient health history and physical examination, which should include, but not be limited to: a review of allergies and health, surgical, medication, and social history; and a focused pain evaluation addressing pain symptoms, identification of pain risk factors, and current and previous pain treatments.[11-18] If available at time of referral, the CRNA should review the results of previous diagnostic testing, psychological evaluation, and diagnosis.

   b. **Diagnosis**
   Both non-interventional and interventional diagnostic procedures may be employed as part of the assessment and evaluation of the patient's pain. These procedures may include, but are not limited to, laboratory testing, diagnostic imaging, electrodiagnostic studies, and focused regional injections as indicated.[19-26]

2. **Management**
   a. **Plan of Care**
   Formulate a patient-specific treatment plan based on a dynamic, comprehensive assessment and evaluation.[27,28] The plan should integrate baseline functional capacity and set realistic functional goals, including measurable targets for pain management.[29] A plan to implement alternative modalities should be considered and developed, as appropriate, if the original goals and targets are not met.

   b. **Education**
   Patient and family education should be made available regarding etiology of pain, treatment plan and goals, potential alternative therapy, and consequences for non-adherence to the treatment plan.[30-33] Discuss possible side effects and complications of the treatment regimen with the patient and family. In addition, provide instruction on the plan to address these side effects and respond to complications, should they occur.[30,32,33] All discussions with the patient's family or other caretakers should be conducted in compliance with state and federal healthcare privacy laws.

   c. **Informed Consent and Treatment Agreement**
   Obtain and document informed consent. The informed consent process should include a

discussion of the individualized treatment plan, planned procedures, alternatives methods of treatment, and risks and benefits of the plan. For additional guidance regarding informed consent, review the AANA's *Informed Consent in Anesthesia*.[34]

CRNAs should be aware of potential drug-seeking behavior. CRNAs should enter into a pain management treatment agreement with the patient, when appropriate. The pain management treatment agreement establishes an understanding of the elements of the treatment plan and outlines patient and provider responsibilities, expectations for compliance, and response to emergency issues.[18,19,27-29,35-37]

d. Non-Pharmacologic Management

Non-pharmacologic treatment modalities may decrease pain and, when appropriate, should be considered as part of the plan of care. These treatments may include, but are not limited to, hypnosis, acupuncture, massage, meditation, reflexology, relaxation techniques, biofeedback, counseling, physical therapy, occupational therapy, or therapeutic manipulation.[6,15,18,38-51] CRNAs should exercise an interdisciplinary approach to patient care and consult with or refer patients to other clinicians, as appropriate.[3,18,19,30]

e. Pharmacologic Management

Pharmacologic interventions may be managed by the CRNA, the patient's primary care provider, or referring clinician. CRNA prescriptive authority varies depending on state law. Pharmacologic treatment of chronic pain may include, but is not limited to, topically applied medications, local anesthetics, steroidal and non-steroidal anti-inflammatory agents, anticonvulsants, antidepressants, sedatives, muscle relaxants, non-opioid analgesics, antispasmodics, opioids, and new agents as released.[12,15,28,52,53] Pharmacologic treatment should be tailored to the patient's level of pain, functionality, and response.[12,18,19] Medications should be titrated incrementally to achieve an adequate level of analgesia.[18,28,54] Tapering or discontinuing medications should be considered if the patient's pain is not adequately controlled when taking appropriate doses or if there is no functional improvement on medication therapy.

f. Interventional Therapeutic Techniques

Interventional techniques may be indicated in the management of chronic pain in conjunction with or following non-pharmacologic and/or pharmacologic treatment modalities. These techniques may include, but are not limited to: trigger point injection, peripheral nerve block, sympathetic nerve block, medial or lateral branch block, joint injection (e.g., facet, sacroiliac), intrathecal injection, epidural steroid injection, nerve ablation techniques, and evaluation and management of implantable systems.[3,15,19,20,55-58]

g. Ongoing Assessment and Evaluation

Monitor, measure, and evaluate the patient's pain, functionality, and response to the treatment plan and adjust the treatment plan accordingly.[17,27,37]

h. Safety

Patient and healthcare provider safety are paramount. CRNAs integrate safety into the delivery of care and adhere to standards, guidelines, applicable laws, and facility policies. Chronic pain management practice incorporates appropriate patient monitoring,[7] procedure time-out,[59]

universal infection control precautions,[60] safe injection practices,[61] and radiation safety.[62] For additional guidance, review the AANA's *Standards for Nurse Anesthesia Practice*,[7] *Patient-Centered Perianesthesia Communication, Practice Considerations*,[59] *Infection Control Guide for Certified Registered Nurse Anesthetists*,[60] and *Safe Injection Guidelines for Needle and Syringe Use*.[61]

3. Imaging Technology

Ultrasound, fluoroscopy, CT guidance, or emerging imaging technology may be used, as appropriate, to enhance patient safety and accuracy of invasive diagnostic and therapeutic procedures.[63-67]

4. Documentation

Document pertinent information on the patient's medical record in an accurate, complete, legible, and timely manner. The patient's record may include: the results of the patient assessment and evaluation; diagnosis with supporting documentation (e.g., diagnostic testing, laboratory results, etc.); the patient-specific treatment plan, goals, and objectives; documentation of informed consent; documentation of the procedure; and images of needle placement, if imaging technology was used.[19,27,30,37]

5. Communication

The CRNA and the patient's treatment team, primary care provider, or referring clinician should have ongoing communication regarding the patient's status, treatment plan, treatment compliance, and prognosis to coordinate the plan for ongoing chronic pain management.[3,27,30]

6. Continuous Quality Improvement

CRNAs demonstrate continued competency for treatment management, procedures performed, and technology employed. CRNAs engage in continuous quality improvement through the use of performance metrics and monitoring of performance outcomes. For additional guidance, review the AANA's *Scope of Nurse Anesthesia Practice*,[8] *Guidelines for Core Clinical Privileges for Certified Registered Nurse Anesthetists*,[68] and *Continued Competency*.[69]

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Board Issued Guidelines	Section 6
Subject:	***Prescribing Controlled Substances***
Implemented:	August 1993
Updated:	June 28, 1997, November 7, 2015

November 7, 2015:
The Board adopted the following Guidelines for Prescribing Controlled Substances:

The Board recognizes that controlled substances are useful and can be essential in the treatment of acute pain that results from trauma or surgery, as well as in the management of certain types of chronic pain. Physicians are expected to be knowledgeable about best clinical practices, aware of associated risks, and to practice in compliance with applicable state and federal laws and relevant practice standards.

The Board will consider inappropriate management of pain, particularly chronic pain, to be a departure from accepted best clinical practices, including, but not limited to the following:

- Practicing pain management without sufficient knowledge, skills, and training, or failure to refer patients to an appropriate pain management physician.
- Inadequate attention to initial assessment to determine what, if any, controlled substances are clinically indicated and to determine risks associated with their use in a particular patient.
- Inadequate monitoring during the use of potentially abusable medications.
- Inadequate attention to patient education and informed consent.
- Unjustified dose escalation without adequate attention to risks or alternative treatments.
- Continued use of ineffective treatments, or failure to reduce or discontinue medications when indicated.
- Excessive reliance on opioids, particularly high dose opioids for chronic pain management.
- Not making use of available tools for risk mitigations, including: participation in the state prescription drug monitoring program (in advance of prescribing and for ongoing monitoring); practice in accordance with Specialty Board practice standards; and practice in accordance with the Guidelines issued by the Federation of State Medical Boards (FSMB) in their Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain.

Previous Guidelines for Prescribing Controlled Substances

Updated:
In June 1997, the board adopted the following regulations that place certain prescribing requirements into law:

> 12 AAC 40.975. PRESCRIBING CONTROLLED SUBSTANCES. When prescribing a drug that is a controlled substance, as defined in AS 11.71.900, an individual licensed under this chapter shall create and maintain a complete, clear, and legible written record of care that includes, at a minimum,
> (1) a patient history and evaluation sufficient to support a diagnosis;
> (2) a diagnosis and treatment plan for the diagnosis;
> (3) monitoring the patient for the primary condition that necessitates the drug, side effects of the drug, and results of the drug, as appropriate;
> (4) a record of drugs prescribed, administered, or dispensed, including the type of drug, dose, and any authorized refills.

In August 1993, the Board implemented the following Guidelines for Prescribing Controlled Substances:

1. Perform a work-up sufficient to support a diagnosis, including all necessary tests.
2. Document a treatment plan that includes the use of non-addictive modalities, and make referrals to specialists within the profession when indicated.
3. Document by history or clinical trial that non-addictive modalities are not appropriate or are ineffective.
4. Identify drug seeking patients. Review records. If the patient is new, discuss drug and chemical use and family chemical history with the patient. If drug abuse is suspected, consider obtaining a chemical dependency evaluation or contacting local pharmacies.
5. Obtain informed consent of the patient before using a drug with the potential to cause dependency. Drug companies, the AMA, and other outlets provide printed material in layman's terms that can be used for patient education.
6. Monitor the patient. It is important to follow the patient for the primary condition that necessitates the drug, and for side effects of the drug, as well as the results of the drug. Drug holidays to evaluate for symptom recurrence or withdrawal are important.
7. Control the supply of the drug. Keep detailed records of the type, dose, and amount of the drug prescribed. Monitor, record, and control refills. Require the patient to return to obtain refill authorization at least part of the time. Records of cumulative dosage and average daily dosage are valuable.

8. Maintain contact with the patient's family as an objective source of information on the patient's response and compliance to the therapy.
9. Create an adequate record of care.

GUIDELINES FOR PRESCRIBING CONTROLLED SUBSTANCES FOR PAIN

MEDICAL BOARD OF CALIFORNIA

NOVEMBER 2014

Edmund G. Brown Jr., Governor
David Serrano Sewell, J.D., President, Medical Board of California
Kimberly Kirchmeyer, Executive Director, Medical Board of California

Guidelines for Prescribing Controlled Substances for Pain

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PREAMBLE

Protection of the public is the highest priority for the Medical Board of California (Board) in exercising its licensing, regulatory, and disciplinary functions. The Board recognizes that principles of high-quality medical practice and California law dictate that the people of California have access to appropriate, safe and effective pain management. The application of up-to-date knowledge and treatment modalities can help to restore function and thus improve the quality of life for patients who suffer from pain, particularly chronic pain.

In 1994, the Medical Board of California formally adopted a policy statement titled, "Prescribing Controlled Substances for Pain." This was used to provide guidance to physicians prescribing controlled substances. Several legislative changes since 1994 necessitated revising these guidelines; most recently in 2007.

In November 2011, the Centers for Disease Control and Prevention declared prescription drug abuse to be a nationwide epidemic. Drug overdose is now the leading cause of accidental deaths, exceeding deaths due to motor vehicle accidents. A majority of those overdose deaths involved prescription drugs. The diversion of opioid medications to non-medical uses has also contributed to the increased number of deaths, although the problem is not limited to the aberrant, drug-seeking patient. Injuries are occurring among general patient populations, with some groups at high risk, (e.g., those with depression). Consequently, the Board called for revision of the guidelines to provide additional direction to physicians who prescribe controlled substances for pain.

These guidelines are intended to help physicians improve outcomes of patient care and to prevent overdose deaths due to opioid use. They particularly address the use of opioids in the long-term treatment of chronic pain. Opioid analgesics are widely accepted as appropriate and effective for alleviating moderate-to-severe acute pain, pain associated with cancer, and persistent end-of-life pain. [1] Although some of the recommendations cited in these guidelines might be appropriate for other types of pain, they are not meant for the treatment of patients in hospice or palliative care settings and are not in any way intended to limit treatment where improved function is not anticipated and pain relief is the primary goal. These guidelines underscore the extraordinary complexity in treating pain and how long-term opioid therapy should only be conducted in practice settings where careful evaluation, regular follow-up, and close supervision are ensured. Since opioids are only one of many options to mitigate pain, and because prescribing opioids carries a substantial level of risk, these guidelines offer several non-opioid treatment alternatives. These guidelines are not intended to mandate the standard of care. The Board recognizes that deviations from these guidelines will occur and may be appropriate depending upon the unique needs of individual patients. Medicine is practiced one patient at a time and each patient has individual needs and vulnerabilities. Physicians are encouraged to document their rationale for each

[1] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

prescribing decision. Physicians should understand that if one is ever the subject of a quality of care complaint, peer expert review will be sought by the Board. The expert reviewer must consider the totality of circumstances surrounding the physician's prescribing practice (e.g., issues relating to access of care, paucity of referral sources, etc.) Specifically, experts are instructed to "define the standard of care in terms of the level of skill, knowledge, and care in diagnosis and treatment ordinarily possessed and exercised by other reasonably careful and prudent physicians in the same or similar circumstances at the time in question."[2]

In an effort to provide physicians with as many sources of information as possible, these guidelines link to numerous references relating to prescribing. Additionally, numerous appendices are attached. The Board recognizes that some of the links/appendices may not be consistent with either each other or the main text of the guidelines. The intent for including as many sources of information as practicable is so that physicians can consider varying perspectives to arrive at the best patient-appropriate treatment decision. The Board does not endorse one treatment option over another and encourages physicians to undertake independent research on this continuously evolving subject matter.

UNDERSTANDING PAIN

The diagnosis and treatment of pain is integral to the practice of medicine. In order to cautiously prescribe opioids, physicians must understand the relevant pharmacologic and clinical issues in the use of such analgesics, and carefully structure a treatment plan that reflects the particular benefits and risks of opioid use for each individual patient. Such an approach should be employed in the care of every patient who receives long-term opioid therapy.

The California Medical Association[3] has defined and clarified key concepts relating to pain, excerpted below:

Pain: The definition of pain proposed by the International Association for the Study of Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." It has also been said that "Pain is what the patient says it is." Both definitions acknowledge the subjective nature of pain and are reminders that, with the rare exception of patients who intentionally deceive, a patient's self-report and pain behavior are likely the most reliable indicators of pain and pain severity. As a guide for clinical decision-making, however, both of these definitions are inadequate. In addition, it is important to remember that the subjectivity of pain, particularly when the cause is not apparent, can lead to the stigmatization of those with pain.

[2] Medical Board of California Expert Reviewer Guidelines (rev. January, 2013)
[3] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

Acute and Chronic Pain: Traditionally, pain has been classified by its duration. In this perspective, "acute" pain is relatively short-duration, arises from obvious tissue injury, and usually fades with healing. "Chronic" pain, in contrast, has been variously defined as lasting longer than would be anticipated for the usual course of a given condition, or pain that lasts longer than arbitrary cut-off times, such as 3 or 6 months. Temporal pain labels, however, provide no information about the biological nature of the pain itself, which is often of critical importance.

Nociceptive and Neuropathic Pain: A more useful nomenclature classifies pain on the basis of its patho-physiological process. Nociceptive pain is caused by the activation of nociceptors, and is generally, though not always, short-lived and is associated with the presence of an underlying medical condition. It is a "normal" process; a physiological response to an injurious stimulus. Nociceptive pain is a symptom. Neuropathic pain, on the other hand, results either from an injury to the nervous system or from inadequately-treated nociceptive pain. It is an abnormal response to a stimulus; a pathological process. It is a neuro-biological disease. Neuropathic pain is caused by abnormal neuronal firing in the absence of active tissue damage. It may be continuous or episodic and varies widely in how it is perceived. Neuropathic pain is complex and can be difficult to diagnose and to manage because available treatment options are limited.

A key aspect of both nociceptive and neuropathic pain is the phenomenon of sensitization, which is a state of hyper-excitability in either peripheral nociceptors or neurons in the central nervous system. Sensitization may lead to either hyperalgia or allodynia. Sensitization may arise from intense, repeated or prolonged stimulation of nociceptors, or from the influence of compounds released by the body in response to tissue damage or inflammation. Importantly, many patients – particularly those with persistent pain --- present with "compound" pain that has both nociceptive and neuropathic components, a situation which complicates assessment and treatment.

Differentiating between nociceptive and neuropathic pain is critical because the two respond differently to pain treatments. Neuropathic pain, for example, typically responds poorly to both opioid analgesics and non-steroidal anti-inflammatory drug (NSAID) agents. Other classes of medications, such as anti-epileptics, antidepressants or local anesthetics, may provide more effective relief for neuropathic pain.

Cancer and Non-Cancer Pain: Pain associated with cancer is sometimes given a separate classification, although it is not distinct from a patho-physiological perspective. Cancer-related pain includes pain caused by the disease itself and/or painful diagnostic or therapeutic procedures [and the sequelae of those processes]. The treatment of cancer-related pain may be influenced by the life expectancy of the patient, by co-morbidities and by the fact that such pain may be of exceptional severity and duration. A focus of recent attention by the public, regulators, legislators, and physicians has been chronic pain that is not associated with cancer. A key feature of such pain, which may be caused by conditions such as musculoskeletal injury, lower back trauma and dysfunctional wound healing, is that the severity of pain may not correspond well to identifiable levels of tissue damage.

Tolerance, Dependence and Addiction: Related to the nomenclature of pain itself is continuing confusion not only among the public, but also in the medical community, about terms used to describe the effects of drugs on the brain and on behavior. To help clarify and standardize understanding, the American Society of Addiction Medicine (ASAM), the American Academy of Pain Medicine (AAPM) and the American Pain Society (APS) have recommended the following definitions:

> *Tolerance:* A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drugs' effects over time.
>
> *Physical Dependence:* A state of adaptation that often includes tolerance and is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug and/or administration of an antagonist.
>
> *Addiction:* A primary, chronic, neurobiological disease, with genetic, psychosocial and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm and craving.

Pain as an Illness: Finally, it may be helpful to point out that pain can be regarded as an illness as well as a symptom or a disease. "Illness" defines the impact a disease has on an organism and is characterized by epiphenomena or co-morbidities with bio-psycho-social dimensions. Effective care of any illness, therefore, requires attention to all of these dimensions. Neuropathic pain, end-of-life pain and chronic pain should all be viewed as illnesses.

SPECIAL PATIENT POPULATIONS

All patients may experience pain. Below are treatment considerations for differing patient populations or scenarios. As previously addressed, these guidelines are intended to particularly address the use of opioids in the long-term treatment of chronic, non-cancer pain. However, since many of the recommendations cited in these guidelines might be appropriate for other types of pain, other scenarios are listed below to provide additional guidance in prescribing opioids, when appropriate.

Acute Pain[4]

Opioid medications should only be used for treatment of acute pain when the severity of the pain warrants that choice and after determining that other non-opioid pain medications or therapies likely will not provide adequate pain relief. When opioid medications are prescribed for treatment of acute pain, the number dispensed should be for a short duration and no more than the number of doses needed based on the usual duration of pain severe enough to require opioids for that condition.

[4] Utah Department of Health (Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain, 2009).

Long (and intermediate) duration-of-action opioids or extended-release/long-acting opioids (ER/LA) should not be used for treatment of acute pain, including post-operative pain, except in situations where monitoring and assessment for adverse effects can be conducted. Methadone is rarely, if ever, indicated for treatment of acute pain. The use of opioids should be re-evaluated carefully, including the potential for abuse, if persistence of pain suggests the need to continue opioids beyond the anticipated time period of acute pain treatment for that condition.

It is important to emphasize that numerous (but not all) recommendations cited in these guidelines may not be relevant for the physician treating a patient for acute pain. For example, a physician treating a patient who presents to an emergency department or primary care physician with a medical condition manifested by objective signs (e.g., a fractured ulna or kidney stones discernible with imaging studies) would not necessarily need to undertake an opioid trial, perform a psychological assessment, utilize a pain management agreement, confer with the Prescription Drug Monitoring Program database, order a drug toxicology screen, etc.

Emergency Departments
Treating patients in an emergency department (ED) or urgent care clinic presents unique challenges in that, oftentimes, there is limited ability to procure adequate patient history and the primary physician is not available. Drug seeking patients may take advantage of this in order to secure controlled substances.

The American College of Emergency Physicians (ACEP) Clinical Policy - Critical Issues in the Prescribing of Opioids for Adult Patients in the Emergency Department (Appendix 1) - identifies acute low back pain as a common presenting complaint in the ED. Opioids are frequently prescribed, expected or requested for such presentations. Consequently, ACEP clinical policy recommends:

(1) For the patient being discharged from the ED with acute low back pain, the emergency physician should ascertain whether non-opioid analgesics and non-pharmacologic therapies will be adequate for initial pain management.
(2) Given a lack of demonstrated evidence of superior efficacy of either opioid or non-opioid analgesics and the individual and community risks associated with opioid use, misuse, and abuse, opioids should be reserved for more severe pain or pain refractory to other analgesics rather than routinely prescribed.
(3) If opioids are indicated, the prescription should be for the lowest practical dose for a limited duration (e.g.,<1 week), and the prescriber should consider the patient's risk for opioid misuse, abuse, or diversion.

For patients presenting to the ED with an acute exacerbation of non-cancer chronic pain, ACEP recommends the following:

(1) Physicians should avoid the routine prescribing of outpatient opioids for a patient with an acute exacerbation of chronic non-cancer pain seen in the ED.
(2) If opioids are prescribed on discharge, the prescription should be for the lowest practical dose for a limited duration (e.g., < 1 week), and the prescriber should consider the patient's risk for opioid misuse, abuse, or diversion.

(3) The physician should, if practicable, honor existing patient-physician pain contracts/treatment agreements and consider past prescription patterns from information sources such as prescription drug monitoring programs.

ACEP recommends that the use of a state prescription monitoring program may help identify patients who are at high risk for prescription opioid diversion or doctor shopping.

End-of-Life Pain[5]
Pain management at the end of life seeks to improve or maintain a patient's overall quality of life in addition to relieving suffering. This focus is important because sometimes a patient may have priorities that compete with, or supersede, the relief of pain. For some patients, mental alertness sufficient to allow lucid interactions with loved ones may be more important than physical comfort. Optimal pain management, in such cases, may mean lower doses of an analgesic and the experience, by the patient, of higher levels of pain.

Fear of inducing severe or even fatal respiratory depression may lead to the clinician[6] under-prescribing and reluctance by patients to take an opioid medication. Despite this fear, studies have revealed no correlation between opioid dose, timing of opioid administration and time of death in patients using opioids in the context of terminal illness. A consult with a specialist in palliative medicine in these situations may be advisable.

Cancer Pain
Pain is one of the most common symptoms of cancer, as well as being one of the most feared cancer symptoms. Opioid pain medications are the mainstay of cancer pain management, and are appropriate to consider for cancer patients with moderate to severe pain, regardless of the known or suspected pain mechanism. However, some cancer survivors with moderate-to-severe pain may additionally or alternatively benefit from the use of non-opioid treatments, and opioids may not be necessary. Other treatments such as surgeries, radiation therapy, and other procedures may provide sufficient pain relief so that opioids are not necessary.

ER/LA opioid formulations may lessen the inconvenience associated with the use of short-acting opioids. Patient-controlled analgesia using an ambulatory infusion device may provide optimal patient control and effective analgesia. The full range of adjuvant medications should be considered for patients with cancer pain, with the caveat that such patients are often on already complicated pharmacological regimens, which raises the risk of adverse reactions associated with polypharmacy.[7]

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[5] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).
[6] The term "clinician" throughout the document means "physician."
[7] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

Older Adults
With appropriate precautions opioid therapy for elderly patients can be efficacious. It is important to begin with lower starting doses, slower titration, longer dosing intervals, and more frequent monitoring. Tapering of benzodiazepines is important to reduce the potential for respiratory depression.

For additional information, see Appendix 2.

Pediatric Patients
Extreme caution should be used in prescribing opioids for pediatric patients. A trial of opioid therapy may be considered with well-defined somatic or neuropathic pain conditions when non-opioid alternatives have failed or are unlikely to be effective for acute pain. Additionally, close monitoring and consultation should be undertaken.

For additional information, see Appendix 3.

Pregnant Women
Clinicians should encourage minimal or no use of opioids during pregnancy unless the potential benefits clearly outweigh risks. Pregnant patients taking long-term opioid therapy should be tapered to the lowest effective dose slowly enough to avoid withdrawal symptoms, and then therapy should be discontinued if possible.

Additional information on the appropriate use of opioids for pregnant patients is available from the American Congress of Obstetricians and Gynecologists (ACOG) committee opinion titled *Opioid Abuse, Dependence, and Addiction in Pregnancy*.

Patients Covered by Workers' Compensation[8]
This population of patients presents its own unique circumstances. Injured workers are generally sent to an occupational medicine facility for treatment. Ideally, the injured worker recovers and returns to work in full capacity. If recovery or healing does not occur as expected, early triage and appropriate, timely treatment is essential to restore function and facilitate a return to work.

The use of opioids in this population of patients can be problematic. Some evidence suggests that early treatment with opioids may actually delay recovery and a return to work. Conflicts of motivation may also exist in patients on workers' compensation, such as when a person may not want to return to an unsatisfying, difficult or hazardous job. Clinicians are advised to apply the same careful methods of assessment, creation of treatment plans and monitoring used for other pain patients but with the added consideration of the psycho-social dynamics inherent in the workers' compensation system. Injured workers should be afforded the full range of treatment options that are appropriate for the given condition causing the disability and impairment.

[8] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

For additional information on treating patients covered by Workers' Compensation please see *State of California Division of Workers' Compensation Guideline for the Use of Opioids to Treat Work-Related Injuries*.

Patients with History of Substance Use Disorder[9]
Use of opioids for patients with a history of substance use disorder is challenging because such patients are more vulnerable to drug misuse, abuse and addiction. In patients who are actively using illicit drugs, the potential benefits of opioid therapy are likely to be outweighed by potential risks, and such therapy should not be prescribed outside of highly controlled settings (such as an opioid treatment program with directly observed therapy). In other patients, the potential benefits of opioid therapy may outweigh potential risks. Although evidence is lacking on best methods for managing such patients, potential risks may be minimized by more frequent and intense monitoring compared with lower risk patients, authorization of limited prescription quantities and consultation or co-management with a specialist in addiction medicine. Clinicians should use the [Controlled Substance Utilization Review and Evaluation System (CURES)/Prescription Drug Monitoring Program (PDMP)] CURES/PDMP to identify patients who obtain drugs from multiple sources.

If either the patient's medical history, self-report or scores on screening assessment tools such as the Opioid Risk Tool (Appendix 4) suggest an above-average risk of substance abuse, clinicians should consider the following steps in proceeding with a pain management strategy:

- Exhaust all non-opioid pain management methodologies prior to considering opioid therapy;
- Consult with a specialist in addiction medicine;
- Create a written treatment plan and patient agreement and review carefully with the patient, obtaining their signed informed consent;
- Closely monitor and assess pain, functioning and aberrant behaviors;
- Regularly check with a PDMP for compliance with prescribed amounts of opioids (using cross-state PDMP systems whenever they are available);
- While the patient is on long-term opioid therapy, implement urine drug testing, if possible; or
- If misuse or abuse of opioid analgesics is suspected or confirmed, initiate a non-confrontational in-person meeting, use a non-judgmental approach to asking questions, present options for referral, opioid taper/discontinuation or switching to non-opioid treatments, and avoid "abandoning" the patient or abruptly stopping opioid prescriptions.

Psychiatric Patients
A higher risk for deleterious side effects exists for patients with psychiatric diagnoses who are receiving opioid treatment. Opioids should only be prescribed for well-defined

[9] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

somatic or neuropathic pain conditions. Physicians should titrate slowly, closely monitor the patient and seek consultation from the appropriate specialist.

Patients Prescribed Benzodiazepines
Patients taking benzodiazepines and opioids are at an increased risk for respiratory depression, particularly elderly patients. Physicians should consider a trial of benzodiazepine tapering in patients concomitantly using opioids or other respiratory depressant medications. If a trial of tapering is not indicated or is unsuccessful, opioids should be titrated more slowly and at lower doses. For additional information, see Benzodiazepines: How They Work and How to Withdraw.

Patients Prescribed Methadone or Buprenorphine for Treatment of a Substance Use Disorder
Patients prescribed methadone or buprenorphine for treatment of a substance use disorder may need relief from acute and/or chronic pain, beyond that provided by their maintenance medication. For more information on pain relief for persons on methadone or buprenorphine, see *Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy*.

PATIENT EVALUATION AND RISK STRATIFICATION

When considering long-term use of opioids for chronic, non-cancer pain, given the potential risks of opioid analgesics, careful and thorough patient assessment is critical. Risk stratification is one of the most important things a physician can do to mitigate potentially adverse consequences of opioid prescribing. The nature and extent of the clinical assessment depends on the type of pain and the context in which it occurs. This includes but is not limited to:

- Completing a medical history and physical examination (Appendix 5).
- Performing a psychological evaluation.
    - Psychological assessment should include risk of addictive disorders. Screening tools that can be considered for use include:
        - CAGE-AID (Appendix 6);
        - PHQ-9 (Appendix 7);
        - Opioid Risk Tool (ORT) (Appendix 4); and
        - SOAPP®-R (Appendix 8).
        - Note: Although the above-listed assessment tools are well-established with proven effectiveness, physicians must be aware that seasoned diverters know the right answers to these tools so they look "normal."
- Establishing a diagnosis and medical necessity (review past medical records, laboratory studies, imaging studies, etc. and order new ones, if necessary or if previous studies are outdated). Screening tools that can be considered for use include:
    - Pain Intensity and Interference (pain scale) (Appendix 9); and
    - Sheehan Disability Scale.
- Exploring non-opioid therapeutic options.

Opioid medications may not be the appropriate first line of treatment for a patient with chronic pain. Other measures, such as non-opioid analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, antiepileptic drugs, and non-pharmacologic therapies (e.g., physical therapy), should be tried and the outcomes of those therapies documented first. Opioid therapy should be considered only when other potentially safer and more effective therapies have proven inadequate. Resources that can be consulted include:
  - Therapeutic Options for Pain Management (Appendix 10); and
  - Non-Opioid Pain Management Tool (Appendix 11).
- Evaluating both potential benefits and potential risks of opioid therapy.
- Being cognizant of aberrant or drug seeking behaviors.
- As a universal precaution, undertaking urine drug testing.
- Reviewing the CURES/PDMP report for the patient. This allows a physician to check to see if a patient is receiving controlled substances from other prescribers in California (assuming the prescription is being filled at a California pharmacy).

CONSULTATION

The treating physician should seek a consultation with, or refer the patient to, a pain, psychiatry, or an addiction or mental health specialist as needed. For example, a patient who has a history of substance use disorder or a co-occurring mental health disorder may require specialized assessment and treatment, if available.

Physicians who prescribe long-term opioid therapy should be familiar with treatment options for opioid addiction (including those available in licensed opioid treatment programs [OTPs]) and those offered by an appropriately credentialed and experienced physician through office-based opioid treatment [OBOT]), so as to make appropriate referrals when needed.

TREATMENT PLAN AND OBJECTIVES

When considering long-term use of opioids for chronic, non-cancer pain, the physician and the patient should develop treatment goals together. The goals of pain treatment include reasonably attainable improvement in pain and function; improvement in pain-associated symptoms such as sleep disturbance, depression, and anxiety; and avoidance of unnecessary or excessive use of medications. Pain relief is important, but it is difficult to measure objectively. Therefore, it cannot be the primary indicator to assess the success of the treatment. Effective pain relief improves functioning, whereas addiction decreases functionality. Effective means of achieving these goals vary widely, depending on the type and causes of the patient's pain, other concurrent issues, and the preferences of the physician and the patient.

The treatment plan and goals should be established as early as possible in the treatment process and revisited regularly, so as to provide clear-cut, individualized objectives to guide the choice of therapies. The treatment plan should contain information supporting the selection of therapies, both pharmacologic (including

medications other than opioids) and non-pharmacologic. It also should specify measurable goals and objectives that will be used to evaluate treatment progress, such as relief of pain and improved physical and psychosocial function.

The plan should document any further diagnostic evaluations, consultations or referrals, or additional therapies that have been considered. The treatment plan should also include an "exit strategy" for discontinuing opioid therapy in the event the tapering or termination of opioid therapy becomes necessary.

PATIENT CONSENT

When considering long-term use of opioids, or in other medically appropriate situations, the physician should discuss the risks and benefits of the treatment plan with the patient, with persons designated by the patient, or with the patient's conservator if the patient is without medical decision-making capacity. If opioids are prescribed, the patient (and possibly family members, if appropriate) should be counseled on safe ways to store and dispose of medications. For convenience, patient consent and a pain management agreement can be combined into one document.

Patient consent typically addresses:

- The potential risks and anticipated benefits of long-term opioid therapy.
- Potential side effects (both short- and long-term) of the medication, such as nausea, opioid-induced constipation, decreased libido, sexual dysfunction, hypogonadism with secondary osteoporosis (Gegmann et al., 2008) and cognitive impairment.
- The likelihood that some medications will cause tolerance and physical dependence to develop.
- The risk of drug interactions and over-sedation.
- The risk of respiratory depression.
- The risk of impaired motor skills (affecting driving and other tasks).
- The risk of opioid misuse, dependence, addiction, and overdose.
- The limited evidence as to the benefit of long-term opioid therapy.

PAIN MANAGEMENT AGREEMENT

Use of a pain management agreement is recommended for patients:

- On short-acting opioids at the time of third visit within two months;
- On long-acting opioids; or
- Expected to require more than three months of opioids.

Pain management agreements typically outline the joint responsibilities of the physician and the patient and should include:

- The physician's prescribing policies and expectations, including the number and frequency of prescription refills, as well as the physician's policy on early refills and replacement of lost or stolen medications.

- Specific reasons for which drug therapy may be changed or discontinued (including violation of the policies and agreements spelled out in the treatment agreement).
- The patient's responsibility for safe medication use (e.g., by not using more medication than prescribed or using the opioid in combination with alcohol or other substances; storing medications in a secure location; and safe disposal of any unused medication to prevent misuse by other household members).
- The patient's agreement to share information with family members and other close contacts on how to recognize and respond to an opiate overdose, including administering an opioid antagonist, such as naloxone, if necessary.(Appendix 12)
- The patient's responsibility to obtain his or her prescribed opioids from only one physician or practice and one pharmacy.
- The patient's agreement to periodic drug testing (blood, urine, hair, or saliva).
- The physician's responsibility to be available or to have a covering physician available to care for unforeseen problems and to prescribe scheduled refills, if appropriate and in accordance with the patient's pain management agreement.

Samples of pain management agreements:

- Patient Pain Medication Agreement and Consent (Appendix 13)
- Treatment Plan Using Prescription Opioids (Appendix 14)

COUNSELING PATIENTS ON OVERDOSE RISK AND RESPONSE

Empirical evidence has shown that lay persons can be trained to recognize the signs of an opiate overdose and to safely administer naloxone, an opiate antagonist. Programs that have trained lay persons in naloxone administration have reported more than 10,000 overdose reversals.[10]

It is important to educate patients and family/caregivers about the danger signs of respiratory depression. Everyone in the household should know to summon medical help immediately if a person demonstrates any of the following signs while on opioids:

- Snoring heavily and cannot be awakened.
- Periods of ataxic (irregular) or other sleep-disordered breathing.
- Having trouble breathing.
- Exhibiting extreme drowsiness and slow breathing.
- Having slow, shallow breathing with little chest movement or no breathing.
- Having an increased or decreased heartbeat.
- Feeling faint, very dizzy, confused or has heart palpitations.
- Blue skin/lips.
- Non-responsiveness to painful stimulation.

[10] Centers for Disease Control and Prevention. Community-based opioid overdose prevention programs providing naloxone-United States, 2010. Morbidity and mortality weekly report, February 17, 2012 / 61(06);101-105

Effective January 1, 2015, California pharmacists will be able to furnish an opioid overdose reversal drug in accordance with standardized procedures or protocols, naloxone, to family members of patients at risk for overdose, those who might be in contact with an individual at risk for overdose, or anyone who requests the drug without a prescription.

SAMHSA's Opiate Overdose Toolkit and Prescribe to Prevent contain numerous documents relating to overdose prevention and management.

INITIATING OPIOID TRIAL

Safer alternative treatments should be considered before initiating opioid therapy for chronic pain. Opioid therapy should be presented to the patient as a therapeutic trial or test for a defined period of time (usually no more than 45 days) and with specific evaluation points. The *Long-Term Chronic Opioid Therapy Discontinuation Rates from the TROUP Study*[11] reveals that "[o]ver half of persons receiving 90 days of continuous opioid therapy remain on opioids years later. Factors most strongly associated with continuation were intermittent prior opioid exposure, daily opioid dose≥120 mg MED, and possible opioid misuse. Since high dose and opioid misuse have been shown to increase the risk of adverse outcomes, special caution is warranted when prescribing more than 90 days of opioid therapy in these patients."

The physician should explain that progress will be carefully monitored for both benefit and harm in terms of the effects of opioids on the patient's level of pain, function, and quality of life, as well as to identify any adverse events or risks to safety.

According to the California Medical Association:[12]

> Oral administration, especially for the treatment of chronic pain, is generally preferred because it is convenient, flexible and associated with stable drug levels. Intravenous administration provides rapid pain relief and, along with rectal, sublingual and subcutaneous administration, may be useful in patients who cannot take medications by mouth. Continuous infusions produce consistent drug blood levels but are expensive, require frequent professional monitoring and may limit patient mobility.
>
> Transdermal administration is a convenient alternate means of continuous drug delivery that does not involve needles or pumps. Patient-controlled analgesia (PCA) allows patients to self-administer pain medications and may be useful if analgesia is required for 12 hours or more and mobility is not required. Intrathecal delivery of opioids is a viable option for patients with chronic pain who have not responded to other treatment options, or for whom the required doses result in unacceptable side-effects. Patients with intrathecal delivery systems typically require ongoing ambulatory monitoring and supportive care.

[11] Journal of General Internal Medicine article (December 2011, Volume 26, Issue 12, pp 1450-1457).
[12] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

Patients on a steady dose of an opioid medication may experience pain that breaks through the analgesic effects of the steady-state drug. Paper or electronic pain diaries may help patients track these breakthrough episodes and spot correlations between the episodes and variables in their lives. A short-acting opioid is typically prescribed for treatment by patients with breakthrough pain.

Continuation of opioid therapy after an appropriate trial should be based on outcomes such as: making progress toward functional goals; presence and nature of side effects; pain status; and a lack of evidence of medication misuse, abuse, or diversion. Patients with no, or modest, previous opioid exposure should be started at the lowest appropriate initial dosage of a short-acting opioid and titrated upward to decrease the risk of adverse effects. The selection of a starting dose and manner of titration are clinical decisions made on a case-by-case basis because of the many variables involved. Some patients, such as frail older persons or those with co-morbidities, may require an even more cautious therapy initiation. Short-acting opioids are usually safer for initial therapy since they have a shorter half-life and may be associated with a lower risk of overdose from drug accumulation. The general approach is to "start low and go slow."

Since opioids are known in some circumstances to worsen pain (hyperalgesia), instances of ongoing pain may suggest opioid insensitivity (or an inadequate dose). Careful assessment must be undertaken. If hyperalgesia is suspected, a dose reduction, opioid rotation or tapering to cessation could be considered.

Dosing Recommendations For Opioid Naïve Patients
There is a plethora of data available regarding recommended dosages for various analgesics. Because this is continuously evolving, physicians are encouraged to review the Food and Drug Administration's website and other relevant information sources.

Morphine Equivalent Dose (MED)
There are differing opinions among reputable experts and organizations as to what MED should trigger a consultation. The Board recommends that physicians proceed cautiously (yellow flag warning) once the MED reaches 80 mg/day. Referral to an appropriate specialist should be considered when higher doses are contemplated. There is no absolute safe ceiling dose of opioids, however, and caution and monitoring are appropriate for applications of these medications.

The patient should be seen more frequently while the treatment plan is being initiated and the opioid dose adjusted. As the patient is stabilized in the treatment regimen, follow-up visits may be scheduled less frequently.

ONGOING PATIENT ASSESSMENT

When a trial of an opioid medication is successful and the physician and patient decide to continue opioid therapy, regular review and monitoring should be undertaken for the duration of treatment.

Continuation, modification or termination of opioid therapy for pain should be contingent on the physician's evaluation of (1) evidence of the patient's progress toward treatment objectives and (2) the absence of substantial risks or adverse events, such as overdose or diversion. A satisfactory response to treatment would be indicated by a reduced level of pain, increased level of function, and/or improved quality of life. Validated brief assessment tools that measure pain and function, such as the three-question "Pain, Enjoyment and General Activity" (PEG) scale or other validated assessment tools, may be helpful and time effective..

Consider the 5-As method for chronic pain management assessment:

Analgesia: the patient is experiencing a reduction in pain.
Activity: the patient is demonstrating an improvement in level of function.
Adverse: the patient is not experiencing side effects.
Aberrance: the patient is complying with the pain management agreement and there are no signs of medication abuse or diversion.
Affect: the patient's behavior and mood are appropriate.

"Opioid rotation," the switching from one opioid to another in order to better balance analgesia and side effects, may be used if pain relief is inadequate, if side effects are bothersome or unacceptable, or if an alternative route of administration is suggested. Opioid rotation must be done with great care, particularly when converting from an immediate-release formulation to an extended-release/long-acting (ER/LA) product. Equianalgesic charts, conversion tables and calculators must be used cautiously with titration and appropriate monitoring. Patients may exhibit incomplete cross-tolerance to different types of opioids because of differences in the receptors or receptor sub-types to which different opioids bind, hence physicians may want to use initially lower-than-calculated doses of the switched-to opioid.

COMPLIANCE MONITORING

Physicians who prescribe opioids or other controlled substances for pain should ensure the provisions of a pain management agreement are being heeded. Strategies for monitoring compliance may include:

CURES/PDMP Report
The CURES/PDMP report can be useful in establishing whether or not an individual is receiving controlled substances from multiple prescribers. The CURES/PDMP report should be requested frequently for patients who are being treated for pain as well as addiction.

Drug Testing
A patient's report of medication use is not always reliable; therefore, drug testing can be an important monitoring tool.

Physicians need to be aware of the limitations of available tests (such as their limited sensitivity for many opioids) and take care to order tests appropriately. For example,

when a drug test is ordered, it is important to specify that it include the opioid being prescribed. Because of the complexities involved in interpreting drug test results, it is advisable to confirm significant or unexpected results with the laboratory toxicologist or a clinical pathologist. Urine toxicology tests can be compromised by variability and limitations in obtaining specimens, custody of specimens, laboratory methodologies and interpreting laboratory data. Laboratories vary in their testing methodologies, thresholds and standards. Results from drug screens may involve diverse drug classes and interpreting them requires clinical understanding well beyond opioids.

"Variability may result from differences between laboratories. Some labs, for example, only report values above a certain preset threshold. So, a patient might have a measureable level of drug, but since it does not exceed the given threshold, it is reported as negative finding. This might lead the physician to suspect that a prescribed drug, which should be present at the time of testing, is absent."[13]

"Limitations to Urine Drug Testing (UDT): There is currently no way to tell from a urine drug test the exact amount of drug ingested or taken, when the last dose was taken, or the source of the drug. A recent systematic review of the use of drug treatment agreements and urine drug testing to discourage misuse when opioids are prescribed for chronic non-cancer pain, found weak, heterogeneous evidence that these strategies were associated with less misuse. Limited research did find that UDT was a valuable tool to detect use of non-prescribed drugs and confirm adherence to prescribed medications beyond that identified by patient self-report or impression of the treating physician."[14] "Consequently, additional testing, including quantitative blood levels of prescribed medications and other laboratory testing, may be deemed necessary to monitor and treat patients receiving chronic opioid treatment and is considered part of a medically necessary treatment and monitoring program."[15]

It is important to be aware of cost barriers related to a patient's ability to pay for the testing. There are numerous Clinical Laboratory Improvement Amendments waived office drug testing kits which are inexpensive and which physicians may wish to consider for use for initial drug testing. However, unexpected results from office-based testing should be confirmed by the more-sensitive laboratory testing before the patient's plan of care is changed.

Pill Counting

Periodic pill counting can be a useful strategy to confirm medication adherence and to minimize diversion (selling, sharing or giving away medications).

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[13] Responsible Opioid Prescribing, A Clinician's Guide, Second Edition, 2012, Scott Fishman, M.D.; Federation of State Medical Boards (FSMB), FSMB Foundation, and University of Nebraska Medical Center.

[14] State Of California Division Of Workers' Compensation Guideline For The Use Of Opioids To Treat Work-Related Injuries (Forum Posting, April 2014) Part D: Comparison Of Recommendations From Existing Opioid Guidelines.

[15] State Of California Division Of Workers' Compensation Guideline For The Use Of Opioids To Treat Work-Related Injuries (Forum Posting, April 2014) Part B Recommendations.

The physician must decide whether or not to revise or augment a pain management agreement and/or treatment plan if the patient's progress is unsatisfactory.
If it is suspected that a patient may be abusing or diverting prescribed medications, or using "street" drugs, a careful re-assessment of the treatment plan must be undertaken. A patient's failure to adhere to a pain management agreement is not necessarily proof of abuse or diversion. Failure to comply may be the consequence of inadequate pain relief, confusion regarding the prescription, a language barrier or economic concerns. A physician should arrange for an in-person meeting in order to have a non-judgmental conversation to clarify his or her concerns. If abuse is confirmed, minimally, consultation with an addiction medicine specialist or mental health specialist trained in substance abuse disorders and/or referral to a substance use disorder treatment program that provides medication-assisted therapy (MAT) should be immediately facilitated. Physicians who prescribe long-term opioid therapy should be knowledgeable in the diagnosis of substance use disorders and able to distinguish such disorders from physical dependence—which is expected in chronic therapy with opioids and many sedatives.

Documented drug diversion or prescription forgery, obvious impairment, and abusive or assaultive behaviors usually require a firmer, immediate response. The degree to which the patient has breached the pain agreement and/or the presence of criminal activity should govern the physician's response. Although an immediate face-to-face meeting with the patient to re-evaluate the treatment plan may be appropriate, in some instances it may be necessary to taper opioid therapy and/or terminate the physician patient relationship. In situations where the patient has engaged in prescription forgery, prescription theft or assaultive behaviors directed towards physician or staff, the physician is strongly encouraged to contact the police/Drug Enforcement Agency (DEA). For other criminal behaviors, the physician is encouraged to contact legal counsel to determine whether it is appropriate to report to law enforcement. Failing to respond can place the patient and others at significant risk of adverse consequences, including accidental overdose, suicide attempts, arrests and incarceration, or even death.

DISCONTINUING OPIOID THERAPY

Discontinuing or tapering of opioid therapy may be required for many reasons and ideally, an "exit strategy" should be included in the treatment plan for all patients receiving opioids at the outset of treatment. Reasons may include:

- Resolution or healing of the painful condition;
- Intolerable side effects;
- Failure to achieve anticipated pain relief or functional improvement (although ensure that this failure is not the result of inadequate treatment);
- Evidence of non-medical or inappropriate use;
- Failure to comply with monitoring, such as urine drug screening (although ensure that this failure is not the result of a cost issue);
- Failure to comply with pain management agreement;

- Exhibition of drug-seeking behaviors (although ensure this behavior is not the result of inadequate treatment) or diversion, such as:
    - Selling prescription drugs;
    - Forging prescriptions;
    - Stealing or borrowing drugs;
    - Aggressive demand for opioids;
    - Injecting oral/topical opioids;
    - Unsanctioned use of opioids;
    - Unsanctioned dose escalation;
    - Concurrent use of illicit drugs;
    - Getting opioids from multiple prescribers and/or multiple pharmacies; or
    - Recurring emergency department visits for chronic pain management.

If opioid therapy is discontinued, the patient who has become physically dependent should be provided with a safely-structured tapering regimen. Opioid withdrawal symptoms are uncomfortable, but are generally not life threatening. Opioids can be stopped abruptly when the risks outweigh the benefits. This is not true for benzodiazepine withdrawals, which can be life threatening. Withdrawal can be managed either by the prescribing physician or by referring the patient to an addiction specialist. "Approaches to weaning range from a slow 10% reduction per week to a more aggressive 25 to 50% reduction every few days. In general, a slower taper will produce fewer unpleasant symptoms of withdrawal."[16] For strategies on tapering and weaning, see Appendix 15. The termination of opioid therapy should not mark the end of treatment, which should continue with other modalities, either through direct care or referral to other health care specialists, as appropriate.

If complete termination of care is necessary (as opposed to termination of a specific treatment modality), physicians should treat the patient until the patient has had a reasonable time to find an alternative source of care, and ensure that the patient has adequate medications, if appropriate, to avoid unnecessary risk from withdrawal symptoms. Physicians can be held accountable for patient abandonment if medical care is discontinued without adequate provision for subsequent care. If a patient is known to be abusing a medication, initiating a detoxification protocol may be appropriate. Consultation with an attorney and/or one's malpractice insurance carrier may be prudent in such cases. Physicians may want to also consult health plan contracts to ensure compliance. The Board also provides guidance on how to terminate/sever the patient relationship.

If a patient is dismissed for not honoring treatment agreements, consider referral to addiction resources. This can also include a 12-step program.

[16] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

MEDICAL RECORDS

Every physician must maintain adequate and accurate medical records. The content of a patient's medical record may vary considerably, depending on numerous factors. For a physician treating a patient with opioids for chronic, non-cancer pain, an adequate medical record includes, but is not limited to, the documentation of:

- the patient's medical history;
- results of the physical examination and all laboratory tests ordered by the physician;
- patient consent;
- pain management agreement;
- results of the risk assessment, including results of any screening instruments used;
- description of the treatments provided, including all medications prescribed or administered (including the date, type, dose and quantity);
- instructions to the patient, including discussions of risks and benefits with the patient and any significant others;
- results of ongoing monitoring of patient progress (or lack of progress) in terms of pain management and functional improvement;
- notes on evaluations by, and consultations with, specialists;
- any other information used to support the initiation, continuation, revision, or termination of treatment and the steps taken in response to any aberrant medication use behaviors (these may include actual copies of, or references to, medical records of past hospitalizations or treatments by other providers);
- authorization for release of information to other treatment providers as appropriate and/or legally required; and
- results of CURES/PDMP data searches.

The medical record should include all prescription orders for opioid analgesics and other controlled substances, whether written, telephoned or electronic. In addition, written instructions for the use of all medications should be given to the patient and documented in the record. The name, telephone number, and address of the patient's pharmacy also should be recorded to facilitate contact as needed, if the pharmacy that the patient will use is known. Records should be up-to-date and maintained in an accessible manner so as to be readily available for review.

Good records demonstrate that a service was provided to the patient and establish that the service provided was medically necessary. Even if the outcome is less than optimal, thorough records protect the physician as well as the patient.

SUPERVISING ALLIED HEALTH PROFESSIONALS

Physicians who supervise physician assistants or nurse practitioners who prescribe opioids should be aware of the specific regulations and requirements governing them and those whom they supervise.

COMPLIANCE WITH CONTROLLED SUBSTANCES LAWS

California laws:

- California laws regarding controlled substances
- Guide to the Laws Governing the Practice of Medicine

Federal laws:

- Title 21 United States Code (USC) Controlled Substances Act

Other information:

- Pharmacist corresponding responsibilities

Appendix 1 - Clinical Policy: Critical Issues in the Prescribing of Opioids for Adult Patients in the Emergency Department

Clinical Policy: Critical Issues in the Prescribing of Opioids for Adult Patients in the Emergency Department

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ABSTRACT

This clinical policy deals with critical issues in prescribing of opioids for adult patients treated in the emergency department (ED). This guideline is the result of the efforts of the American College of Emergency Physicians, in consultation with the Centers for Disease Control and Prevention, and the Food and Drug Administration. The critical questions addressed in this clinical policy are: (1) In the adult ED patient with noncancer pain for whom opioid prescriptions are considered, what is the utility of state prescription drug monitoring programs in identifying patients who are at high risk for opioid abuse? (2) In the adult ED patient with acute low back pain, are prescriptions for opioids more effective during the acute phase than other medications? (3) In the adult ED patient for whom opioid prescription is considered appropriate for treatment of new-onset acute pain, are short-acting schedule II opioids more effective than short-acting schedule III opioids? (4) In the adult ED patient with an acute exacerbation of noncancer chronic pain, do the benefits of prescribing opioids on discharge from the ED outweigh the potential harms?

INTRODUCTION

Pain is a major symptom of many patients presenting to the emergency department (ED), with up to 42% of ED visits being related to painful conditions.[1] Pain management has received increased emphasis in the past decade, including The Joint Commission's focus on patient analgesia[2] and increasing institutional emphasis placed on patient satisfaction surveys covering pain management. Much literature, including the most recent Institute of Medicine report on this topic, has stressed that health care providers have not done as well as possible in the area of pain management.[3] A possible unintended consequence of these efforts is the increase in prescription drug abuse, especially opioid abuse, the fastest-growing drug abuse problem in the United States.[4]

As part of this issue, there has been a startling increase in unintentional drug overdoses and related deaths since the late 1990s.[5,6] Reported overdose deaths involving opioid analgesics increased from 4,030 in 1999 to 14,800 in 2008.[7,8] Data from 2008 reveal that drug overdoses were the second leading cause of injury death in the United States, after motor vehicle crashes.[9] Currently, deaths from opioid analgesics are significantly greater in number than those from cocaine and heroin combined.[8]

The efforts of clinicians to improve their treatment of pain, along with pharmaceutical industry marketing, have been factors in contributing to a significant increase in the sale and distribution of opioids in the United States. For example, the sales of opioid analgesics to hospitals, pharmacies, and practitioners quadrupled between 1999 and 2010.[8] Drug sales and distribution data of opioids show an increase from 180 mg morphine equivalents per person in the United States in 1997 to 710 mg per person in 2010.[8,10] This is the equivalent of 7.1 kg of opioid medication per 10,000 population, or enough to supply every American adult with 5 mg of hydrocodone every 4 hours for a month.[8]

The dilemma of treating pain appropriately while avoiding adverse events is further complicated by insufficient data supporting the long-term use of opioids in the treatment of chronic noncancer pain. Although selective use of opioids in the treatment of acute pain is traditionally accepted, the treatment of chronic noncancer pain is more complex. Many authors have begun to question the routine long-term use of opioids for the treatment of chronic noncancer pain.[11-13] Multiple practice guidelines have been developed to address this issue.[14-19] However, most recommendations in this area are of a consensus nature, being based on experiential or low-quality evidence.

Data from 2009 show that there were more than 201.9 million opioid prescriptions dispensed in the United States during that year.[20] It is difficult to obtain reliable data concerning the degree to which this is an emergency medicine issue, but during 2009, in the 10- to 19-year-old and 20- to 29-year-old patient groups, emergency medicine ranked third among all specialties in terms of number of opioid prescriptions, writing approximately 12% of the total prescriptions in each age group. In the 30- to 39-year-old group, emergency medicine ranked fourth.[20] Although these data do not deal with total doses dispensed by specialty, it is commonly postulated that the population served in EDs as a whole is at high risk for opioid abuse.[21]

The significant increase in opioid-related deaths has raised the concern of many.[5,6,8] This problem has also been observed in the pediatric population.[22-24] Action at the national level includes the recent proposal from the Food and Drug Administration for the establishment of physician education programs for the prescribing of long-acting and extended-release opioids as part of their national opioid risk evaluation and mitigation strategy (the REMS program).[25] State efforts to address this issue have included the development of statewide opioid prescribing guidelines, such as those developed by the Utah Department of Health[17] and statewide ED opioid prescribing guidelines, such as those developed in Washington State by the Washington chapter of the American College of Emergency Physicians (ACEP) working with other state organizations.[16] Some individual EDs and emergency physician groups have also promulgated opioid prescribing guidelines. Some of these policies also deal with the necessity of patient education about the safe use and proper disposal of opioid medications. Early data indicate that, in some cases, these guidelines may decrease prescription opioid overdose.[26] Anecdotal experience suggests that public policies such as these may change patient perceptions of appropriate prescribing and mitigate complaints arising from more stringent prescribing practices. ACEP has approved related policy statements about optimizing the treatment of pain in patients with acute presentations and the implementation of electronic prescription drug monitoring programs.[27,28]

This clinical policy addresses several issues believed to be important in the prescribing of opioids by emergency physicians for adult patients treated and released from the ED for whom opioids may be an appropriate treatment modality. Although relieving pain and reducing suffering are primary emergency physician responsibilities, there is a concurrent duty to limit the personal and societal harm that can result from prescription drug misuse and abuse. Because long-acting or extended-release opioids are not indicated for the treatment of acute pain, the aim of this clinical policy is to provide evidence-based recommendations for prescribing short-acting opioids for adult ED patients with painful acute or chronic conditions while attempting to address the increasing frequency of adverse events, abuse, and overdose of prescribed opioid analgesics.

METHODOLOGY

This clinical policy was created after careful review and critical analysis of the medical literature. The critical questions were formulated in the PICO (patient, intervention, comparison, outcome)[29] format to strengthen the clarity and scientific rigor of the questions. Searches of MEDLINE, MEDLINE InProcess, and the Cochrane Library were performed. All searches were limited to English-language sources, human studies, adults, and years 2000 to 2011. Specific key words/phrases and years used in the searches are identified under each critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members were included.

This policy is a product of the ACEP clinical policy development process, including expert review, and is based on the literature; when literature was not available, consensus of panel members was used. Expert review comments were received from emergency physicians, toxicologists, pain and addiction medicine specialists, pharmacologists, occupational medicine specialists, and individual members of the American Academy of Clinical Toxicology, American Academy of Family Physicians, American Academy of Pain Medicine, American Chronic Pain Association, American College of Occupational and Environmental Medicine, American College of Osteopathic Emergency Physicians, American College of Physicians, American Pain Society, American Society of Health-System Pharmacists, American Society of Interventional Pain Physicians, Emergency Medicine Resident's Association, and Emergency Nurses Association. Their responses were used to further refine and enhance this policy; however, their responses do not imply endorsement of this clinical policy. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology or the practice environment changes significantly. The Centers for Disease Control and Prevention was the funding source for this clinical policy.

All articles used in the formulation of this clinical policy were graded by at least 2 subcommittee members for quality and strength of evidence. The articles were classified into 3 classes of evidence on the basis of the design of the study, with design 1 representing the strongest evidence and design 3 representing the weakest evidence for therapeutic, diagnostic, and prognostic studies, respectively (Appendix A). Articles were then graded on dimensions related to the study's methodological features: blinded versus nonblinded outcome assessment, blinded or randomized allocation, direct or indirect outcome measures (reliability and validity), biases (eg, selection, detection, transfer), external validity (ie, generalizability), and sufficient sample size. Articles received a final grade (Class I, II, III) on the basis of a predetermined formula, taking into account the design and study quality (Appendix B). Articles with fatal flaws or that were not relevant to the critical question were given an "X" grade and were not used in formulating recommendations for this policy. Evidence grading was done with respect to the specific data being extracted and the specific critical question being reviewed. Thus, the level of evidence for any one study may have varied according to the question, and it is possible for a single article to receive different levels of grading as different critical questions were answered. Question-specific level of evidence grading may be found in the Evidentiary Table included at the end of this policy. Evidence grading sheets may be viewed at http://www.acep.org/clinicalpolicies/?pg=1.

Clinical findings and strength of recommendations about patient management were then made according to the following criteria:

Level A recommendations. Generally accepted principles for patient management that reflect a high degree of clinical certainty (ie, based on strength of evidence Class I or overwhelming evidence from strength of evidence Class II studies that directly address all of the issues).

Level B recommendations. Recommendations for patient management that may identify a particular strategy or range of management strategies that reflect moderate clinical certainty (ie, based on strength of evidence Class II studies that directly address the issue, decision analysis that directly addresses the issue, or strong consensus of strength of evidence Class III studies).

Level C recommendations. Other strategies for patient management that are based on Class III studies, or in the absence of any adequate published literature, based on panel consensus.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as heterogeneity of results, uncertainty about effect magnitude and consequences, and publication bias, among others, might lead to such a downgrading of recommendations.

This policy is not intended to be a complete manual on the evaluation and management of adult ED patients with painful conditions where prescriptions for opioids are being considered, but rather is a focused examination of critical issues that have

particular relevance to the current practice of emergency medicine.

The goal of the ACEP Opioid Guideline Panel is to provide an evidence-based recommendation when the medical literature provides enough quality information to answer a critical question. When the medical literature does not contain enough quality information to answer a critical question, the members of the ACEP Opioid Guideline Panel believe that it is equally important to alert emergency physicians to this fact.

Recommendations offered in this policy are not intended to represent the only management options that the emergency physician should consider. ACEP clearly recognizes the importance of the individual physician's judgment. Rather, this guideline defines for the physician those strategies for which medical literature exists to provide support for answers to the critical questions addressed in this policy.

Scope of Application. This guideline is intended for physicians working in hospital-based EDs.

Inclusion Criteria. This guideline is intended for adult patients presenting to the ED with acute noncancer pain or an acute exacerbation of chronic noncancer pain.

Exclusion Criteria. This guideline is not intended to address the long-term care of patients with cancer or chronic noncancer pain.

CRITICAL QUESTIONS

1. In the adult ED patient with noncancer pain for whom opioid prescriptions are considered, what is the utility of state prescription drug monitoring programs in identifying patients who are at high risk for opioid abuse?

Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. The use of a state prescription monitoring program may help identify patients who are at high risk for prescription opioid diversion or doctor shopping.

Key words/phrases for literature searches: opioid, drug prescriptions, drug monitoring, drug utilization review, substance abuse detection, drug-seeking behavior, drug and narcotic control, substance-related disorders, physician's practice patterns, program evaluation, emergency service, and variations and combinations of the key words/phrases with exclusion of cancer.

Emergency physicians must balance oligoanalgesia (undertreatment or ineffectual treatment of pain) with concerns about drug diversion* and doctor shopping.[†30-33] Therefore, the development of mechanisms to address these issues is justified. The expanded use of prescription drug monitoring programs to curb prescription opioid misuse was recommended in the 2011 Prescription Drug Abuse Prevention Plan released by the White House Office of National Drug Control Policy.[34] Prescription drug monitoring programs are state-based monitoring programs for certain controlled substances that are prescribed by licensed practitioners and dispensed by pharmacies. Although existing in various forms for more than 3 decades, the first effort to standardize prescription drug monitoring practice was the passage in 2005 of the National All Schedules Prescription Electronic Reporting Act (NASPER). Unfortunately, this federal legislative mandate that intended to harmonize prescription drug monitoring programs across the various states has yet to be fully funded.

Prescription drug monitoring programs ideally serve multiple functions, including identifying patients who engage in doctor shopping, and patients, providers, or pharmacies who engage in diversion of controlled substances and providing information about prescribing trends for surveillance and evaluation purposes. Such information may serve to benefit the patients, the health care system, epidemiologists, policymakers, regulatory agencies, and law enforcement.[35] Certain large health care systems, particularly closed prescribing systems such as the Veterans Administration and health maintenance organizations, maintain databases that allow prescribers to view recent prescriptions of enrolled clients or patients. Forty-one states have operational prescription drug monitoring programs of various complexity and capability, with an additional 7 states having prescription drug monitoring program legislation in place but with programs that are not yet operational. [36] Most states allow health care providers and pharmacists to access the programs for patients under their care. Other groups such as law enforcement and regulatory boards may also have access. One program tracks only schedule II drug prescriptions, whereas most track drug prescriptions of schedule II to IV or II to V drugs.

Despite prescription drug monitoring programs providing an intuitive perception of benefit for the medical community, there are limited data to indicate any benefit of these programs for improving patient outcomes or reducing the misuse of prescription drugs.[37] In part, this relates to the limited optimization of and standardization between the programs and the lack of a mechanism to allow interstate communication.[35]

*Drug diversion: The diversion of drugs for nonmedical use through routes that do not involve the direct prescription of the drug by a provider. Diverted drugs might be provided by family or friends, purchased on the street market, or obtained through fraudulent prescription. Epidemiologic data suggest that most opioids used nonmedically are obtained through these means.

†Doctor shopping: The practice of obtaining prescriptions for controlled substances from multiple providers, which is regarded as a possible indication of abuse or diversion. There is no rigorous definition, and various authors have defined it in different ways, from 2 or more prescribers within 30 days, greater than 4 during 1 year, and greater than 5 during 1 year.[30-32] It has also been defined as the amount of drug obtained through doctor shopping compared with the amount intended to be prescribed.[33] The use of "pill mills," in which a prescriber provides ready access to prescriptions or pills, can be considered a form of doctor shopping.

One study has demonstrated that compared with states without a prescription monitoring program, those with such a program had a slower rate of increase in opioid misuse.[38]

In an attempt to quantify the effect of a prescription drug monitoring program, Baehren et al[39] conducted a prospective study (Class III) of 18 providers who cared for a convenience sample of adult patients with pain in a single Ohio ED. After the clinical assessment of a patient, the researchers queried the providers about 3 patient-specific issues: (1) the likelihood of querying the state's prescription drug monitoring program, called Ohio Automated Rx Reporting System; (2) the likelihood of providing an opioid prescription at discharge; and (3) if yes, which opioid and what quantity. They were then provided with a printout of the patient data from the prescription drug monitoring program and asked to reassess the same questions. Of the 179 patients with complete data, information from the Ohio Automated Rx Reporting System altered prescribing practice in 74 of 179 (41%). The majority (61%) of these patients received fewer or no opioids, whereas 39% received more. The change in management was attributed to the number of previous prescriptions, 30 of 74 (41%); number of previous prescribers, 23 of 74 (31%); number of pharmacies used, 19 of 74 (26%); and number of addresses listed, 12 of 74 (16%). A limitation of this study was that 4 prescribers accounted for almost two thirds of the total patient encounters. In this study, knowledge of the information provided by a prescription drug monitoring program had an important impact on the prescription practices for controlled substances in an ED, although the actual effect of prescription drug monitoring program data on patient outcomes in this study is unknown.

Although not specifically evaluating the benefit of prescription drug monitoring programs on identifying high-risk patients, Hall et al,[32] in a Class III study, reviewed characteristics of decedents who died of prescription drugs in West Virginia and reported that opioid analgesics accounted for 93% of deaths. Cross-referencing the medical examiner's detailed analysis of the cause of death with the West Virginia prescription monitoring program, the authors determined the prescription history of the drug associated with each fatality. Patients who had received controlled drugs from 5 or more prescribers in the year before death were defined as engaging in "doctor shopping," whereas those whose death was not associated with a valid prescription were considered to have obtained their drugs through "diversion." Of the 295 deaths that were reviewed, the mean age of patients who died was 39 years, and 92% were between ages 18 and 54 years. Diversion was associated with 186 (63%) of the fatalities, and doctor shopping was associated with 63 (21%) of the fatalities. Of the 295 total decedents, 279 (95%) had at least 1 indicator of substance abuse, and these differed according to whether the drug was obtained through diversion or doctor shopping. Deaths involving diversion were associated with a history of substance abuse (82.3% versus 71.6%; odds ratio [OR] 1.8; 95% confidence interval [CI] 1.0 to 3.4), nonmedical route of pharmaceutical administration (26.3% versus 15.6%; OR 1.9; 95% CI 1.0 to 3.8), and a contributory illicit drug (19.4% versus 10.1%; OR 2.1; 95% CI 1.0 to 4.9). Patients with evidence of doctor shopping were significantly more likely to have had a previous overdose (30.2% versus 13.4%; OR 2.8; 95% CI 1.4 to 5.6) and significantly less likely to have used contributory alcohol (7.9% versus 19.8%; OR 0.3; 95% CI 0.1 to 0.9). Few patients (8.1%) were involved in both doctor shopping and diversion. The study suggests that the information provided by a prescription drug monitoring program, with correct interpretation and action based on that knowledge, might have prevented some inappropriate prescribing and poor outcomes in this patient population.

In another Class III study, Pradel et al[33] monitored prescribing trends for buprenorphine in a select area of France, using a prescription drug database during a multiple-year period. During this time, a prescription drug monitoring program was implemented, allowing a before-after comparison of the buprenorphine prescribing pattern for more than 2,600 patients. The doctor shopping drug quantity, which was defined as the total drug quantity received by the patient minus the quantity prescribed by an individual provider, increased from 631 g in the first 6 months of 2000 to a peak of 1,151 g in the first 6 months of 2004, equivalent to 143,750 days of treatment at 8 mg/day. The doctor shopping ratio, determined as the ratio of the quantity delivered to the quantity prescribed, increased steadily from early 2000 (14.9% of the grams of drug prescribed) to a peak value in the first 6 months of 2004 (21.7%). After implementation of the prescription drug monitoring program in early 2004, this value decreased rapidly, in fewer than 2 years reaching the value observed in 2000. The points of inflection of the doctor shopping curves (quantity and ratio) coincided with the implementation of the prescription drug monitoring program, suggesting an immediate benefit of this program. The prescribed quantity did not change after the implementation, indicating that access to treatment may not have changed. Eighty percent of the total doctor shopping quantity of buprenorphine was obtained by approximately 200 (8%) of the total patients. However, it is difficult to make any inferences about the effect of a decrease in doctor shopping, given the fractional amount of total prescribing accounted for by this practice.[33] The authors suggested that the doubling in the street price of buprenorphine after the prescription drug monitoring program implementation was an indicator of success.

An observational study of opioid-related deaths by Paulozzi et al[37] highlights some important considerations in the assessment of the effectiveness of prescription drug monitoring programs. The authors assessed the mortality rate from 1999 to 2005 from schedule II and III prescription opioids in the United States and compared states that had prescription drug monitoring programs with those that did not. They further divided states with prescription drug monitoring programs into those that proactively informed prescribers, generally by mail, of potential

misuse and those that did not. This study found no difference in the mortality rates over time for states with and without a prescription drug monitoring program, nor did states with proactive prescription drug monitoring programs perform better than those with programs that were not proactive. There was a nonsignificantly lower rate of consumption of schedule II opioids and a significantly higher rate of consumption of hydrocodone (schedule III) in states that had a prescription drug monitoring program. A major limitation of this study is that the variability in the prescription drug monitoring program structure, including the ability of health care providers to access the database, was not considered. Current applicability is somewhat limited by substantial changes in the manner in which prescription drug monitoring programs function since the study was conducted, including the extent of physician access and the definition of patient inclusion criteria. Because of the practical limitation of the delay in informing the prescriber of a patient's potential drug misuse, the proactive notification aspect of these programs would have minimal effect on emergency medical practice in states that cannot provide prescription drug monitoring program data in real time.

In conclusion, there are no studies that directly evaluate the effect of real-time, voluntary access to a prescription drug monitoring program on prescribing practices of emergency physicians. In addition, the broader effect of such access on diversion, abuse, doctor shopping, mortality, and the possibility of pain undertreatment remains undefined. Prescription drug monitoring programs have many limitations in their current format, including complex access issues, limitations on access permission, thresholds for patient listing, timeliness, interstate communication, and whether the data are presented to the physician automatically or require physician effort to retrieve. Furthermore, the recent addition of prescription drug monitoring programs in several states and continuing changes in the structure or function of existing programs limit the direct application of even recently published research. Legislation designed to improve prescription drug monitoring program operation (eg, NASPER) has stalled or remained underfunded, and concerns over patient confidentiality have often trumped public health concerns. Until an interstate, frequently updated, multiple-drug-schedule, easily accessible, widely used prescription drug monitoring system is implemented, the likelihood of success is limited.[35]

2. In the adult ED patient with acute low back pain, are prescriptions for opioids more effective during the acute phase than other medications?

Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. (1) For the patient being discharged from the ED with acute low back pain, the emergency physician should ascertain whether nonopioid analgesics and nonpharmacologic therapies will be adequate for initial pain management.

(2) Given a lack of demonstrated evidence of superior efficacy of either opioid or nonopioid analgesics and the individual and community risks associated with opioid use, misuse, and abuse, opioids should be reserved for more severe pain or pain refractory to other analgesics rather than routinely prescribed.

(3) If opioids are indicated, the prescription should be for the lowest practical dose for a limited duration (eg, <1 week), and the prescriber should consider the patient's risk for opioid misuse, abuse, or diversion.

Key words/phrases for literature searches: acute low back pain, opioid, and variations and combinations of the key words/phrases.

Acute low back pain is a common ED presenting complaint. Opioids are frequently prescribed, expected, or requested for such presentations.[40,41] In a recent study, it was estimated that low back pain–related disorders result in approximately 2.6 million annual ED visits in the United States. Of medications either administered in the ED or prescribed at discharge, the most frequently used classes were opioids (61.7%; 95% CI 59.2% to 64.2%), nonsteroidal anti-inflammatory drugs (NSAIDs) (49.6%; 95% CI 46.7% to 52.3%), and muscle relaxants (42.8%; 95% CI 40.2% to 45.4%).[41] The opioid analgesics most commonly prescribed for low back pain, hydrocodone and oxycodone products, are also those most prevalent in a Government Accountability Office study of frequently abused drugs.[42] Low back pain as a presenting complaint was also observed in a recent study to be associated with patients at higher risk for opioid abuse.[43] Low back pain, although a common acute presentation, is also often persistent and recurrent, with 33% of patients continuing to complain of moderate-intensity pain and 15% of severe pain at 1 year from initial presentation. Symptoms recur in 50% to 80% of people within the first year.[44] In one study, 19% reported opioid use at a 3-month follow-up.[40] Emergency physicians, as a specialty, are among the higher prescribers of opioid pain relievers for patients aged 10 to 40 years.[20] Recent data show simultaneous increases in overall opioid sales rates and prescription opioid–related deaths and addiction rates and suggest that widespread use of opioids has adverse consequences for patients and communities.[8]

There is a paucity of literature that addresses the use of opioids after ED discharge for acute low back pain versus the use of NSAIDs or the combination of NSAIDs and muscle relaxants. Two meta-analyses published in the last 5 years identified relatively few valid studies that address the use of opioids for low back pain.[45,46]

In a Class III 2008 Cochrane review, NSAIDs were compared with opioids and muscle relaxants for the treatment of low back pain.[46] Three studies were reviewed that compared opioids (2 of which are no longer in use) with NSAIDs for treatment of acute low back pain, including 1 study considered by the Cochrane reviewers to be of higher quality.[47] None of

the individual studies found statistically significant differences in pain relief. A Class III review by McIntosh and Hall[45] of clinical evidence for treatment of acute low back pain similarly found no evidence for superiority of opioids over other therapies and no direct information to demonstrate that opioids were better than no active therapy; however, the authors concluded that the opioid-related studies were too small to detect any clinically important differences.

A Class III Cochrane review of NSAID treatment for acute low back pain evaluated 65 studies (including more than 11,000 patients) of mixed methodological quality that compared various NSAIDs with placebo, other drugs, other therapies, and other NSAIDs.[46] The review authors concluded that NSAIDs are slightly effective for short-term symptomatic relief in patients with acute and chronic low back pain without sciatica (pain and tingling radiating down the leg). In patients with acute sciatica, no difference in effect between NSAIDs and placebo was found but moderate efficacy was found for opioids. The systematic review also reported that NSAIDs are no more effective than other drugs (acetaminophen, opioids, and muscle relaxants). Placebo and acetaminophen had fewer adverse effects than NSAIDs, and NSAIDS had fewer adverse effects than muscle relaxants or opioids.

A 2003 Cochrane review of muscle relaxants for low back pain (Class X because it did not address the role of opioids) found that muscle relaxants were effective for short-term symptomatic relief in patients with acute and chronic low back pain.[48] However, muscle relaxants were associated with a high incidence of adverse effects. This study cited strong evidence in 4 trials involving a total of 294 people that oral nonbenzodiazepine muscle relaxants are more effective than placebo in patients with acute low back pain for short-term pain relief, global efficacy, and improvement of physical outcomes.

Although no superiority has been demonstrated for opioids over other therapies for treatment of acute low back pain, groups have recommended against use of opioids as first-line therapy for treatment of this problem.[49,50] A guideline for diagnosis and treatment of low back pain endorsed by the American College of Physicians and the American Pain Society recommends opioids only for severe, disabling pain that is not controlled or not likely to be controlled with acetaminophen or NSAIDs.[49] In their 2007 guidelines, the American College of Occupational and Environmental Medicine stated that routine use of opioids for acute, subacute, or chronic low back pain is not recommended.[50]

Several observational non-ED studies also suggest caution with regard to opioid prescribing for back pain. Franklin et al,[51] in a retrospective study (Class X because of the non-ED patient population), found that workers with acute low back injury and worker's compensation claims who were treated with prescription opioids within 6 weeks of acute injury for more than 7 days had a significantly higher risk for long-term disability. In a subsequent Class III population-based prospective study of opioid use among injured Washington State workers with low back pain, Franklin et al[52] observed a strong association between the amount of prescribed opioids received early after injury and long-term use of prescription opioids. A retrospective study of 98 workers with acute low back pain and subsequent disability claims by Mahmud et al[53] found that patients whose treatment of new work-related low back pain involved opioid use for 7 days or more were more likely to have long-term disability (relative risk 2.58; 95% CI 1.22 to 5.47); however, the direct applicability of this study (Class X) was limited because most patients were not seen in the ED. In another study that addressed associations of long-term outcome with opioid therapy for nonspecific low back pain, Volinn et al[54] found that the odds of chronic work loss were 11 to 14 times greater for claimants treated with schedule II ("strong") opioids compared with those not treated with opioids at all. They further observed that the strong associations between schedule II use and long-term disability suggest that for most workers, opioid therapy did not arrest the cycle of work loss and pain. Although this study was also graded as Class X because of the population selected and failure to directly address acute or immediate benefit, the results highlight potential problems of treating acute low back pain with opioids.[54] Unfortunately, causation cannot be directly inferred from these studies because of possible confounding.

In summary, although opioids currently offer the most potent form of pain relief, there is essentially no published evidence that the prescription of opioid analgesics for acute low back pain provides benefit over other available medications or vice versa. Several observational studies suggest associations of both prescription of "strong" opioids or longer prescription duration (greater than 7 days) and early opioid prescribing with worsened functional outcomes. Additionally, as noted, the overall increased rate of opioid sales has been strongly associated with adverse effects in the community (overdose, addiction, aberrant use, and death).[8] Therefore, it can be recommended that opioids not be routinely prescribed for acute low back pain but reserved for select ED patients with more severe pain (eg, sciatica) or pain refractory to other drug and treatment modalities. Prescriptions for opioids should always be provided for limited amounts and for a limited period. Extra caution (such as use of prescription drug monitoring programs and seeking of collateral patient information such as patient visit history) may be indicated for patients identified as possibly having an increased risk for substance dependence or abuse.

3. In the adult ED patient for whom opioid prescription is considered appropriate for treatment of new-onset acute pain, are short-acting schedule II opioids more effective than short-acting schedule III opioids?

Recommendations

Level A recommendations. None specified.

Level B recommendations. For the short-term relief of acute musculoskeletal pain, emergency physicians may prescribe short-acting opioids such as oxycodone or hydrocodone

products while considering the benefits and risks for the individual patient.

Level C recommendations. Research evidence to support superior pain relief for short-acting schedule II over schedule III opioids is inadequate.

Key words/phrases for literature searches: opioids, schedule II narcotics, schedule III narcotics, acute pain, acute disease, emergency service, and variations and combinations of the key words/phrases.

Schedules II and III are classifications established by the Comprehensive Drug Abuse Prevention and Control Act of 1970 and determined by the Drug Enforcement Administration. Among other criteria, classification decisions for specific drugs are based on judgments about the potential for their abuse. Schedule II opioids include morphine (eg, MS Contin), oxymorphone (eg, Opana), oxycodone (eg, Roxicodone) and oxycodone combination products (eg, Percocet, Percodan), as well as hydromorphone (eg, Dilaudid) and fentanyl (eg, Duragesic patch, Actiq). Schedule III opioids include combination products, such as hydrocodone (15 mg or less) combined with acetaminophen (eg, Vicodin, Lortab) or ibuprofen (eg, Vicoprofen), as well as some of the codeine combination products.[55] Schedule classifications for opioids may change over time in response to a number of factors, including their perceived risk of abuse. Calls to reclassify hydrocodone combination products (eg, Vicodin, Lortab) from schedule III to schedule II have increased in recent years in response to increasing levels of abuse of these substances.

These recommendations address only new-onset acute pain. Long-acting or extended-released schedule II products such as oxycodone ER (OxyContin), methadone, fentanyl patches, or morphine extended-release (MS Contin) are indicated for chronic pain and should not be used for acute pain.[56] Long-acting and extended-release opioids are for use in opioid-tolerant patients only and are not intended for use as an "as-needed" analgesic. In addition, the immediate-release oral transmucosal formulations of fentanyl are indicated only for breakthrough pain relief in cancer patients who are already taking sustained-release medications and are opioid tolerant. These formulations should not be used for acute new-onset pain.

As part of the decision to prescribe opioids for new onset of acute pain, the care provider can select between short-acting schedule II or III agents (Table). In general, equianalgesic doses of opioids are equally efficacious in relieving pain. Therefore, *a priori*, there is no reason to consider an equianalgesic dose of a short-acting schedule II opioid more effective in providing pain relief than a short-acting schedule III opioid. However, some studies have compared schedule II and III opioids combined with nonopioid analgesics with one another. Two prospective randomized controlled trials have compared the efficacy of short-acting oxycodone, a schedule II drug, with hydrocodone combination products (schedule III) and found them to be equal.[57,58] In 2005, Marco et al[57] compared single doses of oxycodone 5 mg with hydrocodone 5 mg (both combined with 325 mg acetaminophen). In this single-site Class II study of 67 adolescent and adult subjects with acute fractures, no differences in analgesic efficacy were observed at 30 or 60 minutes. Constipation rates were higher for hydrocodone. In a 2002 Class I study, Palangio et al[58] compared oxycodone 5 mg combined with acetaminophen 325 mg (schedule II) with hydrocodone 7.5 mg combined with ibuprofen 200 mg (schedule III) in a prospective, multicenter, multidose, randomized controlled trial of 147 adults with acute or recurrent low back pain. During an 8-day study period, no differences were found in pain relief, doses taken, global evaluations of efficacy, health status, or pain interference with work. As noted above, equianalgesic doses of opioids have similar efficacy in the treatment of acute pain, no matter their Drug Enforcement Administration classification. Given this understanding, it was not unexpected that 2 randomized controlled trials comparing schedule II with III agents found no differences in analgesic efficacy.

Table. Short-acting oral opioid formulations. Dose and interval are recommended starting dosing ranges.

Medication	Initial Dose/Interval	Schedule
Codeine/APAP	30-60 mg* PO Q4-6h PRN	III
Codeine	30-60 mg PO Q4-6h PRN	II
Hydrocodone/APAP	5-15 mg* PO Q4-6h PRN	III
Hydromorphone	2-4 mg PO Q4-6h PRN	II
Morphine	15-30 mg PO Q4-6h PRN	II
Oxycodone/APAP	5-15 mg* PO Q4-6h PRN	II
Oxycodone	5-15 mg PO Q4-6h PRN	II
Oxymorphone	10-20 mg PO Q4-6h PRN	II

APAP, acetaminophen; *h*, hour; *mg*, milligram; *PO*, by mouth; *PRN*, as needed; *Q*, every.
*Listed dose is of the opioid component. Note that the acetaminophen component is now limited to 325 mg or less per pill.

4. In the adult ED patient with an acute exacerbation of noncancer chronic pain, do the benefits of prescribing opioids on discharge from the ED outweigh the potential harms?

Recommendations

Level A recommendations. None specified.

Level B recommendations. None specified.

Level C recommendations. (1) Physicians should avoid the routine prescribing of outpatient opioids for a patient with an acute exacerbation of chronic noncancer pain seen in the ED.

(2) If opioids are prescribed on discharge, the prescription should be for the lowest practical dose for a limited duration (eg, <1 week), and the prescriber should consider the patient's risk for opioid misuse, abuse, or diversion.

(3) The clinician should, if practicable, honor existing patient-physician pain contracts/treatment agreements and

consider past prescription patterns from information sources such as prescription drug monitoring programs.

Key words/phrases for literature searches: opioid, patient discharge, pain, emergency service, and variations and combinations of the key words/phrases with exclusion of cancer.

Patients with chronic noncancer pain, either already taking opioids or not, commonly present to the ED for treatment of acute exacerbation of their pain. There have been no studies that evaluate the efficacy or potential harms of prescribing opioids specifically for these patients on discharge from the ED. Thus, given the paucity of evidence, this critical question cannot be definitively answered. Despite the biological plausibility that treating any acute exacerbation of pain with parenteral or oral opioids should decrease pain intensity, no studies were found to support this hypothesis.

Only 2 randomized controlled trials were identified that addressed the use of short-acting opioids for the treatment of breakthrough pain in patients taking opioids for chronic noncancer pain; transmucosal fentanyl was the intervention for both trials.[59,60] Because of methodological problems, valid estimates for efficacy of the intervention could not be determined, but adverse event rates among both treated populations were common and similar (range 63% to 65%) (Class III).

A systematic review of nonrandomized studies by Devulder et al[61] examined the effect of rescue medications on overall analgesic efficacy and adverse events. They examined 48 studies of patients treated with long-acting opioids for chronic noncancer pain and compared the analgesic efficacy and adverse events among those that allowed short-acting opioid rescue medications for breakthrough pain with those that did not allow such rescue medications. Although graded Class X because of lack of randomized studies and the limitation of harms studied to adverse effects only, no significant difference in the analgesic efficacy between the rescue and nonrescue studies was found. There was also no difference between these 2 groups in the incidence of nausea, constipation, or somnolence. Kalso et al,[62] in a Class III systematic review, found that 80% of patients receiving opioids for chronic noncancer pain had at least 1 adverse event, including nausea (32%), constipation (41%), and somnolence (29%).

Studies of the use of opioids for chronic pain indicate that adverse effects of these drugs are common. Several studies assessed the adverse effects with the use of tramadol with acetaminophen in the treatment of patients with chronic low back pain.[63-65] All of the studies had high dropout rates and reported adverse event rates of nausea, dizziness, and somnolence between 8% and 17%. Allan et al,[66] in a nonblinded Class III study comparing transdermal fentanyl versus oral morphine, found a constipation rate of 48% in the morphine-treated patients compared with a rate of 31% in the fentanyl-treated patients. Constipation was also the major adverse effect in a Class III study by Hale et al[67] comparing oxymorphone extended release, oxycodone controlled release, and placebo. Furlan et al,[68] in a Class II meta-analysis of 41 randomized studies of opioid use in the treatment of chronic noncancer pain, found that constipation and nausea were the only significant adverse effects. Holmes et al,[69] however, in a Class III study, assessed an opioid screening instrument, the Pain Medication Questionnaire, in chronic noncancer pain patients and found that those patients with a higher score were more likely to have a substance abuse problem or request early refills of their opioid prescription. In a retrospective Class III cohort study, Jensen et al[70] conducted a 10-year follow-up on patients discharged from a pain clinic and found that chronic opioid treatment may put patients at risk for chronic depression. Unfortunately, near-universal shortcomings of these studies include the exclusion of patients with a history of substance abuse, other significant medical problems, or psychiatric disease, and lack of follow-up to detect long-term effects such as aberrant drug-related behaviors, addiction, or overdose. Therefore, studies such as these can be confounded, making the ability to draw conclusions about causality difficult.

Questions of opioid effectiveness involve the assessment of reduction in pain and improvement in function for the patient, potential patient adverse effects, and the potential harm to the community (eg, opioid diversion and abuse) from the drugs prescribed. Hall et al,[32] in a Class III retrospective analysis of 295 unintentional prescription overdose deaths, found that 93% were due to opioids, 63% represented pharmaceutical drug diversion, 21% of the patients had engaged in doctor shopping, and 95% of the patients had a history of substance abuse. Although no studies have addressed the effects related to dose and duration of prescribed opioids in this specific patient population, 2 general studies have shown a correlation between high daily opioid dose and overdose death.[71,72]

Patient assessment tools such as the Screener and Opioid Assessment for Patients with Pain (SOAPP), Opioid Risk Tool (ORT), Diagnosis, Intractability, Risk, and Efficacy (DIRE), and others to assess the risk of prescription opioid misuse and abuse have yet to be fully validated in the ED in terms of sensitivity, specificity, and utility.[73] Many, however, believe that use of these tools, as imperfect as they are, represents a beginning in the ability to better quantify potential risks related to opioid prescribing for outpatients.

Many patients undergoing treatment for chronic noncancer pain have pain contracts/treatment agreements with their primary care providers. These should be honored if possible in treating any acute exacerbation of their pain.[74,75] As discussed in critical question 1, use of prescription drug monitoring programs may also assist the emergency physician in making appropriate clinical decisions about the use of outpatient opioid prescriptions for these patients.

FUTURE RESEARCH

Provider pain management practices related to opioids are highly variable. In part, this variability reflects the lack of evidence to guide many of these therapeutic decisions.[76]

Although there is high-quality research assessing the treatment of acute pain with opioid analgesics during the ED encounter, there is a paucity of studies assessing the benefits of prescribing opioids for discharged ED patients with acute pain and chronic noncancer pain, especially in comparison to other analgesic drugs and pain treatment modalities. Therefore, clinical decisions and practice recommendations must rely on practice experience and consensus rather than research evidence.

ED populations typically include patients with unmet substance abuse treatment needs and psychiatric comorbidities, and many of these patients present with acute pain.[77] In almost all pain studies, these patients are excluded, leaving clinicians with little evidence-based guidance for their pain management. There are also significant research gaps in clearly understanding the long-term harms of opioids, including drug abuse and addiction, aberrant drug-related behaviors, and diversion. As mentioned above, further research and validation is needed on ED patient abuse and addiction-related assessment tools. Additional studies to characterize individual patient-related risks for opioid abuse are also greatly needed.

Although there has been recent widespread adoption of prescription monitoring programs, there remains a dearth of evidence about the effectiveness of these programs in altering physician prescribing patterns or diminishing the adverse effects of opioids in the community. For research in this area to advance, further refinement of prescribing metrics (quantity, duration, and frequency) and public health measures is required. Comparison of the functionality and effectiveness of the various state prescription drug monitoring program models may provide additional insight into developing best practices that could be adopted nationally, including the sharing of data between states. Important distinctions among the states, such as immediate online prescriber access to the prescription monitoring program, should be examined for their relative contributions. However, this type of analysis must consider baseline variability among states for prescription opioid misuse (versus heroin or methadone, for example) and other state-specific issues (such as prescription-writing regulations).

With respect to the treatment of acute low back pain in the ED, there is a need for quality studies comparing the effectiveness of the more commonly prescribed opioids (hydrocodone and oxycodone congeners and other semisynthetic opioids) and nonopioid therapies, with attention to confounding variables such as depression or other psychopathology. Further study is needed to validate or refute the reported associations of early or potent opioid prescribing with increased rates of disability.[51] Given the frequency of acute low back pain as an ED presentation and its association with perceived drug-seeking behavior,[78] and with apparent higher risk for misuse,[43] more attention needs to be paid to discriminatory historical or physical factors that may be predictive of drug-seeking or abuse to allow better matching of treatment modality for individual patients.

Future studies should include additional multiple-dose analgesic protocols to better understand the postdischarge experience of patients with acute pain and what would constitute optimum patient follow-up provisions. Investigators should include clinically relevant study periods (days to weeks), which vary by diagnosis; thus, trials should be stratified by specific presenting complaints, pain site, discharge diagnosis, and classification of pain type, ie, nociceptive, neuropathic, and visceral pain. In addition to measuring pain and adverse effects, functional outcomes, such as return to work or pain-related quality-of-life measures, should be included.[79] Straightforward observational studies are needed to determine the relative duration of different acute pain presentations, thus informing decisions to prescribe an appropriate number of opioid doses per prescription. Current prescribing practice often involves a "one size fits all" pattern that is encouraged by electronic prescribing software. Prescribing practices that ignore variable durations of acute pain syndromes will predictably result in undertreatment for some patients and overtreatment for others. The latter increases the likelihood that unused opioids will be diverted into nonmedical use in communities at risk.

Additional research should include evaluation of the appropriateness of patient satisfaction as a quality metric as related to patient expectations of opioids and the prevalence of providers reporting pressure through low patient satisfaction scores or administrative complaints to provide opioids when the providers believe these drugs are not medically indicated. This issue may gain increased importance with the institution of the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey, which may tie some reimbursement to patient satisfaction scores. Additional work is needed to investigate what constitutes an appropriate educational curriculum in both medical school and residency for physician education concerning safe, appropriate, and judicious use of opioids.

Research addressing the treatment of chronic noncancer pain would be enhanced by the use of accepted case definitions, standardized definitions of adverse events, and validated pain measurements. Case definitions should use a similar definition of chronic, nociceptive (musculoskeletal or visceral) versus neuropathic pain, or pain by disease type (headache, low back pain, etc). Research reporting also requires more refined descriptions of opioid potency and routes of administration.

Although opioids represent a treatment modality that has long been used in patient care, it is clear by the paucity of definitive answers to the questions posed in this document and the significant number of future research issues that much work remains to be done to clarify the best use of opioids in the care of patients.

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American Chronic Pain Association and has previously been a consultant to the pharmaceutical industry.

Relevant industry relationships are those relationships with companies associated with products or services that significantly impact the specific aspect of disease addressed in the critical questions.

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Evidentiary Table.

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Hall et al[32]	2008	Retrospective, population based, observational study	Comparison of West Virginia medical examiner data with patient data from the state prescription monitoring program and opioid abuse treatment program records	Behaviors of those who died of a pharmaceutical overdose; diversion; doctor shopping; substance abuse history; type of drug	295 deaths; 67% male; 92% aged 18-54 y; 63% pharmaceutical diversion; 21% doctor shopping; 95% substance abuse history; 93% opioids	Actual source of opioids involved in death not known; single state; not validated definitions; retrospective	III
Pradel et al[33]	2009	Database	Review of prescription drug database (not prescription monitoring program) to identify amount of buprenorphine delivered, prescribed, and obtained by doctor shopping; extension of 2004 study, used multiple time period comparisons; evaluation of trends in doctor shopping over time	Determined prescribed quantity of buprenorphine, delivered quantity, and the doctor shopping quantity	Although there was some variation over time, the trend for prescribing stayed constant overall and doctor shopping decreased after 2004, associated with the change in the mechanism by which prescriptions are monitored	Reasons for multiple providers or overlapping or interrupted prescriptions unclear; did not examine risk factors for abuse	III
Baehren et al[39]	2010	Prospective, uncontrolled	Physicians prescribing analgesics for nonacute pain were asked details about the patient's prescription and then again after being informed of the prescription monitoring program search result for that patient	Change in prescription for the specific patient	179 enrolled; management changed in 41%; 61% received fewer opioids, 39% received more	Convenience sample; majority of data from 4 prescribers	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
McIntosh and Hall[45]	2011	Review of randomized controlled trials, systematic reviews, and observational studies found searching MEDLINE 1966-12/2009, EMBASE 1980 to 12/2009, and Cochrane database up to 12/2009; 49 studies met inclusion criteria	Multiple treatment modalities for acute low back pain, including oral drugs, local injections, and nondrug treatment	Clinical improvement of low back pain	NSAIDs shown to effectively improve symptoms compared with placebo, but use associated with gastrointestinal adverse effects; muscle relaxants may reduce pain and improve clinical assessment but are associated with adverse effects including drowsiness, dizziness, nausea	The studies examining the effects of analgesics such as acetaminophen or opioids were generally too small to detect any clinically important differences	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Roelofs et al[46]	2008	Cochrane review: search of MEDLINE, EMBASE, and Cochrane central registry of controlled trials up to 7/2007; 65 trials qualified for review	NSAIDs and COX-2 inhibitors administered to treat low back pain	Clinical improvement of low back pain	Review authors found NSAIDs are not more effective than other drugs (acetaminophen, opioids, and muscle relaxants); placebo and acetaminophen had fewer adverse effects than NSAIDs, although the latter had fewer adverse effects than muscle relaxants and opioids; the new COX-2 NSAIDs do not seem to be more effective than traditional NSAIDs but are associated with fewer adverse effects, particularly stomach ulcers, although other literature has shown that some COX-2 NSAIDs are associated with increased cardiovascular risk	7 studies reported on acute low back pain, 5 of which, including 1 higher-quality study, did not find any statistical differences between NSAIDs and opioids or muscle relaxants; there is moderate evidence that NSAIDs are not more effective than other drugs for acute low back pain	III
Videman et al[47]	1984	Double-blind parallel study	70 patients; comparative trial of meptazinol vs diflunisal for up to 3 wk	Patients examined at 1-wk intervals for task capability, range of motion, and subjective pain self-assessment	Both regimens produced marked improvement in most parameters, similar adverse effect profiles	No mention of patient randomization	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Franklin et al[52]	2009	Prospective cohort; Washington State workers with back injury; n=1,883	Prospective cohort of workers with back injuries interviewed at 18 days (medial) and 1 y after injury; pharmacy data obtained from computerized records; analyzed for demographic and covariates	Injury severity, pain, function, and quantities of opioids used	For long-term users total number of medications increased significantly (P=.01) from the first to the fourth quarter; after adjustment for baseline pain, function, and injury severity, the strongest predictor of longer-term opioid prescriptions was total number of medications in the first quarter; receipt of ≥10 mg/day medicine in first quarter more than tripled the odds of receiving opioids long term, and receipt of ≥40 mg/day medicine in first quarter had 6-fold odds of receiving long-term opioids; amount of prescribed opioid received early after injury predicts long-term use	Addressed progression to long-term use according to initial treatment and continuation of same	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Marco et al[57]	2005	Single site; prospective; double blind; randomized controlled trial; concealment method described; ED patients with fractures	Single dose of oxycodone 5 mg/acetaminophen 325 mg schedule II vs hydrocodone 5 mg/acetaminophen 325 mg schedule III	Primary outcomes were numeric pain scores (0-10) at 30 and 60 min	88 subjects evaluated, 73 enrolled, 67 completed ED study period, 35 to oxycodone, 32 to hydrocodone; no baseline differences, no differences in outcomes at 30 min: -0.6 (95% CI -1.8 to 0.5); 60 min -0.5 (95% CI -2.0 to 1.0); adverse effects higher for constipation with hydrocodone (21% vs 0%; (95% CI 3% to 39%)	Small sample size powered to address acute pain during the first 30 to 60 min in the ED; study also assessed adverse effects during a longer period of time; excluded history of alcohol or opioid or other substance abuse; limited time period	II
Palangio et al[58]	2002	Prospective multicenter (18 sites), randomized controlled trial, sequential assignment by computer-generated randomization schedule	Hydrocodone 7.5 mg/ibuprofen 200 mg (schedule III) vs oxycodone 5 mg/acetaminophen 325 mg (schedule II)	Primary outcome was mean daily pain relief score at endpoint (day 8 or day of discontinuation), study period up to 8 days, intention-to-treat analysis	147 subjects enrolled (75 hydrocodone/ibuprofen, 72 oxycodone/acetaminophen), adults with acute or recurrent low back pain requiring opioids, 85% completed study in both groups, mean days to endpoint 6.5 vs 6.9 days, no baseline differences, no differences in pain relief, number of pills, global evaluations, SF-36, pain interference with work, adverse events	Excluded drug or alcohol abuse, concealment methods described	I

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Portenoy et al[59]	2007	Randomized, double blind, placebo controlled	Fentanyl buccal tablet for breakthrough pain in chronic low back pain patients	Pain before treatment and for 2 h after treatment	Fentanyl buccal tablet effective for breakthrough pain in chronic low back pain; adverse effects in 65%; 34% during double-blind phase	Severe selection bias in initial screening; industry sponsored	III for adverse effects
Simpson et al[60]	2007	Randomized, double blind, placebo controlled	Fentanyl buccal tablet for breakthrough pain in chronic pain patients	Pain before treatment and for 2 h after treatment	Fentanyl buccal tablet effective for breakthrough pain; adverse effects in 63%; 22% dropout	Severe selection bias in initial screening; industry sponsored	III for adverse effects
Kalso et al[62]	2004	Systematic review	Randomized trials in chronic noncancer pain comparing potent opioids with placebo	Pain intensity outcomes	15 randomized trials were included; 11 studies compared oral opioids for 4 wk; pain intensity decrease was 30% compared with placebo; only 44% were taking opioids by mo 7 to 24; 80% of patients experienced at least 1 adverse event: constipation (41%), nausea (32%), somnolence (29%)	4-wk duration on average; differing causes of pain; open label in many of the studies; limited power calculations; concealment not maintained in some studies	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Peloso et al[63]	2004	Prospective, randomized, blinded study	Tramadol/acetaminophen vs placebo; patients with chronic low back pain requiring daily medication for at least 3 mo	Pain VAS; pain relief rating scale; Short Form Magill Pain Questionnaire SF-36; 3-mo trial	336 patients randomized; improved mean final pain scores (47 vs 63; $P<.001$), adverse effects: nausea 12%, dizziness 11%, constipation 10%, somnolence 9%	35%-40% dropout rate; pharmaceutical-sponsored research	II
Ruoff et al[64]	2003	Prospective, randomized, blinded study	Tramadol/acetaminophen vs placebo; patients with chronic low back pain requiring daily medication for at least 3 mo	Pain VAS; pain relief rating scale; Short Form Magill Pain Questionnaire SF-36; Roland Disability Questionnaire	318 patients randomized; tramadol improved pain VAS ($P=.15$) and final Pain Relief Rating Scale ($P<.001$); adverse effects: nausea 13%, somnolence 12%, constipation 11%, dizziness 8%	153 of 318 dropped out; pharmaceutical-sponsored research	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Schnitzer et al[65]	2000	Prospective, randomized, blinded study	Tramadol/acetaminophen vs placebo; patients with chronic low back pain requiring daily medication for at least 3 mo	Time to discontinuation because of inadequate pain relief; Short Form Magill Pain Questionnaire; Roland Disability Questionnaire	380 patients in open-label phase; 254 entered into blinded phase; time to therapeutic failure was greater in the placebo group ($P<.0001$); other parameters showed improvement; adverse effects: nausea 17%, dizziness 15%, somnolence 14%, headache 12%	The dropout rate was the primary outcome; pharmaceutical-sponsored research	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Allan et al[66]	2005	Nonblinded, randomized comparison of 2 treatments in patients with chronic low back pain	Transdermal fentanyl vs sustained-release oral morphine; 680 total patients; dose titrated to effect; followed for 13 mo; outpatient setting; not applicable to ED	Pain relief (VAS scale); bowel function (validated questionnaire); quality of life (SF-36); disease, progression (3-point scale), days not working, adverse events all during 13 mo	Comparable pain relief, noninferior, VAS score for fentanyl (56) vs morphine (55); fentanyl had lower constipation rate: fentanyl (31%) vs morphine (48%)	Both groups had half of the participants drop out; vague definition of chronic low back pain; not blinded	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Hale et al[67]	2005	Randomized trial, blinded	Comparison of oxymorphone extended-release vs oxycodone controlled release vs placebo in patients with chronic low back pain who were taking a stable dose of opioids	VAS of pain score 4 h after morning dose; use of breakthrough pain medications; categorical pain intensity, pain intensity, global assessment, adverse events	Opioids were superior to placebo at reducing VAS for pain compared with placebo, oxymorphone (-27), oxycodone (-36); oxymorphone was comparable to oxycodone in pain efficacy and adverse effects; sedation and constipation were more common with opioids (35% vs 29% vs 11%)	Only 22 of 75 patients in the placebo group completed the study; included only patients receiving stable opioids and then randomized to opioids or placebo; baseline characteristics between groups not specified; pharmaceutical-sponsored research	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/ Comments	Class
Furlan et al[68]	2006	Meta-analysis	Study included randomized trials of any opioid for chronic noncancer pain (defined as pain for longer than 6 mo) vs placebo or some other nonopioid treatment	41 randomized studies with 6,019 patients evaluated for effectiveness and adverse effects; most (80%) had nociceptive pain	81% of the studies were believed to be of high quality; dropout rates were 33% in the opioid group and 38% in the placebo group; opioids improved pain and functional outcomes compared with placebo in nociceptive and neuropathic pain; strong opioids were superior to naproxen and nortriptyline for pain relief; weak opioids were not superior; constipation and nausea were the only significant adverse effects observed	Average duration of the study was 5 wk (range 1-16 wk); adequate random patient assignment in only 17 of 41 trials; 90% of trials were pharmaceutical-sponsored research	II

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Holmes et al[69]	2006	Prospective cohort	Convenience sample of patients who were new at a pain clinic; Pain Medication Questionnaire was administered; patients were treated with interdisciplinary treatment and/or medications alone, depending on the results of an initial evaluation	Beck Depression Inventory; Confidential Pain questionnaire; SF-36; Million VAS; Oswestry Disability Questionnaire; Physician Risk Assessment; VAS	271 patients, divided into low-, medium-, and high-score pain medication questionnaire; high-score group was more likely to have a known substance use problem (OR 2.6), request early refills (OR 3.2), or drop out of treatment (OR 2.3)	Only 26% of patients completed the full treatment program; heterogeneous types of pain diagnosis; differing treatment plans	III

Evidentiary Table (continued).

Study	Year	Design	Intervention(s)/Test(s)/Modality	Outcome Measure/Criterion Standard	Results	Limitations/Comments	Class
Jensen et al[70]	2006	Retrospective review of cohort	Patients who were treated and discharged from a pain clinic 10 y ago; medical records were abstracted and questionnaires were sent to willing participants	Demographics, health care utilization, SF-36; Hospital Anxiety and Depression Scale; Coping Strategy Questionnaire; CAGE* test	160 patients; 60% of patients were still taking long-acting opioids; dose escalation was unusual; chronic users had lower health-related quality of life and higher occurrence of depression	160 of 279 possible patients participated; no control group	III

COX-2, cyclooxygenase-2; *ED*, emergency department; *h*, hour; *mg*, milligram; *min*, minute; *mo*, month; *NSAID*, nonsteroidal anti-inflammatory drug; *OR*, odds ratio; *SF-36*, Short-Form Health Survey; *VAS*, visual analog scale; *vs*, versus; *wk*, week; *y*, year.
*CAGE (Cutting down, Annoyed, Guilty, Eye-opener) test is a method of screening for alcoholism.

Appendix A. Literature classification schema.*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)	Case series Case report Other (eg, consensus, review)

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome, including mortality and morbidity.

Appendix B. Approach to downgrading strength of evidence.

	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix 2 - Older Adults

Older Adults[17]

The prevalence of pain among older adults has been estimated between 25% and 50%. The prevalence of pain in nursing homes is even higher. Unfortunately, managing pain in older adults is challenging due to: underreporting of symptoms; presence of multiple medical conditions; polypharmacy; declines in liver and kidney function; problems with communication, mobility and safety; and cognitive and functional decline in general.

Acetaminophen is considered the drug of choice for mild-to-moderate pain in older adults because it lacks the gastrointestinal, bleeding, renal toxicities, and cognitive side-effects that have been observed with NSAIDs in older adults (although acetaminophen may pose a risk of liver damage). Opioids must be used with particular caution and clinicians should "start low, go slow" with initial doses and subsequent titration. Clinicians should consult the American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults for further information on the many medications that may not be recommended.

The various challenges of pain management in older adults, only sketched here, suggest that early referral and/or consultation with geriatric specialists or pain specialists may be advisable.

[17] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

Appendix 3 - Pediatric Patients

Pediatric Patients[18]

Children of all ages deserve compassionate and effective pain treatment. In fact, due to their more robust inflammatory response and immature central inhibitory influences, infants and young children actually may experience greater pain sensations and pain-related distress than adults. Effective pain management in the pediatric population is critical since children and adolescents experience a variety of acute and chronic pain conditions associated with common childhood illnesses and injuries, as well as some painful chronic diseases that typically emerge in childhood such as sickle cell anemia and cystic fibrosis.

The same basic principles of appropriate pain management for adults apply to children and teens, which means that opioids have a place in the treatment armamentarium. Developmental differences, however, can make opioid dosing challenging, especially in the first several months of life. In the first week of a newborn's life, for example, the elimination half-life of morphine is more than twice as long as that in older children and adults, as a result of delayed clearance. For older children, dosing must be adjusted for body weight.

Although a thorough discussion of this topic is not possible in this document, the following are summary recommendations for pain management in children and teens from the American Pain Society and the American Academy of Pediatrics:

- Provide a calm environment for procedures that reduce distress-producing stimulation;
- Use age-appropriate pain assessment tools and techniques;
- Anticipate predictable painful experiences, intervene and monitor accordingly;
- Use a multimodal approach (pharmacologic, cognitive, behavioral and physical) to pain management and use a multidisciplinary approach when possible;
- Involve families and tailor interventions to the individual child; and
- Advocate for the effective use of pain medication for children to ensure compassionate and competent management of their pain.

[18] California Medical Association (Prescribing Opioids: Care amid Controversy, March 2014).

Appendix 4 - Opioid Risk Tool (ORT)

Date _____

Patient Name _____

OPIOID RISK TOOL

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

Total Score Risk Category Low Risk 0 – 3 Moderate Risk 4 – 7 High Risk ≥ 8

Appendix 5 - Patient Evaluation and Risk Stratification

Patient Evaluation and Risk Stratification[19]

The medical record should document the presence of one or more recognized medical indications for prescribing an opioid analgesic and reflect an appropriately detailed patient evaluation. Such an evaluation should be completed before a decision is made as to whether to prescribe an opioid analgesic.

The nature and extent of the evaluation depends on the type of pain and the context in which it occurs. For example, meaningful assessment of chronic pain, including pain related to cancer or non-cancer origins, usually demands a more detailed evaluation than an assessment of acute pain. Assessment of the patient's pain typically would include the nature and intensity of the pain, past and current treatments for the pain, any underlying or co-occurring disorders and conditions, and the effect of the pain on the patient's physical and psychological functioning.

For every patient, the initial work-up should include a systems review and relevant physical examination, as well as laboratory investigations as indicated. Such investigations help the physician address not only the nature and intensity of the pain, but also its secondary manifestations, such as its effects on the patient's sleep, mood, work, relationships, valued recreational activities, and alcohol and drug use.

Social and vocational assessment is useful in identifying supports and obstacles to treatment and rehabilitation; for example: Does the patient have good social supports, housing, and meaningful work? Is the home environment stressful or nurturing?.

Assessment of the patient's personal and family history of alcohol or drug abuse and relative risk for medication misuse or abuse also should be part of the initial evaluation, and ideally should be completed prior to a decision as to whether to prescribe opioid analgesics. This can be done through a careful clinical interview, which also should inquire into any history of physical, emotional or sexual abuse, because those are risk factors for substance misuse. Use of a validated screening tool (such as the Screener and Opioid Assessment for Patients with Pain [SOAPP-R] or the Opioid Risk Tool [ORT]), or other validated screening tools, can save time in collecting and evaluating the information and determining the patient's level of risk.

All patients should be screened for depression and other mental health disorders, as part of risk evaluation. Patients with untreated depression and other mental health problems are at increased risk for misuse or abuse of controlled medications, including addiction, as well as overdose.

[19] Federation of State Medical Boards - Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain, July 2013.

Patients who have a history of substance use disorder (including alcohol) are at elevated risk for failure of opioid analgesic therapy to achieve the goals of improved comfort and function, and also are at high risk for experiencing harm from this therapy, since exposure to addictive substances often is a powerful trigger of relapse. Therefore, treatment of a patient who has a history of substance use disorder should, if possible, involve consultation with an addiction specialist before opioid therapy is initiated (and follow-up as needed). Patients who have an active substance use disorder should not receive opioid therapy until they are established in a treatment/recovery program or alternatives are established such as co-management with an addiction professional. Physicians who treat patients with chronic pain should be encouraged to also be knowledgeable about the treatment of addiction, including the role of replacement agonists such as methadone and buprenorphine. For some physicians, there may be advantages to becoming eligible to treat addiction using office-based buprenorphine treatment.

Information provided by the patient is a necessary but insufficient part of the evaluation process. Reports of previous evaluations and treatments should be confirmed by obtaining records from other providers, if possible. Patients have occasionally provided fraudulent records, so if there is any reason to question the truthfulness of a patient's report, it is best to request records directly from the other providers.

If possible, the patient evaluation should include information from family members and/or significant others. Where available, the state prescription drug monitoring program (PDMP) should be consulted to determine whether the patient is receiving prescriptions from any other physicians, and the results obtained from the PDMP should be documented in the patient record.

In dealing with a patient who is taking opioids prescribed by another physician—particularly a patient on high doses—the evaluation and risk stratification assume even greater importance. With all patients, the physician's decision as to whether to prescribe opioid analgesics should reflect the totality of the information collected, as well as the physician's own knowledge and comfort level in prescribing such medications and the resources for patient support that are available in the community.

Appendix 6 - CAGE-AID

CAGE-AID Questionnaire

CAGE-AID Questionnaire

Patient Name _____ Date of Visit _____

When thinking about drug use, include illegal drug use and the use of prescription drug other than prescribed.

Questions:	YES	NO
1. Have you ever felt that you ought to cut down on your drinking or drug use?	☐	☐
2. Have people annoyed you by criticizing your drinking or drug use?	☐	☐
3. Have you ever felt bad or guilty about your drinking or drug use?	☐	☐
4. Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover?	☐	☐

Scoring
Regard one or more positive responses to the CAGE-AID as a positive screen.

Psychometric Properties

The CAGE-AID exhibited:	Sensitivity	Specificity
One or more Yes responses	0.79	0.77
Two or more Yes responses	0.70	0.85

(Brown 1995)

Appendix 7 - PHQ-9 Nine Symptom Checklist

PHQ-9 — Nine Symptom Checklist

Patient Name _____ **Date** _____

1. Over the last 2 weeks, how often have you been bothered by any of the following problems? Read each item carefully, and circle your response.

   a. Little interest or pleasure in doing things
   Not at all **Several days** **More than half the days** **Nearly every day**

   b. Feeling down, depressed, or hopeless
   Not at all **Several days** **More than half the days** **Nearly every day**

   c. Trouble falling asleep, staying asleep, or sleeping too much
   Not at all **Several days** **More than half the days** **Nearly every day**

   d. Feeling tired or having little energy
   Not at all **Several days** **More than half the days** **Nearly every day**

   e. Poor appetite or overeating
   Not at all **Several days** **More than half the days** **Nearly every day**

   f. Feeling bad about yourself, feeling that you are a failure, or feeling that you have let yourself or your family down
   Not at all **Several days** **More than half the days** **Nearly every day**

   g. Trouble concentrating on things such as reading the newspaper or watching television
   Not at all **Several days** **More than half the days** **Nearly every day**

   h. Moving or speaking so slowly that other people could have noticed. Or being so fidgety or restless that you have been moving around a lot more than usual
   Not at all **Several days** **More than half the days** **Nearly every day**

   i. Thinking that you would be better off dead or that you want to hurt yourself in some way
   Not at all **Several days** **More than half the days** **Nearly every day**

2. If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

   Not Difficult at All **Somewhat Difficult** **Very Difficult** **Extremely Difficult**

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PHQ-9 — Scoring Tally Sheet

Patient Name _____ **Date** _____

1. **Over the last 2 weeks, how often have you been bothered by any of the following problems? Read each item carefully, and circle your response.**

	Not at all	Several days	More than half the days	Nearly every day
	0	1	2	3
a. Little interest or pleasure in doing things				
b. Feeling down, depressed, or hopeless				
c. Trouble falling asleep, staying asleep, or sleeping too much				
d. Feeling tired or having little energy				
e. Poor appetite or overeating				
f. Feeling bad about yourself, feeling that you are a failure, or feeling that you have let yourself or your family down				
g. Trouble concentrating on things such as reading the newspaper or watching television				
h. Moving or speaking so slowly that other people could have noticed. Or being so fidgety or restless that you have been moving around a lot more than usual				
i. Thinking that you would be better off dead or that you want to hurt yourself in some way				
Totals				

2. **If you checked off any problem on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?**

Not Difficult At All	Somewhat Difficult	Very Difficult	Extremely Difficult
0	1	2	3

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How to Score PHQ-9

Scoring Method For Diagnosis

Major Depressive Syndrome is suggested if:

- Of the 9 items, 5 or more are circled as at least "More than half the days"
- Either item 1a or 1b is positive, that is, at least "More than half the days"

Minor Depressive Syndrome is suggested if:

- Of the 9 items, b, c, or d are circled as at least "More than half the days"
- Either item 1a or 1b is positive, that is, at least "More than half the days"

Scoring Method For Planning And Monitoring Treatment

Question One

- To score the first question, tally each response by the number value of each response:

  Not at all = 0

  Several days = 1

  More than half the days = 2

  Nearly every day = 3
- Add the numbers together to total the score.
- Interpret the score by using the guide listed below:

Score	Action
≤4	The score suggests the patient may not need depression treatment.
> 5-14	Physician uses clinical judgment about treatment, based on patient's duration of symptoms and functional impairment.
≥15	Warrants treatment for depression, using antidepressant, psychotherapy and/or a combination of treatment

Question Two

In question two the patient responses can be one of four: not difficult at all, somewhat difficult, very difficult, extremely difficult. The last two responses suggest that the patient's functionality is impaired. After treatment begins, the functional status is again measured to see if the patient is improving.

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How to Score PHQ-9

Appendix 8 - SOAPP®-R

Screener and Opioid Assessment for Patients with Pain- Revised (SOAPP®-R)

The Screener and Opioid Assessment for Patients with Pain- Revised (SOAPP®-R) is a tool for clinicians to help determine how much monitoring a patient on long-term opioid therapy might require. This is an updated and revised version of SOAPP V.1 released in 2003.

Physicians remain reluctant to prescribe opioid medication because of concerns about addiction, misuse, and other aberrant medication-related behaviors, as well as liability and censure concerns. Despite recent findings suggesting that most patients are able to successfully remain on long-term opioid therapy without significant problems, physicians often express a lack of confidence in their ability to distinguish patients likely to have few problems on long-term opioid therapy from those requiring more monitoring.

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

- A brief paper and pencil questionnaire
- Developed based on expert consensus regarding important concepts likely to predict which patients will require more or less monitoring on long-term opioid therapy (content and face valid)
- Validated with 500 chronic pain patients
- Simple to score
- 24 items
- <10 minutes to complete
- Ideal for documenting decisions about the level of monitoring planned for a particular patient or justifying referrals to specialty pain clinic.
- The SOAPP-R is for clinician use only. The tool is not meant for commercial distribution.
- The SOAPP-R is NOT a lie detector. Patients determined to misrepresent themselves will still do so. Other clinical information should be used with SOAPP-R scores to decide on a particular patient's treatment.
- The SOAPP-R is NOT intended for all patients. The SOAPP-R should be completed by chronic pain patients being considered for opioid therapy.
- It is important to remember that all chronic pain patients deserve treatment of their pain. Providers who are not comfortable treating certain patients should refer those patients to a specialist.

SAMPLE

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PainEDU.org

SOAPP®-R

The following are some questions given to patients who are on or being considered for medication for their pain. Please answer each question as honestly as possible. There are no right or wrong answers.

	Never	Seldom	Sometimes	Often	Very Often
	0	1	2	3	4
1. How often do you have mood swings?	○	○	○	○	○
2. How often have you felt a need for higher doses of medication to treat your pain?	○	○	○	○	○
3. How often have you felt impatient with your doctors?	○	○	○	○	○
4. How often have you felt that things are just too overwhelming that you can't handle them?	○	○	○	○	○
5. How often is there tension in the home?	○	○	○	○	○
6. How often have you counted pain pills to see how many are remaining?	○	○	○	○	○
7. How often have you been concerned that people will judge you for taking pain medication?	○	○	○	○	○
8. How often do you feel bored?	○	○	○	○	○
9. How often have you taken more pain medication than you were supposed to?	○	○	○	○	○
10. How often have you worried about being left alone?	○	○	○	○	○
11. How often have you felt a craving for medication?	○	○	○	○	○
12. How often have others expressed concern over your use of medication?	○	○	○	○	○

SAMPLE

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	Never	Seldom	Sometimes	Often	Very Often
	0	1	2	3	4
13. How often have any of your close friends had a problem with alcohol or drugs?	○	○	○	○	○
14. How often have others told you that you had a bad temper?	○	○	○	○	○
15. How often have you felt consumed by the need to get pain medication?	○	○	○	○	○
16. How often have you run out of pain medication early?	○	○	○	○	○
17. How often have others kept you from getting what you deserve?	○	○	○	○	○
18. How often, in your lifetime, have you had legal problems or been arrested?	○	○	○	○	○
19. How often have you attended an AA or NA meeting?	○	○	○	○	○
20. How often have you been in an argument that was so out of control that someone got hurt?	○	○	○	○	○
21. How often have you been sexually abused?	○	○	○	○	○
22. How often have others suggested that you have a drug or alcohol problem?	○	○	○	○	○
23. How often have you had to borrow pain medications from your family or friends?	○	○	○	○	○
24. How often have you been treated for an alcohol or drug problem?	○	○	○	○	○

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

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Scoring Instructions for the SOAPP®-R

All 24 questions contained in the SOAPP®-R have been empirically identified as predicting aberrant medication-related behavior six months after initial testing.

To score the SOAPP, add the ratings of all the questions. A score of 18 or higher is considered positive.

Sum of Questions	SOAPP-R Indication
> or = 18	+
< 18	-

What does the Cutoff Score Mean?

For any screening test, the results depend on what cutoff score is chosen. A score that is good at detecting patients at-risk will necessarily include a number of patients that are not really at risk. A score that is good at identifying those at low risk will, in turn, miss a number of patients at risk. A screening measure like the SOAPP-R generally endeavors to minimize the chances of missing high-risk patients. This means that patients who are truly at low risk may still get a score above the cutoff. The table below presents several statistics that describe how effective the SOAPP-R is at different cutoff values. These values suggest that the SOAPP-R is a sensitive test. This confirms that the SOAPP-R is better at identifying who is at high risk than identifying who is at low risk. Clinically, a score of 18 or higher will identify 81% of those who actually turn out to be at high risk. The Negative Predictive Values for a cutoff score of 18 is .87, which means that most people who have a negative SOAPP-R are likely at low-risk. Finally, the Positive likelihood ratio suggests that a positive SOAPP-R score (at a cutoff of 18) is 2.5 times (2.53 times) as likely to come from someone who is actually at high risk (note that, of these statistics, the likelihood ratio is least affected by prevalence rates). All this implies that by using a cutoff score of 18 will ensure that the provider is least likely to miss someone who is really at high risk. However, one should remember that a low SOAPP-R score suggests the patient is very likely at low-risk, while a high SOAPP-R score will contain a larger percentage of false positives (about 30%); at the same time retaining a large percentage of true positives. This could be improved, so that a positive score has a lower false positive rate, but only at the risk of missing more of those who actually do show aberrant behavior.

SOAPP-R Cutoff Score	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ratio
Score 17 or above	.83	.65	.56	.88	2.38	.26
Score 18 or above	.81	.68	.57	.87	2.53	.29
Score 19 or above	.77	.75	.62	.86	3.03	.31

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How does the SOAPP-R help determine appropriate treatment?
The SOAPP-R should only be one step in the assessment process to determine which patients are high-risk for opioid misuse. The following discussion examines the assessment and treatment options for chronic pain patients who are at risk (high risk or medium risk) and those who are likely not at risk.

Who is at a high risk for opioid misuse? (SOAPP-R score = 22 or greater)*

Patients in this category are judged to be at a high risk for opioid misuse. These patients have indicated a history of behaviors or beliefs that are thought to place them at a higher risk for opioid misuse. Some examples of these behaviors or beliefs include a current or recent history of alcohol or drug abuse, being discharged from another physician' care because of his/her behavior, and regular noncompliance with physicians' orders. These patients may have misused other prescription medications in the past. It is a good idea to review the SOAPP-R questions with the patient, especially those items the patient endorsed. This will help flesh out the clinical picture, so the provider can be in the best position to design an effective, workable treatment plan.

Careful and thoughtful planning will be necessary for patients in this category. Some patients in this category are probably best suited for other therapies or need to exhaust other interventions prior to entering a treatment plan that includes chronic opioid therapy. Others may need to have psychological or psychiatric treatment prior to or concomitant with any treatment involving opioids. Patients in this category who receive opioid therapy should be required to follow a strict protocol, such as regular urine drug screens, opioid compliance checklists, and counseling.

Specific treatment considerations for patients in this high-risk category:

- Past medical records should be obtained and contact with previous and current providers should be maintained.
- Patients should also be told that they would be expected to initially give a urine sample for a toxicology screen during every clinic visit. They should also initially be given medication for limited periods of time (e.g., every 2-weeks).
- Ideally, family members should be interviewed and involvement with an addiction medicine specialist and/or mental health professional should be sought.
- Less abusable formulations should be considered (e.g., long-acting versus short-acting opioids, transdermal versus oral preparation, tamper-resistant medications).
- Early signs of aberrant behavior and a violation of the opioid agreement should result in a change in treatment plan. Depending on the degree of violation, one might consider more restricted monitoring, or, if resources are limited, referring the patient to a program where opioids can be prescribed under stricter conditions. If violations or aberrant behaviors persist, it may be necessary to discontinue opioid therapy.

** Note these are general ranges. Clinicians should also complement SOAPP scores with other clinical data such as urine screens and psychological evaluations.*

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Who is at a moderate risk for opioid misuse? (SOAPP-R score = 10 to 21)*

Patients in this category are judged to be at a medium or moderate risk for opioid misuse. These patients have indicated a history of behaviors or beliefs that are thought to place them at some risk for misuse. Some examples of these behaviors or beliefs are family history of drug abuse, history of psychological issues such as depression or anxiety, a strong belief that medications are the only treatments that will reduce pain and a history of noncompliance with other prescription medications. It is a good idea to review the SOAPP-R items the patient endorsed with the patient present.

Some of these patients are probably best treated by concomitant psychological interventions in which they can learn to increase their pain-coping skills, decrease depression and anxiety, and have more frequent monitoring of their compliance. They may need to be closely monitored until proven reliable by not running out of their medications early and having appropriate urine drug screens.

Additional treatment considerations for patients in this category:

- Periodic urine screens are recommended.
- After a period in which no signs of aberrant behavior are observed, less frequent clinic visits may be indicated. If there are any violations of the opioid agreement, then regular urine screens and frequent clinic visits would be recommended.
- After two or more violations of the opioid agreement, an assessment by an addiction medicine specialist and/or mental health professional should be mandated.
- After repeat violations referral to a substance abuse program would be recommended. A recurrent history of violations would also be grounds for tapering and discontinuing opioid therapy

** Note these are general ranges. Clinicians should also complement SOAPP scores with other clinical data such as urine screens and psychological evaluations.*

Who is at a low risk for opioid misuse? (SOAPP-R score < 9)*

Patients in this category are judged to be at a low risk for opioid misuse. These patients have likely tried and been compliant with many other types of therapies. They should be able to handle their medication safely with minimal monitoring. They are apt to be responsible in their use of alcohol, not smoke cigarettes, and have no history of previous difficulties with alcohol, prescription drugs, or illegal substances. This patient probably reports few symptoms of affective distress, such as depression or anxiety.

As noted previously, the SOAPP-R is not a lie detector. The provider should be alert to inconsistencies in the patient report or a collateral report. Any sense that the patient's story "doesn't add up" should lead the provider to take a more cautious approach until experience suggests that the person is reliable.

Patients in this category would be likely to have no violations of the opioid treatment agreement. These patients are least likely to develop a substance abuse disorder. Additionally, they may not require special monitoring or concomitant psychological treatment.

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Additional treatment considerations for patients in this category:

- Review of SOAPP-R questions is not necessary, unless the provider is aware of inconsistencies or other anomaly in patient history/report.
- Frequent urine screens are not indicated.
- Less worry is needed about the type of opioid to be prescribed and the frequency of clinic visits.
- Efficacy of opioid therapy should be re-assessed every six months, and urine toxicology screens and update of the opioid therapy agreement would be recommended annually.

** Note these are general ranges. Clinicians should also complement SOAPR scores with other clinical data such as urine screens and psychological evaluations.*

SAMPLE

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Appendix 9 - Pain Intensity and Interference (pain scale)

Pain Intensity and Interference (pain scale)[20]

Pain Intensity and Interference

In the last month, on average, how would you rate your pain? Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be"? [*That is, your usual pain at times you were in pain.*]

No pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

In the last month, how much has pain interfered with your daily activities? Use a scale from 0 to 10, where 0 is "no interference" and 10 is "unable to carry on any activities"?

No interference										Unable to carry on any activities
0	1	2	3	4	5	6	7	8	9	10

Interpretation of the Two Item Graded Chronic Pain Scale – This two item version of the Graded Chronic Pain Scale is intended for brief and simple assessment of pain severity in primary care settings. Based on prior research, the interpretation of scores on these items is as follows:

Pain Rating Item	Mild	Moderate	Severe
Average/Usual Pain Intensity	1–4	5–6	7–10
Pain-related interference with activities	1–3	4–6	7–10

Although pain intensity and pain-related interference with activities are highly correlated and tend to change together, it is recommended that change over time be tracked for pain intensity and pain-related interference with activities separately when using these two items.

For an individual patient, a reduction in pain intensity and improvement in pain-related interference with activities of two points is considered moderate but clinically significant improvement.

Similar pain ratings have been widely used in the Brief Pain Inventory, the Multidimensional Pain Inventory, and the Pain Severity Scale of the SF-12.

There is extensive research on the reliability, validity and responsiveness to change of these pain severity ratings, which is summarized in the following reference:

Von Korff M. Chronic Pain Assessment in Epidemiologic and Health Services Research: Empirical Bases and New Directions. Handbook of Pain Assessment: Third Edition. Dennis C. Turk and Ronald Melzack, Editors. Guilford Press, New York., In press

[20] Interagency Guideline on Opioid Dosing for Chronic Non-cancer Pain: An educational aid to improve care and safety with opioid therapy (Washington State Agency Medical Directors' Group)

Appendix 10 - Therapeutic Options for Pain Management

Therapeutic Options for Pain Management[21]

In treating pain, clinicians can avail themselves of five basic modalities of pain-management tools:

1. Cognitive-behavioral approaches
2. Rehabilitative approaches
3. Complementary and alternative therapies
4. Interventional approaches
5. Pharmacotherapy

Not all of these options are necessary or appropriate for every patient, but clinical guidelines suggest that all options should be considered every time a health care provider decides to treat a patient with chronic pain. These options can be used alone or in combinations to maximize pain control and functional gains. Only one of these options involves medications and opioids are only one of many types of medications with potential analgesic utility. Which options are used in a given patient depends on factors such as the type of pain, the duration and severity of pain, patient preferences, co-occurring disease states or illnesses, patient life expectancy, cost and the local availability of the treatment option.

Cognitive-behavioral Approaches

The brain plays a vitally important role in pain perception and in recovery from injury, illness or other conditions involving pain. Psychological therapies of all kinds, therefore, may be a key element in pain management. At the most basic level, such therapy involves patient education about disease states, treatment options or interventions, and methods of assessing and managing pain. Cognitive therapy techniques may help patients monitor and evaluate negative or inaccurate thoughts and beliefs about their pain. For example, some patients engage in an exaggeration of their condition called "catastrophizing" or they may have an overly passive attitude toward their recovery which leads them to inappropriately expect a physician to "fix" their pain with little or no work or responsibility on their part. Another way to frame this is to assess whether a patient has an internal or external "locus of control" relative to their pain. Someone with an external locus of control attributes the cause/relief of pain to external causes and they expect that the relief comes from someone else. Someone with an internal locus of control believes that they are responsible for their own well being; they own the experience of pain and recognize they have the ability and obligation to undertake remediation, with the help of others.

Some chronic pain patients have a strong external locus of control, and successful management of their pain hinges, in part, on the use of cognitive or other types of

[21] California Medical Association (Prescribing Opioids: Care amid Controversy March 2014)

therapy to shift the locus from external to internal. Individual, group or family psychotherapy may be extremely helpful for addressing this and other psychological issues, depending on the specific needs of a patient.

In general, psychological interventions may be best suited for patients who express interest in such approaches, who feel anxious or fearful about their condition, or whose personal relationships are suffering as a result of chronic or recurrent pain. Unfortunately, the use of psychological approaches to pain management can be hampered by such barriers as provider time constraints, unsupportive provider reimbursement policies, lack of access to skilled and trained providers, or a lack of awareness on the part of patients and/or physicians about the utility of such approaches for improving pain relief and overall function.

Rehabilitative Approaches

In addition to relieving pain, a range of rehabilitative therapies can improve physical function, alter physiological responses to pain and help reduce fear and anxiety. Treatments used in physical rehabilitation include exercises to improve strength, endurance, and flexibility; gait and posture training; stretching; and education about ergonomics and body mechanics. Exercise programs that incorporate Tai Chi, swimming, yoga or core-training may also be useful. Other noninvasive physical treatments for pain include thermotherapy (application of heat), cryotherapy (application of cold), counter-irritation and electroanalgesia (e.g., transcutaneous electrical stimulation). Other types of rehabilitative therapies, such as occupational and social therapies, may be valuable for selected patients.

Complementary and Alternative Therapies

Complementary and alternative therapies (CAT) of various types are used by many patients in pain, both at home and in comprehensive pain clinics, hospitals or other facilities.27 These therapies seek to reduce pain, induce relaxation and enhance a sense of control over the pain or the underlying disease. Meditation, acupuncture, relaxation, imagery, biofeedback and hypnosis are some of the therapies shown to be potentially helpful to some patients. CAT therapies can be combined with other pain treatment modalities and generally have few, if any, risks or attendant adverse effects. Such therapies can be an important and effective component of an integrated program of pain management.

Interventional Approaches

Although beyond the scope of this paper, a wide range of surgical and other interventional approaches to pain management exist, including trigger point injections, epidural injections, facet blocks, spinal cord stimulators, laminectomy, spinal fusion, deep brain implants and neuro-augmentative or neuroablative surgeries. Many of these approaches involve some significant risks, which must be weighed carefully against the potential benefits of the therapy.

Pharmacotherapy

Many types of medications can be used to alleviate pain, some that act directly on pain signals or receptors, and others that contribute indirectly to either reduce pain or improve function. For patients with persistent pain, medications may be used concurrently in an effort to target various aspects of the pain experience.

NSAIDs and Acetaminophen

Non-steroidal anti-inflammatory drugs (NSAIDs), which include aspirin and other salicylic acid derivatives, and acetaminophen, are categorized as non-opioid pain relievers. They are used in the management of both acute and chronic pain such as that arising from injury, arthritis, dental procedures, swelling or surgical procedures. Although they are weaker analgesics than opioids, acetaminophen and NSAIDs do not produce tolerance, physical dependence or addiction. Acetaminophen and NSAIDs are also frequently added to an opioid regimen for their opioid-sparing effect. Since non-opioids and opioids relieve pain via different mechanisms, combination therapy can provide improved relief with fewer side effects.

These agents are not without risk, however. Adverse effects of NSAIDs as a class include gastrointestinal problems (e.g., stomach upset, ulcers, perforation, bleeding, liver dysfunction), bleeding (i.e., antiplatelet effects), kidney dysfunction, hypersensitivity reactions and cardiovascular concerns, particularly in the elderly. The threshold dose for acetaminophen liver toxicity has not been established, although the FDA recommends that the total adult daily dose should not exceed 4,000 mg in patients without liver disease (although the ceiling may be lower for older adults).

In 2009, the FDA required manufacturers of products containing acetaminophen to revise their product labeling to include warnings of the risk of severe liver damage associated with its use. In 2014, new FDA rules went into effect that set a maximum limit of 325 mg of acetaminophen in prescription combination products (e.g. Vicodin and Percocet) in an attempt to limit liver damage and other ill effects from the use of these products. Of note, aspirin (> 325 mg/d), ibuprofen, ketoprofen, naproxen and other non-cyclooxygenase-selective NSAIDs, are listed as "potentially inappropriate medications" for use in older adults in the American Geriatrics Society 2012 Beers Criteria because of the range of adverse effects they can have at higher doses.

Nonetheless, with careful monitoring, and in selected patients, NSAIDs and acetaminophen can be safe and effective for long-term management of persistent pain.

Opioids

Opioids can be effective pain relievers because, at a molecular level, they resemble compounds, such as endorphins, which are produced naturally in the human central nervous system. Opioid analgesics work by binding to one or more of the three major types of opioid receptors in the brain and body: mu, kappa and delta receptors. The

most common opioid pain medications are called "mu agonists" because they bind to and activate mu opioid receptors. The binding of mu agonist opioids to receptors in various body regions results in both therapeutic effects (such as pain relief) and side effects (such as constipation).

Physical tolerance develops for some effects of opioids, but not others. For example, tolerance develops to respiratory suppressant effects within 5-7 days of continuous use, whereas tolerance to constipating effects is unlikely to occur. Tolerance to analgesia may develop early, requiring an escalation of dose, but tolerance may lessen once an effective dose is identified and administered regularly, as long as the associated pathology or condition remains stable.

Opioids, as a class, comprise many specific agents available in a wide range of formulations and routes of administration. Short-acting, orally-administered opioids typically have rapid onset of action (10-60 minutes) and a relatively short duration of action (2-4 hours). They are typically used for acute or intermittent pain, or breakthrough pain that occurs against a background of persistent low-level pain. Extended-release/long-acting (ER/LA) opioids have a relatively slow onset of action (typically between 30 and 90 minutes) and a relatively long duration of action (4 to 72 hours). The FDA states that such drugs are "indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate."

These agents achieve their extended activity in various ways. Some have intrinsic pharmacokinetic properties that make their effects more enduring than short-acting opioids, while others are modified to slow their absorption or to slow the release of the active ingredient. A given patient might be appropriate for ER/LA therapy only, short-acting only or a combination of an ER/LA opioid with a short-acting opioid. Note that patients may respond in very different ways to any given medication or combination of medications. One size does not fit all, and treatment is best optimized by titrating a given regimen on an individual basis. Combination products that join an opioid with a non-opioid analgesic entail the risk of increasing adverse effects from the non-opioid co-analgesic as doses are escalated, even if an increase of the opioid dose is appropriate.

In response to concerns about opioid misuse and abuse, abuse-deterrent and tamper-resistant opioid formulations have been developed. One class of deterrent formulation incorporates an opioid antagonist into a separate compartment within a capsule; crushing the capsule releases the antagonist and neutralizes the opioid effect. Another strategy is to modify the physical structure of
tablets or incorporate compounds that make it difficult or impossible to liquefy, concentrate, or otherwise transform the tablets. Although abuse-deterrent opioid formulations do not prevent users from simply consuming too much of a medication, they may help reduce the public health burden of prescription opioid abuse.

Patients who receive opioids on a long-term basis to treat pain are considered to be receiving long-term opioid analgesic therapy, which is differentiated from opioid use by

patients who have an established opioid use disorder who use an opioid (e.g. methadone) as part of their treatment program.

Potential Adverse Effects of Opioids

Although opioid analgesics (of all formulations) may provide effective relief from moderate-to-severe pain, they also entail the following significant risks:

- Overdose
- Misuse and diversion
- Addiction
- Physical dependence and tolerance
- Potentially grave interactions with other medications or substances
- Death

At the heart of much of the current controversy over the use of opioid analgesics for chronic pain are beliefs about the degree to which these pain medications are potentially addicting. Unfortunately, it is difficult to quantify the degree of addictive risk associated with opioid analgesics, either for an individual patient or the population of pain patients in general.

In this context, it is critical to differentiate addiction from tolerance and physical dependence which are common physiological responses to a wide range of medications and even to widely-consumed non-prescription drugs (e.g. caffeine). Physical dependence and tolerance alone are not synonymous with addiction. Addiction is a complex disease state that severely impairs health and overall functioning. Opioid analgesics may, indeed, be addicting, but they share this potential with a wide range of other drugs such as sedatives, alcohol, tobacco, stimulants and anti-anxiety medications.

Rigorous, long-term studies of both the potential effectiveness and potential addictive risks of opioid analgesics for patients who do not have co-existing substance-use disorders have not been conducted. The few surveys conducted in community practice settings estimate rates of prescription opioid abuse of between 4% to 26%. A 2011 study of a random sample of 705 patients undergoing long-term opioid therapy for non-cancer pain found a lifetime prevalence rate of opioid-use disorder of 35%.41 The variability in results reflect differences in opioid treatment duration, the short-term nature of most studies and disparate study populations and measures used to assess abuse or addiction. Although precise quantification of the risks of abuse and addiction among patients prescribed opioids is not currently possible, the risks are large enough to underscore the importance of stratifying patients by risk and providing proper monitoring and screening when using opioid analgesic therapy.

Particular caution should be exercised when prescribing opioids to patients with conditions that may be complicated by adverse effects from opioids, including chronic obstructive pulmonary disease (COPD), congestive heart failure, sleep apnea, current

or past alcohol or substance misuse, mental illness, advanced age or patients with a history of kidney or liver dysfunction.

In addition, opioids generally should not be combined with other respiratory depressants, such as alcohol or sedative-hypnotics (benzodiazepines or barbiturates) unless these agents have been demonstrated to provide important clinical benefits, since unexpected opioid fatalities can occur in these combination situations at relatively low opioid doses.

In addition to the potential risks just described, opioids may induce a wide range of side effects including respiratory depression, sedation, mental clouding or confusion, hypogonadism, nausea, vomiting, constipation, itching and urinary retention. With the exception of constipation and hypogonadism, many of these side effects tend to diminish with time. Constipation requires prophylaxis that is prescribed at the time of treatment initiation and modified as needed in response to frequent monitoring. With the exception of constipation, uncomfortable or unpleasant side effects may potentially be reduced by switching to another opioid or route of administration (such side effects may also be alleviated with adjunctive medications). Although constipation is rarely a limiting side effect, other side effects may be intolerable. Because it is impossible to predict which side effects a patient may experience, it is appropriate to inquire about them on a regular basis.

Patients should be fully informed about the risk of respiratory depression with opioids, signs of respiratory depression and about steps to take in an emergency. Patients and their caregivers should be counseled to immediately call 911 or an emergency service if they observe any of these warning signs.

As of January 2014, a California physician may issue standing orders for the distribution of an opioid antagonist to a person at risk of an opioid-related overdose or to a family member, friend, or other person in a position to assist a person at risk of an opioid-related overdose. A physician may also issue a standing order for the administration of an opioid antagonist to a person at risk of an opioid-related overdose to a family member, friend, or other person in a position to assist a person experiencing or reasonably suspected of experiencing an opioid overdose.

The potential of adverse effects and the lack of data about the addictive risks posed by opioids do not mean these medications should not be used. Common clinical experience and extensive literature document that some patients benefit from the use of opioids on a short or long term basis. Existing guidelines from many sources, including physician specialty societies (American Academy of Pain Medicine, The American Pain Society), various states (Washington, Colorado, Utah), other countries (Canada) and federal agencies (Department of Defense, Veterans Administration), reflect this potential clinical utility.

Recommendations from authoritative consensus documents have been summarized in concise, user-friendly formats such as: Responsible Opiate Prescribing: A Clinician's

Guide for the Federation of State Medical Boards; the 2013 Washington State Labor and Industries Guideline for Prescribing Opioids to Treat Pain in Injured Workers; and the Agency Medical Directors' Group 2010 Opioid Dosing Guideline for Chronic Non-Cancer Pain.

Methadone

Particular care must be taken when prescribing methadone. Although known primarily as a drug used to help patients recovering from heroin addiction, methadone can be an effective opioid treatment for some pain conditions. Methadone is a focus of current debate because it is frequently involved in unintentional overdose deaths. These deaths have escalated as methadone has increasingly been used to treat chronic pain.

Methadone must be prescribed even more cautiously than other opioids and with full knowledge of its highly variable pharmacokinetics and pharmacodynamics. Of critical importance is the fact that methadone's analgesic half-life is much shorter than its elimination half-life. This can lead to an accumulation of the drug in the body. In addition, methadone is metabolized by a different group of liver enzymes than most other opioids, which can lead to unexpected drug interactions.

When rotating from another opioid to methadone, extreme caution must be used when referring to equianalgesic conversion tables. Consensus recommendations suggest a 75 to 90% decrement in the equianalgesic dose from conventional conversion tables when a switch is made from another opioid to methadone.

Because the risk of overdose is particularly acute with methadone, patients should be educated about these risks and counseled to use methadone exactly as prescribed. They should also be warned about the dangers of mixing unauthorized substances, especially alcohol and other sedatives, with their medication. This should be explicitly stated in any controlled substance agreement that the patient receives, reads and signs before the initiation of treatment [...].

Although uncommon, potentially lethal cardiac arrhythmias can be induced by methadone. The cardiac health of patients who are candidates for methadone should be assessed, with particular attention paid to a history of heart disease or arrhythmias. An initial ECG may be advisable prior to starting methadone, particularly if a patient has a specific cardiac disease or cardiac risk factors or is taking agents that may interact with methadone. In addition, it is important that an ECG be repeated periodically, because QT interval prolongation has been demonstrated to be a function of methadone blood levels and/or in response to a variety of other medications.

Adjuvant Pain Medications

Although opioid medications are powerful pain relievers, in the treatment of neuropathic pain and some other centralized pain disorders such as fibromyalgia, they are of limited effectiveness and are not preferred. Other

classes of medications, however, may provide relief for pain types or conditions that do not respond well to opioids. Some of these adjuvant medications exert a direct analgesic effect mediated by non-opioid receptors centrally or peripherally. Others have no direct analgesic qualities but may provide pain relief indirectly via central or peripheral affects.

Commonly-used non-opioid adjuvant analgesics include antiepileptic drugs (AEDs), tricyclic antidepressants (TCAs) and local anesthetics (LAs). AEDs, such as gabapentin and pregabalin, are used to treat neuropathic pain, especially shooting, stabbing or knife-like pain from peripheral nerve syndromes.TCAs and some newer types of antidepressants may be valuable in treating a variety of types of chronic and neuropathic pain, including post-herpetic neuralgia and diabetic neuropathy. LAs are used to manage both acute and chronic pain. Topical application provides localized analgesia for painful procedures or conditions with minimal systemic absorption or side effects. Topical Las are also used to treat neuropathic pain. Epidural blocks with LAs, with or without opioids, play an important role in managing postoperative and obstetrical pain.

Non-Opiod Pain Management Tool by Jeremy Biggs MD MSPH

Area/Type of Pain	Treatment Options (Strongest Recommendations listed first)	When to Initiate	Population	Duration/Indication of Treatment	Cautions/MISC
Back Pain <4 weeks	Directed Exercise Program 1, 2, 3, 4, 5, 6	Within 7-10 days of injury	All ages	Life long	Consider co morbities
	Controlled Weight Loss 2	Immediately	All ages	Life long	Consider co morbidities
	Ice/Heat 2, 4, 6, 7	During the first 1-4 days	All ages	Most effective in first 1-3 days	Consider co morbidities
	Acetaminophen up to 4 g/day 1, 2, 4, 6, 8, 9	Immediately	Adults	Can be long term	Consider co morbidities
	Physical therapy 4, 6, 10, 11	After 3 weeks of conservative therapy	Adults	1-2 visits	Consider co morbidities
	NSAIDs 2, 4, 6, 9, 12	Immediately (recommended to try Acetaminophen first)	Younger adults, without any CV, Renal or GI risk factors	Short term treatment	Consider co morbidities, no CV, renal or GI risk factors
	Muscle Relaxers 4, 9, 13	Immediately	Adults	Short term treatment	Significant side effects profile, use cautions in prescribing
	Cox-2 Inhibitors 1, 2	If unable to tolerate NSAIDs and failed Acetaminophen therapy	Adults , not to be used in people with any CV risk factors	Short term treatment	Consider co morbidities, no CV risk factors
	Back School 14, 15	After 1-2 weeks of conservative therapy	Adults	For length of program	This has shown to speed return to work, but not any significance in lowering of pain scores or duration of pain.
	Tramadol/acetaminophen 2	After failing acetaminophen for 1-2 weeks	Adults	Can be long term	Consider co morbidities
	Tramadol 2	After initial acetaminophen trail	Adults	Can be long term	Consider co morbidities
	Manipulation 1, 4, 6, 16, 17, 18, 19	Most effective when used for pain <6 weeks of duration without radiculopathy	Adults	3-4 weeks of treatment has been studied. Up to 8 treatments.	Consider co morbidities, not shown to be better than other therapies. Not to be used with herniated disks
Back Pain >4 weeks	Directed Exercise Program 1, 2, 3, 4, 5, 8, 18, 19	Immediately	Adults	Life Long	Consider co morbidities
	Yoga exercises (viniyoga) 20	Immediately	Adults	Life Long, studies for 12 weekly sessions	Has been shown to be as or more beneficial than exercise in some studies.
	Controlled Weight Loss 2	Immediately	Adults	Life Long	Consider co morbidities
	Acetaminophen up to 4 g/day 1, 2, 4, 8	Immediately	Adults	Can be long term	Consider co morbidities
	NSAIDs 2, 4, 12	Immediately, recommend acetaminophen trial first. Some evidence that NSAIDs are equal with acetaminophen in chronic low back pain (21) Some	Adults with no CV, Renal or GI risk factors	Short term	Consider co morbidities, no CV, renal or GI risk factors

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		evidence that it is superior at pain control. (22)			
	Muscle Relaxers 4, 13	Immediately	Adults	Short term treatment	Significant side effects profile, use cautions in prescribing, some studies did not show any benefit after 3-4 weeks of injury
	Cox-2 Inhibitors 1, 2	If unable to tolerate NSAIDs and no CV risk factors	Adults with no CV risk factors	Short term	Consider co morbidities, no CV risk factors
	Back School 14, 15, 18	After 1-2 weeks of conservative therapy	Adults	For length of program	This has shown to speed return to work, but not any significance in lowering of pain scores or duration of pain. Swedish Back School program was studied.
	Tricyclic antidepressants 9, 23	After 3-4 weeks and failing conservative therapy, acetaminophen	Adults	As long as deemed beneficial	Have significant side effects profile, consider co morbidities
	Tramadol/acetaminophen 2	After failing acetaminophen for 1-2 weeks	Adults	Can be long term	Consider co morbidities
	Tramadol 2	After failing acetaminophen trial, co administration with acetaminophen has been shown to have more favorable results	Adults	Can be long term	Consider co morbidities
	Injections, epidural/facet joints 24, 25	After failing conservative treatment	Adults	As long as beneficial, if effective often last 1-4 months in duration, can be used to help diagnosis and evaluate for additional treatment options	Choose population according to guidelines. There are conflicting opinions on efficacy
	Physical Therapy 10, 11	Recommend starting immediately	Adults	1-2 visits	Consider co morbidities
	Message Therapy 26, 27, 28	Recommended in conjunction exercise and education	Adults	As long as beneficial has been shown to effective for up to one year, >5 visits shows better results, most studies showed results in 6-10 treatments	Some disagreement in literature, but done by licensed therapist found to be more effective
	Neuroreflexotherapy 29	Only in Chronic LBP	Adults	Undetermined	Preliminarily this has shown some effect. Requires lengthy training of practitioner to be considered effective
Neck Pain	Directed Exercise Program 1, 2, 3, 6, 30	Within 7-10 days of injury	All ages	Life long	Consider co morbidities, can add mechanical manipulation to an exercise program
	Acetaminophen 4g/day maximum 2, 6, 31	Immediately	Adults	Can be long term	Consider co morbidities

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	NSAIDs 6, 12, 31	Immediately (recommended to try Acetaminophen first)	Younger adults, without any CV, Renal or GI risk factors	Short term treatment	Consider co morbidities, no CV, renal or GI risk factors
	Physical Therapy 6	After 2 weeks of conservative treatment	Adults	1-2 visits for education, counseling of home exercise	Consider co morbidities
	Manipulation 6	Once more conservative measures fail	Adults	Best when combined with exercise	Consider co morbidites, rare instances of CVA
	IV methylprednisolone 31	Within 8 hours of injury for acute whiplash	Adults	One time treatment	Any contraindications to IV steroids.
	IM Lidocaine 31	Chronic neck pain with arm symptoms	Adults	Only a few treatments indicated	Consider co morbidities
	Muscle Relaxers 31	Immediately	Adults	Short term	Consider co morbidities
	Acupuncture 32	After failing exercise and/or acetaminophen/NSAIDs	Adults	Ideally 6 or more treatments, effects have been shown for short-term pain relief	Consider co morbidities
Headache	Directed exercise program 33	Immediately	Adults	When the HA is a result of a mechanical neck disorder	Consider co morbidities
	Acetaminophen 4g/day maximum 34	Immediately	Adults	Long term, has not been shown to be effective in migraines	Consider co morbidities
	NSAIDS 12, 35, 36	Immediately	Adults	Short term, shown to be effective in both migraine and non-migraine HAs	Consider co morbidities, not to be used with CV, renal or GI risk factors
	Triptans 36, 37	Use if unable to control HA with NSAIDs and or acetaminophen	Adults	Beneficial for migraine headaches. IM has been shown to be more effective than oral, but both are superior to placebo. Sumatriptan most studied	Consider co morbidities
	Excedrin 36	Immediately	Adults	Shown to be beneficial in Acute migraines	Consider co morbidities
	Amitriptyline 35	Immediately	Adults	Best for migraine headaches, can be started immediately	Monitor for side effects and complications of medication, can cause drowsiness
	Antidepressants (other TCAs, SNRIs, SSRIs) 38, 39	After failing conservative therapy	Adults	Migraine, tension, and mixed. Studies lasted 4-27 weeks	Independent of depression, SSRI least effective
	Antiemetics 36	With migraine associated nausea	Adults	Has been shown to help with pain and nausea with migraines	Consider co morbidities
	Anticonvulsants 40	After failing other therapies, for prevention	Adults	For prevention of migraine headache	Sodium valproate/divalproex sodium and topiramate are the best studied
	NSAIDS combined with metoclopromide 41	After failing acetaminophen	Adults	Migraine	Consider co morbidities, metoclopromide can cause dystonia. NNT 3.5
	DHE IM/SC/IV 36	After failing more conservative therapies	Adults	Have shown to help migraines, more effective in combination with antiemetics	Consider co morbidities
	Isometheptene 36	After failing more conservative	Adults	Found effective for mild-	Consider co morbidities

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		therapies		moderate migraine	
	Normal barometric oxygen therapy 42	Immediately	Adults	For use in Cluster Headaches	Unknown
	TENS 35	Immediately	Adults	Best for cervical tension headaches, mildly affective in some migraine headaches	Do not use in patients with pacemakers, cardiac conduction abnormalities, or over the carotid body or sinus
	Manipulation 35	Immediately	Adults	Best for tension, post-traumatic headache. Can be helpful in some migraine headaches	Choose population according to literature
	Acupuncture 43	As adjuvant treatment	Adults	Shown to be effective for both tension and migraine	Choose population according to literature, not effective for all
Osteoarthritis	Directed Exercise Program1, 2, 3, 6, 44	Within 7-10 days of injury	All ages	Life long	Consider co morbidities
	Controlled Weight Loss 2	Immediately	All ages	Life long	Consider co morbidities
	Acetaminophen 4g/day maximum 2, 8	Immediately first line	Adults	Can be long term	Consider co morbidities
	NSAIDs 2, 12	Immediately	Younger adults, without any CV, Renal or GI risk factors	Short term	Consider co morbidities, no CV, renal or GI risk factors
	Non-acetylated salicylates 2	Immediately	Adults	Short term	Consider co morbidities, watch for ototoxicity
	Topical capsaicin 2	Immediately	Adults	Short term	Consider co morbidities
	Intra-articular steroid injection 2, 45	Immediately	Adults	Can be long term, but if too long can consider joint replacement.	This should be considered first-line therapeutic intervention if OA is confined to a single joint.
	Cox-2 Inhibitors 1, 2	If unable to tolerate NSAIDs and failed Acetaminophen therapy	Adults , not to be used in people with any CV risk factors	Short term treatment	Consider co morbidities, no CV risk factors
	Diacerein 46, 47	After failing other therapies	Adults	Studies lasted 2 months to 3 years	Consider co morbidities, shown to have minimal pain relief
Acute Sports Injury	Ice/Heat 2	Immediately for first 1-4 days	All ages	For first 1-4 days	Instruct on timing to not cause tissue damage
	Acetaminophen 4g/day maximum 2	Immediately	Adults	Can be long term	Consider co morbidities
	NSAIDs 2, 12	Immediately, recommended to try acetaminophen first	Adults	Short term	Consider co morbidities
Neuropathic Pain	Acetaminophen 4g/day maximum 48	Immediately	Adults	Can be long term	Consider co morbidities
	Anticonvulsants 49, 50	After failing acetaminophen	Adults	Can be long term	Have a side effect profile that must be monitored. Carbamezapine and gabapentin found to most effective, some showing crabamezapine to be more

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					effective with lower NNT and higher NNH
	Systemic administration of local anesthetics 51	After failing acetaminophen	Adults	Undetermined	Can be as effective as anticonvulsants. Monitor for side effects
	Antidepressantsv34, 52	After failing acetaminophen.	Adults	Can be long term, TCAs (amitriptyline) and Venlafaxine shown to be most effective. Not shown to be effective in HIV neuropathies	Monitor for side effects, follow black box warnings. Newer SSRIs have less evidence supporting their use in neuropathic pain
Post-Herpetic Pain	Anticonvulsants 49	Immediately	Adults	While symptoms last	Can cause drowsiness
Fibromyalgia	Supervised Aerobic/Strength training exercise 53, 54, 55	Immediately, for at least 20 minutes a day 3 times a week	All ages	Life long, most studies were conducted on average for 12 weeks, 3-24 weeks.	Consider co morbidities.
	Cognitive Behavioral Therapy 54, 56	Immediately	Adults	Data showed results from 6-30 months	Works best as a multidisciplinary approach
	Amitriptyline 54, 57, 58	Immediately	Adults	While beneficial	Does have side effect profile, tolerance to effect can occur.
	Cyclobenzaprine 54, 57	Typically is after exercise, acetaminophen and amitriptyline	Adults	While beneficial	Significant side effects
	Acupuncture 54, 59, 60	After exercise and amitriptyline	Adults	While beneficial	Mild/weak evidence
	Deep tissue message 54	Immediately	Adults	While beneficial	Mild/weak evidence
	Fluoxetine 54	Typically start with exercise, acetaminophen, and amitriptyline first	Adults	While beneficial	Secondary to amitriptyline, can be used in conjunction with tricyclics
	Dual-reuptake inhibitors (SNRIs): 54	Immediately	Adults	While beneficial	Weaker evidence than previous medications
	Gabapentin 61	Immediately	Audits	While beneficial, studied over a 12 week period	Consider co morbidities
	Pregabalin 54, 62, 63	Immediately	Adults	While beneficial	Still under investigation, one study showing positive results
Dental Pain	Acetaminophen 64, 65	Immediately	All ages	As needed	Consider co morbidities
	NSAIDs 65	Immediately	Adults	As needed	Consider co morbidities
	Acupuncture 57, 66	Immediately postop	Adults	1-4 sessions	
Pelvic Pain (dysmenorrheal)	Directed exercise program 67	Immediately	All ages	Life long	Consider co morbidities
	Acetaminophen 68	During first 3 days of menstruation	Adults	While beneficial	Consider co morbidities
	NSAIDs 68, 69	During first 3 days of menstruation	Adults	While beneficial	Consider co morbidities
	Oral contraceptives 70	Immediately	Adults/Adolescents	While beneficial	Consider co morbidities, can be traditional or extended continuous cycle
	Acupuncture 71	Immediately	Adults	10 visits over 3 months	Consider co morbidities
	Chinese herbal medication 72	After other interventions	Adults	While beneficial	Not all interactions known

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					with other medications
Pelvic Pain (chronic pelvic pain)	Directed exercise program 73	Immediately	All ages	Life long	Consider co morbidities
	Medroxyprogesterone acetate 73	Immediately	Adults	Not found to be effected after 9 months	Consider co morbidities
	Goserelin 73	After failing more conservative therapies	Adults	As long as beneficial, cannot be taken longer than six months	Consider co morbidities, extensive side effects
Pelvic Pain (Endometriosis)	Danazol 74	After failing conservative therapy	Adults	For up to 6 months	Consider co morbidities, extensive side effects
	OCPs 75	Immediately	Adults	While beneficial	Consider co morbidities
	Goserelin 75	After failing more conservative therapies	Adults	While beneficial, cannot be taken for longer than six months	Consider co morbidities, extensive side effects

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Appendix 12 – Suggested Language on Naloxone for Pain Management Agreement

- I understand that "overdose" is a risk of opioid therapy which can lead to death. I understand and can recognize the signs and symptoms of overdose including respiratory depression.

- I understand that I will be prescribed naloxone because overdose is a risk of opioid therapy. I understand that naloxone is a drug that can reverse opioid overdose. I understand when and how to use naloxone.
  - I understand it is strongly encouraged to share information about naloxone with my family and friends.
  - I understand it is strongly encouraged to teach family and friends how to respond to an overdose.

PATIENT PAIN MEDICATION AGREEMENT AND CONSENT

This agreement is important for you:

- *You will have a safe and controlled pain treatment plan.*
- *Your medicines have a high potential for abuse. They can be dangerous if used in the wrong way. You need to understand the risks that come from use of pain medicines.*

Please read and make sure you understand each statement here. Here are rules about refills and health risks. Here are also reasons for stopping your pain control treatment.

I WILL:

- ☐ I will only get my pain medicine from this clinic during scheduled appointments.
- ☐ I will take my pain medicine the way that my healthcare provider has ordered.
- ☐ I will be honest with all my healthcare providers if I am using street drugs.
- ☐ I will be honest about all the medicine I use. This includes medicine from stores and herbal medicines.
- ☐ I will be honest about my full health history.
- ☐ I will tell my healthcare provider if I go to an emergency room for any reasons.
- ☐ If I get pain medicine from an emergency room, I will tell my healthcare provider.
- ☐ I will call this office if I am prescribed any new medicine.
- ☐ I will call this office if I have a reaction to any medicine.
- ☐ I will tell all other healthcare providers that I have a pain medication agreement.
- ☐ I will tell the emergency room people that I have a pain medication agreement.
- ☐ I will take drug tests and other tests when I am told to do so.
- ☐ I will go to office visits when I am told to do so.
- ☐ I will go to physical therapy when I am told to do so.
- ☐ I will go to counseling when I am told to do so.
- ☐ I will follow directions for all treatment.
- ☐ I will show up on time for all appointments.
- ☐ I will make an appointment for refills before I run out of medicine.
- ☐ I will tell my health provider if I will be out of town so that I can get my refills.
- ☐ I will get past health records from other offices when needed.
- ☐ I will deliver these records by hand if needed. I will do this within one month of being asked. I will pay for these records if needed.
- ☐ I will give permission to this clinic to talk about my treatment with pharmacies, doctors, nurses, and others who are helping me.
- ☐ I will give permission to any healthcare provider to get information from this clinic about my health and my pain treatment.
- ☐ I will take responsibility if I overdose myself accidentally or on purpose.
- ☐ I will tell my healthcare provider if I plan to become pregnant.
- ☐ I will tell my healthcare provider if I am pregnant while I am taking pain medicine.
- ☐ I will only take this medicine the way I was told to take it.

CONTINUED ON NEXT PAGE

I WILL NOT:

- ☐ I will not share or sell, or trade any of my medicine.
- ☐ I will not drink alcohol or take street drugs while I am taking pain medicine.
- ☐ I know that I cannot call the office to have my medicine refilled over the phone.
- ☐ I will not go to the emergency room or other doctors for more pain medicine or other drugs.
- ☐ I know that when I drive a car, I must be fully alert. I know that when I use machines, I must also be fully alert. Pain medicines can make me less alert. When I am taking pain medicines, I need to be sure that I am alert. I need to be sure that it is safe for me to drive a car or use a machine.
- ☐ I will not stand in high places or do anything to hurt others after I have taken pain medicine.
- ☐ I will not leave my medicine where it can be stolen or where others can take it.
- ☐ I will not leave my medicine where children can find it.
- ☐ I will not suddenly stop taking my medicine. I know that if I do this, I can have withdrawals.

WHEN USING A PHARMACY, I WILL:

- ☐ I will use the same pharmacy for all my medicines. This is the pharmacy that I have picked: _____
- ☐ I will not ask for early refills or more pain medicine, even if I lose my medicine.

I KNOW THAT

- ☐ Pain management may include other treatment. Some treatment may not include medicine.
- ☐ Pain medicine will probably not get rid of all of my pain. Pain medicine can reduce my pain so that I can do more and have a better life.
- ☐ Part of my treatment is to reduce my need for pain medicine.
- ☐ If the pain medicines work, I will continue to use them. If the pain medicine does not help me, it will be stopped.
- ☐ My medicines will not be replaced if any of these things happen: Medicine is lost. Medicine gets wet. Medicine is destroyed
- ☐ If my medicine is stolen, I might be able to get more medicine if I get a report from the police about the medicine being stolen.
- ☐ Any of my healthcare providers can find out from the California Prescription Drug Monitoring Program about any other medicines I get from any other pharmacy in California. This is called a CURES report.
- ☐ My healthcare provider may contact the drug enforcement agency, if I try to get other doctors to give me pain medicine.
- ☐ Healthcare providers may contact the drug enforcement agency if I am not honest about how I take pain medicine.
- ☐ My doctor and my clinic will help with any investigation if I am suspected of prescription drug abuse.
- ☐ I may be sent somewhere else for drug abuse or addiction help if I need it.
- ☐ Pain medicine can be addictive. This means that my body may need more and more pain medicine or that it can be hard for me to stop taking this medicine.
- ☐ If I suddenly stop using the medicine, I can get withdrawals.
- ☐ If I use too much pain medicine, I can end up with health problems. I could die.
- ☐ If I mix medicines, I could also end up with health problems. I could die.
- ☐ Here are some things that could go wrong if I use too much medicine or mix medicines:

Overdose	Addiction	Constipation	Vomiting	Sleepiness
Slower reflexes	Nausea	Difficulty with urination	Confusion	Itching
Problems with sex	Dry mouth	Depression	Trouble breathing	Death

CAUSE FOR DISMISSAL FROM THIS CLINIC

- ☐ I know that the pain medicines may be stopped if I break any part of this contract.

My signature below means that I have read this contract. I am signing this to say that I understand all of this contract.

Patient Name _____ Doctor Name _____

Patient Signature _____ Doctor Signature _____

Date: _____

Appendix 14 – Suggested Treatment Plan Using Prescription Opioids

Treatment Plan Using Prescription Opioids

Patient name: _____

Prescriber name: _____

THE PURPOSE OF THIS AGREEMENT IS TO STRUCTURE OUR PLAN TO WORK TOGETHER TO TREAT YOUR CHRONIC PAIN. THIS WILL PROTECT YOUR ACCESS TO CONTROLLED SUBSTANCES AND OUR ABILITY TO PRESCRIBE THEM TO YOU.

I (patient) understand the following (initial each):

____ Opioids have been prescribed to me on a trial basis. One of the goals of this treatment is to improve my ability to perform various functions, including return to work. If significant demonstrable improvement in my functional capabilities does not result from this trial of treatment, my prescriber may determine to end the trial.

Goal for improved function: _____

____ Opioids are being prescribed to make my pain tolerable but may not cause it to disappear entirely. If that goal is not reached, my physician may end the trial.

Goal for reduction of pain: _____

____ Drowsiness and slowed reflexes can be a temporary side effect of opioids, especially during dosage adjustments. If I am experiencing drowsiness while taking opioids, I agree not to drive a vehicle nor perform other tasks that could involve danger to myself or others.

____ Using opioids to treat chronic pain will result in the development of a physical dependence on this medication, and sudden decreases or discontinuation of the medication will lead to symptoms of opioid withdrawal. These symptoms can include: runny nose, yawning, large pupils, goose bumps, abdominal pain and cramping, diarrhea, vomiting, irritability, aches and flu-like symptoms. I understand that opioid withdrawal is uncomfortable but not physically life threatening.

____ There is a small risk that opioid addiction can occur. Almost always, this occurs in patients with a personal or family history of other drug or alcohol abuse. If it appears that I may be developing addiction, my physician may determine to end the trial.

Continued on other side.

I agree to the following (initial each):

_____ I agree not to take more medication than prescribed and not to take doses more frequently than prescribed.

_____ I agree to keep the prescribed medication in a safe and secure place, and that lost, damaged, or stolen medication will not be replaced.

_____ I agree not to share, sell, or in any way provide my medication to any other person.

_____ I agree to obtain prescription medication from one designated licensed pharmacist. I understand that my doctor may check the Utah Controlled Substance Database at any time to check my compliance.

_____ I agree not to seek or obtain **ANY** mood-modifying medication, including pain relievers or tranquilizers from **ANY** other prescriber without first discussing this with my prescriber. If a situation arises in which I have no alternative but to obtain my necessary prescription from another prescriber, I will advise that prescriber of this agreement. I will then immediately advise my prescriber that I obtained a prescription from another prescriber.

_____ I agree to refrain from the use of **ALL** other mood-modifying drugs, including alcohol, unless agreed to by my prescriber. The moderate use of nicotine and caffeine are an exception to this restriction.

_____ I agree to submit to random urine, blood or saliva testing, at my prescriber's request, to verify compliance with this, and to be seen by an addiction specialist if requested.

_____ I agree to attend and participate fully in any other assessments of pain treatment programs which may be recommended by the prescriber at any time.

I understand that ANY deviation from the above agreement may be grounds for the prescriber to stop prescribing opioid therapy at any time.

_____ _____

Patient Signature Date

_____ _____

Prescriber Signature Date

Appendix 15 – Suggested Strategies for Tapering and Weaning

Strategies for Tapering & Weaning

Strategies for tapering:

From a medical standpoint, weaning from opioids can be done safely by slowly tapering the opioid dose and taking into account the following issues:

- A decrease by 10% of the original dose per week is usually well tolerated with minimal physiological adverse effects. Some patients can be tapered more rapidly without problems (over 6 to 8 weeks).
- If opioid abstinence syndrome is encountered, it is rarely medically serious although symptoms may be unpleasant.
- Symptoms of an abstinence syndrome, such as nausea, diarrhea, muscle pain and myoclonus can be managed with clonidine 0.1 – 0.2 mg orally every 6 hours or clonidine transdermal patch 0.1mg/24hrs (Catapres TTS-1™) weekly during the taper while monitoring for often significant hypotension and anticholinergic side effects. In some patients it may be necessary to slow the taper timeline to monthly, rather than weekly dosage adjustments.
- Symptoms of mild opioid withdrawal may persist for six months after opioids have been discontinued.
- Consider using adjuvant agents, such as antidepressants to manage irritability, sleep disturbance or antiepileptics for neuropathic pain.
- Do not treat withdrawal symptoms with opioids or benzodiazepines after discontinuing opioids.
- Referral for counseling or other support during this period is recommended if there are significant behavioral issues.
- Referral to a pain specialist or chemical dependency center should be made for complicated withdrawal symptoms.

Recognizing and managing behavioral issues during opioid weaning:

Opioid tapers can be done safely and do not pose significant health risks to the patient. In contrast, extremely challenging behavioral issues may emerge during an opioid taper.

Behavioral challenges frequently arise in the setting of a prescriber who is tapering the opioid dose and a patient who places great value on the opioid he/she is receiving. In this setting, some patients will use a wide range of interpersonal strategies to derail the opioid taper. These may include:

- Guilt provocation ("You are indifferent to my suffering")
- Threats of various kinds
- Exaggeration of their actual suffering in order to disrupt the progress of a scheduled taper

There are no fool-proof methods for preventing behavioral issues during an opioid taper, but strategies implemented at the beginning of the opioid therapy are most likely to prevent later behavioral problems if an opioid taper becomes necessary.

TOOLS

Michigan Guidelines for the Use of Controlled Substances for the Treatment of Pain

Section I: Preamble

The Michigan Boards of Medicine and Osteopathic Medicine & Surgery recognize that principles of quality medical practice dictate that the people of the State of Michigan have access to appropriate and effective pain relief. The appropriate application of up-to-date knowledge and treatment modalities can serve to improve the quality of life for those patients who suffer from pain as well as reduce the morbidity and costs associated with untreated or inappropriately treated pain. The Board encourages physicians to view effective pain management as a part of quality medical practice for all patients with pain, acute or chronic, and it is especially important for patients who experience pain as a result of terminal illness. All physicians should become knowledgeable about effective methods of pain treatment as well as statutory requirements for prescribing controlled substances.

Inadequate pain control may result from physicians' lack of knowledge about pain management or an inadequate understanding of addiction. Fears of investigation or sanction by federal, state and local regulatory agencies may also result in inappropriate or inadequate treatment of chronic pain patients. Accordingly, these guidelines have been developed to clarify the Boards' position on pain control, specifically as related to the use of controlled substances, to alleviate physician uncertainty and to encourage better pain management.

The Boards recognize that controlled substances, including opioid analgesics, may be essential in the treatment of acute pain due to trauma or surgery and chronic pain, whether due to cancer or non-cancer origins. Physicians are referred to the *U.S. Agency for Health Care and Research Clinical Practice Guidelines* for a sound approach to the management of acute[1] and cancer-related pain[2]. The medical management of pain should be based on current knowledge and research and include the use of both pharmacologic and non-pharmacologic modalities. Pain should be assessed and treated promptly, and the quantity and frequency of doses should be adjusted according to the intensity and duration of the pain. Physicians should recognize that tolerance and physical dependence are normal consequences of sustained use of opioid analgesics and are not synonymous with addiction.

The Boards are obligated under the laws of the State of Michigan to protect the public health and safety. The Boards recognize that inappropriate prescribing of controlled substances, including opioid analgesics, may lead to drug diversion and abuse by individuals who seek them for other than legitimate medical use. Physicians should be diligent in preventing the diversion of drugs for illegitimate purposes.

1. Acute Pain Management Guideline Panel. Acute Pain Management: Operative or Medical Procedures and Trauma. *Clinical Practice Guideline*. AHCPR Publication No. 92-0032. Rockville, Md. Agency for Health Care Policy and Research. U.S. Department of Health and Human Resources, Public Health Service. February 1992.

2. Jacox A, Carr DB, Payne R, et al. Management of Cancer Pain. *Clinical Practice Guideline No. 9*. AHCPR Publication No. 94-0592. Rockville, Md. Agency for Health Care Policy and Research. U.S. Department of Health and Human Resources, Public Health Service. March 1994.

Physicians should not fear disciplinary action from the Board or other state regulatory or enforcement agency for prescribing, dispensing or administering controlled substances, including opioid analgesics, for a legitimate medical purpose and in the usual course of professional practice. The Board will consider prescribing, ordering, administering or dispensing controlled substances for pain to be for a legitimate medical purpose if based on accepted scientific knowledge of the treatment of pain or if based on sound clinical grounds. All such prescribing must be based on clear documentation of unrelieved pain and in compliance with applicable state or federal law.

Each case of prescribing for pain will be evaluated on an individual basis. The board will not take disciplinary action against a physician for failing to adhere strictly to the provisions of these guidelines, if good cause is shown for such deviation. The physician's conduct will be evaluated to a great extent by the treatment outcome, taking into account whether the drug used is medically and/or pharmacologically recognized to be appropriate for the diagnosis, the patient's individual needs—including any improvement in functioning—and recognizing that some types of pain cannot be completely relieved.

The Boards will judge the validity of prescribing based on the physician's treatment of the patient and on available documentation, rather than on the quantity and chronicity of prescribing. The goal is to control the patient's pain for its duration while effectively addressing other aspects of the patient's functioning, including physical, psychological, social and work-related factors. The following guidelines are not intended to define complete or best practice, but rather to communicate what the Boards consider to be within the boundaries of professional practice.

Section II: Guidelines

The Boards have adopted the following guidelines when evaluating the use of controlled substances for pain control:

1. Evaluation of the Patient

   A complete medical history and physical examination must be conducted and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting diseases or conditions, the effect of the pain on physical and psychological function, and history of substance abuse. The medical record also should document the presence of one or more recognized medical indications for the use of a controlled substance.

2. Treatment Plan

   The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychosocial function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment.

3. Informed Consent and Agreement for Treatment

   The physician should discuss the risks and benefits of the use of controlled substances with the patient, persons designated by the patient or with the patient's surrogate or guardian if the patient is incompetent. The patient should receive prescriptions from one physician and one pharmacy where possible. If the patient is determined to be at high risk for medication abuse or have a history of substance abuse, the physician may employ the use of a written agreement between physician and patient outlining patient responsibilities, including

   - urine/serum medication levels screening when requested;
   - number and frequency of all prescription refills; and
   - reasons for which drug therapy may be discontinued (i.e., violation of agreement).

4. Periodic Review

At reasonable intervals based on the individual circumstances of the patient, the physician should review the course of treatment and any new information about the etiology of the pain. Continuation or modification of therapy should depend on the physician's evaluation of progress toward stated treatment objectives, such as improvement in patient's pain intensity and improved physical and/or psychosocial function, i.e., ability to work, need of health care resources, activities of daily living and quality of social life. If treatment goals are not being achieved, despite medication adjustments, the physician should reevaluate the appropriateness of continued treatment. The physician should monitor patient compliance in medication usage and related treatment plans.

5. Consultation

The physician should be willing to refer the patient as necessary for additional evaluation and treatment in order to achieve treatment objectives. Special attention should be given to those pain patients who are at risk for misusing their medications and those whose living arrangement pose a risk for medication misuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care, monitoring, documentation and consultation with or referral to an expert in the management of such patients.

6. Medical Records

The physician should keep accurate and complete records to include

- the medical history and physical examination;
- diagnostic, therapeutic and laboratory results;
- evaluations and consultations;
- treatment objectives;
- discussion of risks and benefits;
- treatments;
- medications (including date, type, dosage and quantity prescribed);
- instructions and agreements; and
- periodic reviews.

Records should remain current and be maintained in an accessible manner and readily available for review.

7. Compliance With Controlled Substances Laws and Regulations

To prescribe, dispense or administer controlled substances, the physician must be licensed in the state and comply with applicable federal and state regulations. Physicians are referred to the Physicians Manual of the U.S. Drug Enforcement Administration and (any relevant documents issued by the state medical board) for specific rules governing controlled substances as well as applicable state regulations.

Section III: Definitions

For the purposes of these guidelines, the following terms are defined as follows:

Acute Pain

Acute pain is the normal, predicted physiological response to an adverse chemical, thermal or mechanical stimulus and is associated with surgery, trauma and acute illness. It is generally time-limited and is responsive to opioid therapy, among other therapies.

Addiction

Addiction is a neurobehavioral syndrome with genetic and environmental influences that results in psychological dependence on the use of substances for their psychic effects and is characterized by compulsive use despite harm. Addiction may also be referred to by terms such as "drug dependence" and "psychological dependence." Physical dependence and tolerance are normal physiological consequences of extended opioid therapy for pain and should not be considered addiction.

Analgesic Tolerance

Analgesic tolerance is the need to increase the dose of opioid to achieve the same level of analgesia. Analgesic tolerance may or may not be evident during opioid treatment and does not equate with addiction.

Chronic Pain

A pain state which is persistent and in which the cause of the pain cannot be removed or otherwise treated. Chronic pain may be associated with a long-term incurable or intractable medical condition or disease.

Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Physical Dependence

Physical dependence on a controlled substance is a physiologic state of neuro-adaptation which is characterized by the emergence of a withdrawal syndrome if drug use is stopped or decreased abruptly, or if an antagonist is administered. Physical dependence is an expected result of opioid use. Physical dependence, by itself, does not equate with addiction.

Pseudoaddiction

Pattern of drug-seeking behavior of pain patients who are receiving inadequate pain management that can be mistaken for addiction.

Substance Abuse

Substance abuse is the use of any substance(s) for non-therapeutic purposes or use of medication for purposes other than those for which it is prescribed.

Tolerance

Tolerance is a physiologic state resulting from regular use of a drug in which an increased dosage is needed to produce the same effect, or a reduced effect is observed with a constant dose.

Opioid Prescribing Guidelines

A PROVIDER AND COMMUNITY RESOURCE

OPG

OREGON PAIN GUIDANCE

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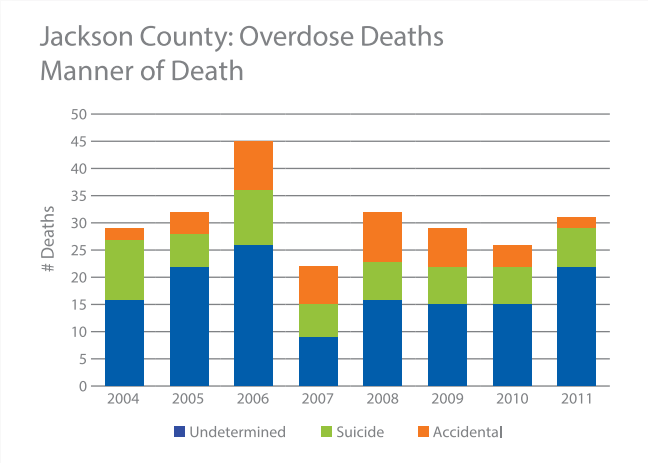
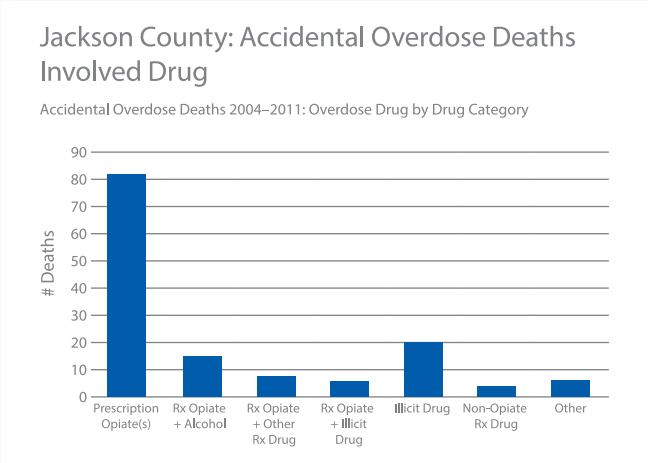
INTRODUCTION

Oregon Pain Guidance (OPG) of Southern Oregon created these guidelines in response to the alarming rise in opioid overdose deaths in our community and the need for a standard of care for the treatment of chronic pain. Each year overdoses claim scores of our citizens' lives, and the fact is the majority of these deaths are related to the misuse of medications that have been prescribed by healthcare providers. Our goal is to furnish resources to local prescribers to help them understand and adopt best practices for the treatment of complex chronic non-cancer pain (CCNP).





In 2011, more than 70 local healthcare professionals formed the OPG group. We have been meeting monthly ever since—first to brainstorm, then to create a guidance document, and now to encourage the practice of safe, scientifically based chronic pain management.

Who is the OPG? We are local professionals: nurses, prescribing healthcare providers, pharmacists, behavioral health clinicians, and administrators. We represent private medical groups, public health, coordinated care organization (CCOs), hospitals, emergency departments, the Veterans Administration, specialty care, chemical dependency treatment centers, and federally qualified health centers (FQHCs).

In addition to helping reduce the morbidity and the mortality associated with the inappropriate use of opiate drugs, we hope that by shifting the focus from opioid use to non-opioid treatments, patients will experience an overall improvement in well-being.

An OPG website has been developed that includes all of the information included in these guidelines, as well as links to important documents, community and web-based resources, and our educational video. We encourage you to use these helpful tools within your practice.

We are grateful to the members of the OPG group for all of their hard work, as well as to the subject-matter experts both within and outside our community for their invaluable assistance.

How to Use These Guidelines

SIX MAIN SECTIONS

1. Tools
2. Non-opioid treatments
3. Opioid management strategies
4. Special issues
5. Tapering
6. Difficult conversations

TREATMENT AND TAPERING FLOW SHEETS

In addition to the main sections of these guidelines there are two flow sheets, which can be laminated for easy reference. One is an overview of the assessment and treatment of CCNP. It is color coded to match the sections of this book to provide easy access to further reading on each subject matter. The other contains a flow sheet for the tapering of opioids and benzodiazepines.

If you have decided to treat your patient with opioids for CCNP, the five-step approach to treating patients with CCNP on page 6 will lead you through recommended steps for the best possible outcomes. The chronic pain checklist (Appendix L on page 59) will help assure that you have considered all of your options and complied with recommended procedures.

WEBSITE

These guidelines, plus links, videos, and other useful information can be found at **www.oregonpainguidance.org**.

VIDEO

In collaboration with AllCare Health Plan, a CCO in Grants Pass, Oregon, the Oregon Pain Guidance has created an educational video to help prescribers and their staff understand the new paradigms and best practices for the treatment of CCNP. The tools referenced in the video are included in these guidelines, either reproduced in their entirety or provided as links. For more information, you can access the video and this document at www.oregonpainguidance.org.

GUIDELINES FLOWCHART

FOR THE EVALUATION AND THE TREATMENT OF COMPLEX CHRONIC NON-CANCER PAIN

BEGIN

ASSESSMENT[1]

- Review medical history, including records from previous providers.
- Administer a physical exam to determine baseline function and pain.
- What prior attempts were made to treat this pain with non-opioid modalities?
- Is the diagnosis appropriate for opioid treatment?[2]
- Psychosocial and risk assessment:[3] risk of medication abuse (e.g. ORT, SOAPP, etc.), psychiatric co-morbidity (e.g. PHQ 2,4, etc.).
- Sleep risk assessment (e.g. S T O P B A N G or equivalent).
- It is seldom appropriate to prescribe chronic opioids on the first visit.

GREEN LIGHT

NON-OPIOID OPTIONS

- Create a plan of treatment with the patient that incorporates non-opioid interventions.
- Patient lifestyle improvement: exercise, weight loss.
- Behavioral therapies: CBT, peer-to-peer or other peer support, case management, psychotherapy, and case management.
- Physiotherapy modalities: OT, PT, passive modalities.
- Medical interventions: pharmacological, procedural, surgical.

AT EVERY VISIT

ESTABLISHED PATIENTS

- Use these guidelines with established patients.
- Reassess your patient and work your way through the flowchart.
- Continue to prescribe, or taper, as you do so.

CAUTION

OPIOID TREATMENT

PROCEED WITH CAUTION!

- Perform UDS prior to prescribing.[4]
- Check for evidence of possible misuse (PDMP).[5]
- Patient signs a material risk notice and a treatment agreement.[6]
- Agree on and document treatment goals.

AT *EVERY* VISIT!

- Assess for changes in function and pain.
- Evaluate progress on treatment goals.
- Assess for aberrant behaviors.[7]
- Assess for adverse side effects.[8]

If no improvement or if aberrant behavior or adverse side effects are observed, stop and reassess!

STOP!

STOP! REASSESS.

- If you have concerns from your visit assessment, seek help from community partners or other specialists.

CAUTION: Re-evaluate your treatment plan/seek help from specialists if you are:

- prescribing more than 120 mg MED/day without obvious functional improvement.[9]
- prescribing opioids with benzodiazepines.
- prescribing more than 40 mg of methadone/day.
- or if your patient shows signs of significant misuse or illicit drug use.

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Footnotes to the Guidelines Flowchart for the Evaluation and the Treatment of Complex Chronic Non-Cancer Pain

1 Prior to prescribing opioids, fully assess the patient for appropriateness. This is recommended whether the patient is new or established, already taking opioids, or opioid-naïve. This implies that it is unlikely you will prescribe opioids on the first visit. We recommend that the patient be informed of this by clinic support staff before meeting with the provider.

2 Certain medical conditions, such as fibromyalgia, low-back pain, chronic pelvic pain, and headaches, are relative contraindications for opioid treatment. Benzodiazepines should be used with extreme caution in combination with opioids.

3 Individuals who are at risk of misusing opioids can be predicted, to some extent, by evaluating for mental health disorders and substance abuse risk (using the Opioid Risk Tool (ORT)). There is a very strong correlation between certain psychiatric conditions and the misuse of opioids. These may include depression (PHQ-4), bipolar disorder, ADD, and PTSD.

4 Urine drug screenings (UDSs) come in many panel configurations. They can be point-of-care (POC) or lab-based. Be sure you have a plan in place to handle unexplained positive and negative tests. We recommend direct and compassionate intervention with patients upon any indication that they may be addicted to the medicines or if they are unable to use them safely.

5 The Oregon Prescription Drug Monitoring Program (PDMP) (www.orpdmp.com) provides instant feedback concerning opioid prescribing.

6 Treatment agreements come in many forms, but certain elements are considered essential. They include: utilizing one provider and one pharmacy, no early refills, and consequences for falsification, substitution, sales/distribution, use of illicit or contraindicated drugs, misuse, and disruptive behaviors. The consequences of such violations must be clearly communicated to the patient and documented in the chart. In addition to the treatment agreement, a Material Risk Notice is required by the Oregon Medical Board. Samples of both are provided in the Appendix of these guidelines.

7 Aberrant behaviors violate the treatment agreement. To identify such behaviors, monitoring tools such as UDSs, patient call-backs for pill counts, and PDMP reviews should be considered. The frequency of such monitoring should be determined by the degree of risk identified in the assessment phase. For example, if you choose to treat someone with a high ORT score, you might perform a UDS every three months, whereas for someone with a low score, only once or twice a year.

8 Frequent reassessments of improvement in pain and function are recommended. Assessment of the side effects of medication is important, too. Sexual dysfunction, endocrine dysfunction, and constipation are almost universal. Sleep disturbance, drowsiness, emotional disruption, and interactions with other medications are common.

9 Escalation of patient dose should be gradual. Increases and high doses should be tied to improvement of pain and function. Morphine equivalent doses (MEDs) can be determined by using the following online calculator: http://agencymeddirectors.wa.gov/mobile.html. Seek consultation for doses above 120mg MED. Methadone should be used cautiously. Generally, doses should not exceed 40mg/day.

TAPERING FLOWCHART

START HERE

Consider opioid taper for patients with opioid MED > 120/methadone > 40, aberrant behaviors, significant behavioral/physical risks, lack of improvement in pain and function.

Consider benzodiazepine taper for patients with aberrant behaviors, behavioral risk factors, impairment, or concurrent opioid use.

1. Explain to the patient the reason for the taper: "I am concerned…"
2. Determine rate of taper based on degree of risk.
3. If multiple drugs involved, taper one at a time (e.g., start with benzos, follow with opioids).
4. Set a date to begin, provide information to the patient, and set up behavioral supports, prior to instituting the taper. See page 26 of OPG guidelines.

OPIOID TAPER

Opioids (not methadone)

Basic principle: For longer acting drugs and a more stable patient, use slower taper. For shorter acting drugs, less stable patient, use faster taper.

1. Utilize the drug the patient is taking as the tapering medication. If you switch medications, follow MED equivalency chart and then reduce the dose by 25–50% as starting dose. Metabolic variability can be quite significant. Utilize a 90% dose reduction if switching to methadone. See dose calculator link below.
2. Decrease total daily starting dose by 5–15% per week in divided doses.
3. See patient frequently during process and stress behavioral supports. Consider UDS, pill counts, and PDMP to help determine adherence.
4. After ¼ to ½ of the dose has been reached, with cooperative patient, you can slow the process down.
5. Consider adjuvant medications: antidepressants, NSAIDs, clonidine, anti-nausea, anti-diarrhea agents.

Methadone

Basic principle: Very long half life may necessitate a more protracted tapering process. Otherwise follow opioid principles.

MED for Selected Opioids

Opioid	Approximate Equianalgesic Dose (oral and transdermal)
Morphine (reference)	**30mg**
Codeine	200mg
Fentanyl transdermal	12.5mcg/hr
Hydrocodone	30mg
Hydromorphone	7.5mg
Methadone	Chronic: 4mg†
Oxycodone	20mg
Oxymorphone	10mg

Link to Morphine Equivalent Dosing (MED) Calculator

agencymeddirectors.wa.gov/mobile.html

OPG
OREGON PAIN GUIDANCE

BENZODIAZEPINE TAPER

Basic principle: Expect anxiety, insomnia, and resistance. Patient education and support very important. Risk of seizures with abrupt withdrawal increases with higher doses. The slower the taper, the better tolerated.

1. **Slow taper:** Calculate total daily dose. Switch from short acting agent (alprazolam, lorazepam) to longer acting agent (diazepam, clonazepam). Upon initiation of taper reduce the calculated dose by 25–50% to adjust for possible metabolic variance.
2. First follow up visit 2–4 days after initiating taper to determine need to adjust initial calculated dose.
3. Reduce the total daily dose by 5–10% per week in divided doses.
4. After ¼ to ½ of the dose has been reached, with cooperative patient, you can slow the taper.
5. Consider adjunctive agents to help with symptoms: trazodone, buspirone, hydroxyzine, clonidine, antidepressants, neuroleptics, and alpha blocking agents.

1. **Rapid taper:** See the tapering guidelines on page 28 of the OPG guidance documents.

Benzodiazepine Equivalency Chart

Drug	Half-life (hrs)	Dose Equivalent
Chlordiazepoxide (Librium)	5–30 h	25mg
Diazepam (Valium)	20–50 h	10mg
Alprazolam (Xanax)	6–20 h	0.5mg
Clonazepam (Klonopin)	18–39 h	0.5mg
Lorazepam (Ativan)	10–20 h	1mg
Oxazepam (Serax)	3–21 h	15mg
Triazolam (Halcion)	1.6–5.5 h	0.5mg

Five-Step Approach to Treating Patients with Chronic Complex Non-Cancer Pain (CCNP)

The five steps listed below are recommended for treating patients with CCNP. These steps can be followed whether the patient is already receiving opioid therapy or coming to you for the first time. Implementation of the five steps may require multiple visits.

Step 1 Practice Assessment

Establish a standard policy regarding chronic pain treatment, with uniform guidelines for all patients. This will help minimize some of the challenges surrounding opiate prescribing and ensure consistent policies for all. New patients should be advised of these policies prior to receiving care. After determining your policy, it's important that you identify current patients receiving opioid therapy for more than 90 days and schedule them for a full assessment. At that time, inform them of your new policies. See Difficult Conversations on page 34.

Step 2 Patient Assessment

We've found that taking the time to learn about a patient's goals, preferences, and views about opioids can be enormously helpful. With this information, you can formulate strategies and set realistic expectations for chronic pain treatment. You'll find that many chronic pain patients are ambivalent about opioids. Some are concerned about dependency or side effects. Others may fear that opioids will be abruptly withdrawn. Keep the following in mind:

- Risk assessments such as the ORT, PHQ and the S T O P B A N G will help determine whether opioids are appropriate for a patient and, if so, guide the frequency of monitoring. See Tools section, starting on page 11.
- Careful screening can reduce the possibility of opioid misuse.
- For new patients, you should rarely prescribe opioids on the first visit, even if they come to your office with pill bottles and old records in hand. You will need time to thoroughly review each patient's history and determine the appropriateness and the safety of prescribing opioids.

Step 3 Non-Opioid Treatment

It is best to begin chronic pain treatment without opioids and instead use patient self-management strategies. (During this process, it may become clear that a patient has PTSD, depression or anxiety and would benefit from professional help.) Treating patients with chronic pain requires a care plan and consistent follow-through. During these sessions, focus on the functional goals (see Graded Pain and Function Scale on page 55), not on pain relief alone. This type of care planning is an ongoing process and may involve other members of your team. To keep other clinicians informed, documentation is necessary, including:

- Treatment goals outlining pain and functional expectations.
- Possible steps to achieve those goals.
- A schedule for periodic monitoring and what monitoring will include.
- If needed, documentation of discussion regarding the risks and the benefits of any opioid treatment.

Step 4 Patient Reassessment

Over time, you can determine if the treatment plan has improved patient functionality and reduced pain. Following non-opioid treatment, you may determine that low-dose opioid therapy will be beneficial. As you share information about opioid risks and benefits, it's important to show your patients that you understand and sympathize with the frustration and the difficulties of living with chronic pain.

It's also essential that you discuss with your patients the medical, psychosocial, and addiction risks of opioids. The Oregon Medical Board mandates that a discussion occur between providers and patients regarding risks and benefits of opioid treatment. If you choose to prescribe opioids, the Oregon Medical Board requires that a Material Risk Notice be signed by both patient and provider and that it remain on the chart.

In addition to the Material Risk Notice, many practices require that patients sign a treatment agreement. Samples of treatment agreements can be found in Appendix F, starting on page 48. Remember: Patient safety is your primary concern.

Step 5 Follow-Up Visits

Whether or not opioids are prescribed, you should schedule periodic follow-up visits to assess safety and progress toward treatment goals. Nurses, medical assistants, and other support staff can assist with follow-up monitoring by assessing progress toward treatment goals and noting problems with medications.

Periodic follow-up visits are necessary and the frequency of both visits and screening for aberrancy should be determined by degree of risk established during the assessment process. During these visits:

- Watch for opioid adverse effects, including problems with affect and sedation.
- Remember that exacerbations of chronic pain are expected and should not automatically result in a dose increase.
- Remind patients that chronic pain ebbs and flows.
- Reinforce realistic expectations of opioid benefits.
- If a patient achieves reasonable pain reduction with stable doses and makes progress toward self-management goals, you can consider less frequent follow-ups.
- Chronic pain is a chronic condition with bio-psychosocial determinants. Behavioral health collaboration is strongly recommended in the care of patients with CCNP.

It's important to avoid dose escalating when treating acute pain in a patient with chronic pain using opiates. If necessary, use a short-acting opioid for a short period of time.

TOOLS

There are various tools which can assist you in evaluating and managing your chronic pain patients. The following is a brief description, while the tools themselves can be found in the appendix.

Assessment Tools

Opioid Risk Tool (ORT)

The ORT is one of the easiest assessment tools for establishing a patient's susceptibility to misuse of opioids. Other excellent tools are available and are equally appropriate. The ORT is provided in Appendix A on page 41.

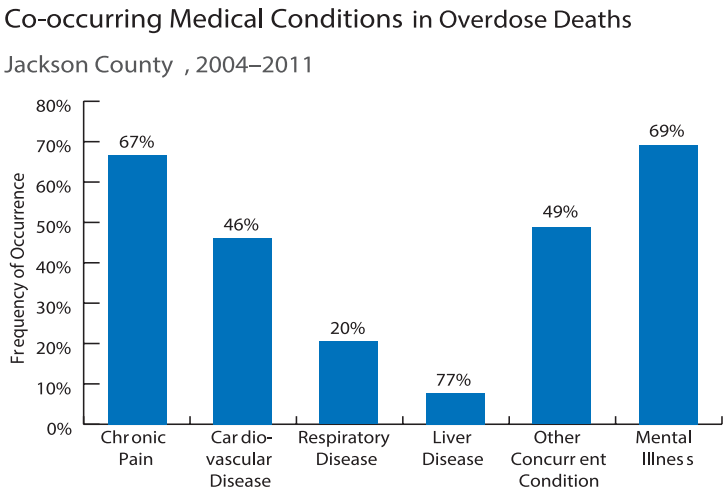
Patient Health Questionnaire (PHQ)

The correlation between mental health issues and opioid misuse is well established. The PHQ is a tool to help you identify individuals who are at risk of misusing opioids and benzodiazepines because of mental health issues. Depression and, to a lesser extent, anxiety are well-known risk factors. Bipolar disorder, PTSD, and certain personality disorders are risk factors, as well. Tools like the PHQ are especially useful when used in the context of behavioral health evaluation and/or physical exam. The PHQ-4 is a short questionnaire and can be found in Appendix B on page 42.

PTSD in the form of childhood trauma is a very common confounding problem in patients with CCNP, and in those who become dependent on benzodiazepines. Ensuring you practice "trauma-informed care" is essential to managing chronic pain patients.

A positive score, the presence of suicidal ideation, and/or your clinical judgment can indicate that further assessment is warranted. Immediate referral is recommended for those with suicidal ideation and/or a severe score. The PHQ-4 is only a screening tool and does not diagnose depression—that is done by appropriately licensed healthcare personnel.

The chart in this section represents actual Jackson County, Oregon, deaths data (2004–2011) from the Jackson County Medical Examiner's Office and illustrates the importance of screening for substance abuse and mental health disorders.



The graph on this page illustrates the importance of screening for mental illness and substance abuse. (See Assessment section of this document.) More than half of all overdose deaths, when patient documentation was obtained, included a history of either mental illness, substance abuse, or both. Almost half of all overdoses included a benzodiazepine as a co-existing factor.

Source: Medical Examiners Data, Jim Shames, MD.

S T O P B A N G

S T O P B A N G helps evaluate the risk of respiratory depression with opioids.

Snoring. **T**iredness. **O**bstruction symptoms. High blood **P**ressure **B**MI. **A**ge. **N**eck circumference. **G**ender

Pain often disrupts sleep in chronic pain patients, and the resulting insomnia may increase pain intensity and reduce the pain threshold. Narcotic administration can significantly increase the chance of obstructive sleep apnea, and must be used with caution, especially in those patients identified to have possible obstructive sleep apnea (OSA) prior to the initiation of opioid therapy. Assessment of sleep disturbances is a key metric for evaluating patient risk as well as for monitoring opioid therapy.[1]

The S T O P B A N G assessment is provided in Appendix C on page 43.

Aberrancy Screening

Urine Drug Screen (UDS)

UDS helps monitor for unexpected licit and illicit drugs that may be present in your patient's urine. UDSs should be used with every chronic pain patient as a standard part of your office policy. There are two basic types of UDS: POC testing (in office) and confirmatory (laboratory-based). See Appendix D on page 44 for Urine Drug Screening Frequently Asked Questions.

Point-of-Care (POC)

Advantages and limitations. POC tests are inexpensive and easily performed. Testing kits can be configured to your needs. Most common drugs to be included: opiates, benzodiazepines, methadone, amphetaminemethamphetamine, cocaine, THC, and oxycodone. Other tests commonly included are: PCP, barbiturates, and alcohol, but many others are often optional single tests (fentanyl, buprenorphine, for example).

Remember that these are management tools, not definitive tests to determine deception or illicit use. These tests have a fairly high rate of false negative and false positives. Their interpretation is fraught with difficulties. Understanding of metabolic pathways, cutoff levels, drug-drug interactions, and what drugs are and are not picked up on a particular test are essential to the interpretation of POC testing. Some examples:

- Hydrocodone often is not detected on the POC opioid strip
- Hydrocodone can metabolize to hydromorphone and be detected as dilaudid when in fact none was prescribed
- Diazepam metabolizes to oxazepam and can present as a drug "not prescribed"
- Clonazepam and lorazepam are sometimes not detected on the benzodiazepine screen.

1. Manchikanti L, Malla Y, Wargo BW, et al. Protocol for accuracy of point-of-care (POC) or in-office urine drug screening (immunoassay) in chronic pain patients: a prospective analysis of immunoassay and liquid chromatography tandem mass spectometry. Pain Physician Journal. 2010;13:E1-E22.

Confirmatory Lab-Based Tests

Advantages. These tests, GC-MS and LC/MS-MS, can be highly accurate, depending on the type used. For instance, LC/MS-MS testing allows for extremely low opiate cutoffs.

Limitations. Many lab-based tests are quite expensive. Use them for verification purposes. We recommend using POC testing first and, if results are unexpected, following up with a laboratory test.

Prescription Drug Monitoring Program (PDMP)

The PDMP is an online tool available to all prescribers, pharmacists, and patients in Oregon. Once a prescriber is registered with the program, he or she can learn exactly which prescription medications a patient has taken and is taking. The value of this information cannot be overstated. We strongly encourage its regular use as an assessment and management tool. Below is a sample of the kind of information that can be obtained within minutes. Without question, a query of the PDMP should be completed for each patient prior to prescribing. Prescribers can now delegate "look-up authority" to their support staff. Go to www.orpdmp.com for details.

A sample PDMP printout in provided in Appendix E on page 47.

Patient-provider Communication

Patient Treatment Agreements

Many providers wish to have conditions of treatment clearly stated in a written document prior to prescribing. Samples patient agreements are provided in Appendix F on page 48.

Material Risk Notice

The Oregon Medical Board states that a material risk notice needs to be signed by the patient whenever opioids are prescribed chronically. A Material Risk Notices is provided in Appendix G on page 53.

Medical Risks of Long-term Opioid Use – Patient Education Handout

Many patients are not familiar with the wide range of medical risks of long-term opioid use. When they understand the risks involved, they are more likely to be receptive to reducing or discontinuing opioid use. We recommend that you print out this one-page document, give it to your patient and go over with them the many risks and side effects of using opioids long term. This patient education handout is provided in Appendix H on page 54.

Assessing Progress

Graded Pain and Function Scale

The goal of opioid treatment is to improve function, both physical and emotional. Activities of daily living (ADLs) are critical to evaluate at each visit, as are other quality of life indicators This is a very simple tool to track function and pain over time.

The Graded Pain and Function Scale is provided in Appendix I on page 55.

Oswestry Low-back Pain Disability Questionnaire

A comprehensive functional assessment tool provided in Appendix J on page 56.

Opioid Dose Calculator

This tool helps calculate opioid doses and find Morphine Equivalent Doses (MED) for commonly used opioids. A sample calculator can be found at www.agencymeddirectors.wa.gov/Files/DosingCalc.xls.

Additional Assessment Tools

See Appendix K on page 58 for additional assessment tools.

NON-OPIOID OPTIONS

Treatment Comparison

Studies show that opioids are only moderately successful in relieving pain and, in fact, are inferior to sleep restoration, mindfulness training, and physical exercise in providing long-term benefit.

Any non-opioid treatment should include the following:

- Encouraging patients to resume rewarding and enjoyable activities to reduce their attention on pain.
- Asking patients to practice relaxation exercises and to apply heat or cold for counterstimulation to distract during times of pain flare-up.
- Encouraging patients to perform exercises that gradually increase flexibility, strength, and aerobic capacity.
- Encouraging patients to join facilitated group discussions concerning attitudes and beliefs about pain.
- Asking patients to think about and address unrealistic fears regarding causes and consequences of chronic pain.
- Suggesting ways that patients can change their sleep behavior so that they benefit from restorative sleep.

Reduction in Pain Intensity	Numeric Rating Scale
Physical fitness	30–60%
CBT/mindfulness	30–50%
Sleep restoration	30–40%
Opioids	<30%
Tricyclics	<30%
Anti-epileptics	<30%
Acupuncture	>10%

Source: David Tauben, MD, UW Center for Pain Relief.

Table of Non-Opioid Treatment Options

Patient Lifestyle	Physiotherapy Interventions
› Healthy sleep management › Weight reduction › Diet/nutrition › Stress reduction › Exercise	› Functional therapies — Physical therapy (PT) — Occupational therapy (OT) — Passive modalities

Behavioral Interventions	Medical Interventions
› Educational groups — Preventive — Support — Peer-to-peer/Living Well workshops — Shared medical appointments › Psychotherapy — Individual counseling — Group therapy — Cognitive behavioral therapy › Supportive care — Case management › Substance abuse treatment — Residential — Outpatient — Medication-assisted treatment referral › Trauma-informed care — PTSD screening — Domestic violence screening — Child abuse screening	› Non-opioid medications that may aid in chronic pain management — NSAIDS, acetaminophen — Tricyclic antidepressants (neuropathic pain) — Anti-epileptics (neuropathic pain) — Antidepressants (treating underlying depression) — Topical medications › Minimally invasive surgical procedures — Nerve blocks, steroid injections — Interventional treatments: ablations, restorative injections, stimulators, implantable devices — Surgical treatment › Complementary and alternative treatments — Manipulation therapy — Acupuncture

Behavioral Treatment Options

Peer-to-Peer, Living Well, and Shared Medical Appointments for Chronic Pain Patients

- Self-management classes such as Living Well with Chronic Illness workshops and other peer-to-peer groups may be offered in your community and are a valuable tool. Some clinics employ a shared-medical appointment model when treating CCNP. Patients are seen in a group setting to address health concerns surrounding chronic pain, controlled medications, and related issues.
- The Patient and Community Resources list (Appendix Q on page 64) shows local options for behavioral treatment and peer-to-peer programs.
- The previous table is a list of non-opioid treatment options you may want to consider. These same treatments can also be used with patients whom you are tapering off opioids.

Cognitive Behavioral Therapy

What is CBT?

CBT is a form of psychotherapy that emphasizes the importance of "thinking" in how we feel and what we do. Simply put: the cognitive, or thinking part of our experience, very much affects the behavioral, or action, part of our experience. Indeed, there is a causal relationship between our thinking and our feelings and behaviors. With training, we can change the way we think in order to feel and behave more comfortably and acceptably, even if the situation has not changed. CBT has an educational focus and teaches rational self-counseling skills.

What does the research say about CBT for the treatment of chronic pain?

Studies show that a patient's report of chronic pain intensity is far more about that individual's capacity to manage his or her pain than it is about stimulation of nociceptors (source: Wilbur Fordyce, PhD c 1970). Additional studies show that patients experience between 30% to 60% reduction in pain intensity by learning and applying CBT techniques (source: David Tauben, MD, UW Center for Pain Relief). This compares favorably to the estimated efficacy of 30% for chronic opioids.

What are some of the key components of CBT for patients with CCNP?

In general, CBT for chronic pain works to reduce patients' pain, distress, and pain behavior while improving their daily functioning. Components of CBT may include helping patients to decrease negative emotional responses to pain and perceptions of disability while increasing their acceptance of pain and orientation toward selfmanagement. CBT helps patients change the way they relate to pain so they can experience life more fully.

What is the goal of CBT for patients with CCNP?

Two fundamental concepts are at play. One is that a person must accept the aspects of the pain that cannot be changed, including all the difficult thoughts, feelings, and bodily sensations that come with it. The second is that this acceptance allows for the possibility of the patient opening to the pain and committing to acting in ways that make the patient feel vital and energized. Learning to accept pain to live life is often referred to as "victory by surrender."

Source: Living Beyond Your Pain by J. Dahl and T. Lundgreen, 2006

OPIOID MANAGEMENT STRATEGIES

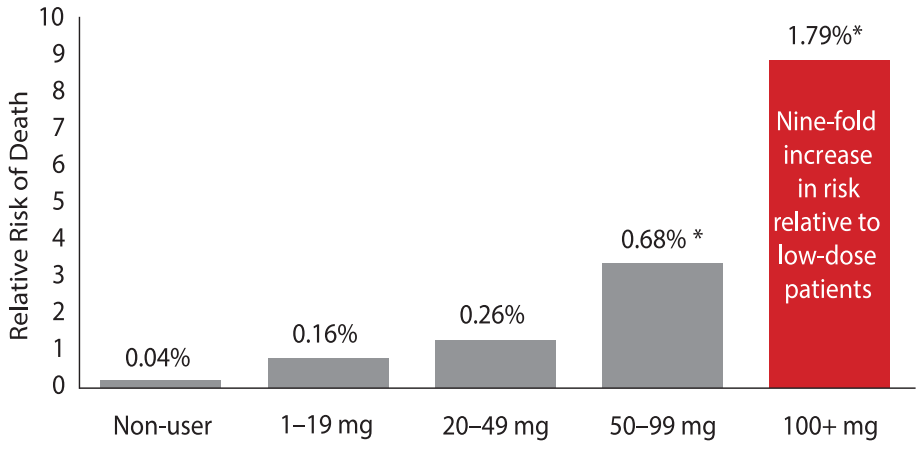
Pharmacological Treatment and Tools

This section provides tools and resources for patients who are currently being treated with opioids and for those who are at low-risk of misuse. The basic principles of using opioids for chronic pain management can be summarized by the phrase start low, go slow. Sometimes, intermittent use of a short-acting opioid may be preferable to daily, continuous use of long-acting opioids. Notice on the daily Morphine Equivalency Dose (MED) mortality graph to the right that overdose deaths increase dramatically as the MED dose gets above 50mg per day. There is little evidence that most people achieve significant improvement in CCNP with higher doses.

The Importance of MED

Significant Increment in Risk p<0.05*

Source: Dunn et al., Annals of Int. Med., 2010.



Pharmacological Considerations in Chronic Opioid Therapy (COT)

Under limited circumstances, patients can benefit from chronic opioid use. In these situations, please consider the following:

Opioid Selection

- Consider previous treatment.
- Start with short-acting medications.

Managing Doses and Expectations

- Consider a 30 percent pain reduction with narcotics alone to be a success.
- Keep total daily dose below 120mg MED.
- Refer to **www.oregonpainguidance.org** for other resources and links.

Conversion/Rotation of Opioid

- Consider alternate opioid if treatment goal is not reached.
- Some opioids will not be as effective in some patients due to variations in CYP2D6 enzymes.
- Use clinical calculators such as: http://agencymeddirectors.wa.gov/mobile.html.
- Monitor periodically according to risk group. Refer to Opioid Risk Stratification table on page 21.

Discontinuation and Tapering

Please refer to the Tapering section, beginning on page 23, for more information as well as the Tapering Flowchart on page 8.

Safety and Concerns

- Total daily acetaminophen dose should not exceed 2500mg, long term (1500mg for patients with liver disease/alcohol misuse).
- Benzodiazepines: Discontinue sedative medications to reduce risk of fatal drug-drug interactions. Discontinuing benzodiazepines can be difficult and prolonged. Residential treatment may be necessary. For additional guidance, visit: www.benzo.org.uk/manual.
- Drug-specific considerations:
  - **Hydromorphone.** Increased risk of unintentional overdose.
  - **Tramadol.** Increased risk of seizures (especially with SSRIs).
  - **Meperidine**, Neurotoxic metabolite; its use is discouraged.
  - **Methadone.** Long half-life, can prolong Q/T interval, unpredictable dosing, high-dose/lethality ratio. This drug is overrepresented in overdose statistics, and its use should be restricted. The dose for the treatment of chronic pain in an outpatient setting should be limited to 40mg per day or fewer.
  - **Fentanyl.** Not appropriate for opioid-naïve patients. Be aware that the patches can be cut, licked, and abused.
  - For geriatric patients, refer to the AGS Beers Criteria at: www.americangeriatrics.org/files/documents/beers/PrintableBeersPocketCard.pdf.
  - **Naloxone (Narcan).** Recent legislation in Oregon allows naloxone to be prescribed to individuals who may witness a friend's or relative's opioid overdose (similar to the situation with epinephrine or glucagon for emergency use by lay people). There is excellent data concerning successful overdose rescues when naloxone is available to this population. The medication is available as I.M. or intra-nasal spray. The Oregon Health Plan will pay for Naloxone. We strongly recommend that you consider prescribing naloxone to family members, friends, or others who may accompany your chronic opioid patients to appointments.

Morphine Equivalent Dose

Opioid doses above the MED of 120mg are associated with greater adverse outcomes without a corresponding increase in benefit. The Washington State Agency Medical Directors' Group has developed a calculator to help clinicians determine the total daily MED dose for their patients. This is an approximation of equivalency and caution should be exercised when adjusting medications. Methadone should be treated separately since its pharmacodynamics are widely variable.

MED for Selected Opioids

Opioid	Approximate Equianalgesic Dose (oral and transdermal)*
Morphine (reference)	30mg
Codeine	200mg
Fentanyl transdermal	12.5mcg/hr
Hydrocodone	30mg
Hydromorphone	7.5mg
Methadone	Chronic: 4mg †
Oxycodone	20mg
Oxymorphone	10mg

www.agencymeddirectors.wa.gov/Files/DosingCalc.xls

*Adapted from VA 2003 and FDA labeling
†Equianalgesic dosing ratios between methadone and other opioids are complex; thus, requiring slow, cautious conversion (Ayonrinde 2000).
Source: Interagency Guideline on Opioid Dosing for Chronic Non-Cancer Pain, 2010 Update, page 16, Table 4. Available at: www.agencymeddirectors.wa.gov/opioiddosing.asp.

Medication Refill Considerations

For more information on side effects, contraindications, and other pharmacy-related issues, consult a pharmacist. Before refilling a prescription, clinicians are encouraged to:

- Calculate and document the total morphine equivalent dose (MED); doing this can help assess the magnitude of seemingly small incremental dosage changes over time.
- Calculate and document the total acetaminophen dose (including prescribed and over the counter):
  - Acute use: Maximum single dose 1000mg, maximum daily dose 4000mg. (For elderly patients and patients with alcohol or liver disease, maximum single dose 650mg, maximum daily dose 2000mg.)
  - Long-term use (>10 days): Maximum daily dose 2500mg.
- Follow best prescribing practices:
  - Order medication in multiples of 7 days and include "to last __ days."
  - Provide specific instructions (e.g., schedule for taking).
- Ask patients about potential medication problems or concerns related to chronic opioid therapy.

Clinicians involved in treating a patient on COT are expected to clarify—both among themselves and for the patient—which clinician holds primary responsibility for prescribing.

An electronic Morphine Equivalent Dose Calculator is available at:
www.agencymeddirectors.wa.gov/Files/DosingCalc.xls

All conversions between opioids are estimates generally based on "equianalgesic dosing," or ED. Patient variability in response to these EDs can be large, due primarily to genetic factors and incomplete cross-tolerance. Additionally, methadone has unique characteristics that make it difficult to translate dose to MED.

Patient Education

All candidates for chronic opioid therapy must be informed of the side effects of opioids, your policies, and the patient's responsibilities.

See page 34, Questions to Use with Patients, to facilitate a discussion with each patient. Before prescribing opioids, the state of Oregon requires that both patient and provider sign a Material Risk Notice (see Appendix G on page 53).

In addition to the Material Risk Notice, a treatment agreement is a tool that many providers use to manage opioid treatment. If a patient refuses to sign your treatment agreement, consider that a red flag.

Treatment Agreements

There are some variations in treatment agreements, but all have the following essential components in common. Sample agreements can be found in Appendix F on page 48.

- Patients should utilize one prescriber and one pharmacy.
- No early refills and no telephone refills.
- Expect certain monitoring: pill counts, recall visits, and UDSs.
- Behavioral expectations: following advice, respectful behavior, and working toward goals.
- Consequences for concerning behaviors: substance abuse referrals, increased scrutiny, or discontinuation of opioid prescribing (without dismissal from care).

Opioid Risk Stratification

Risk stratification is based on several factors: the opioid dosage level, whether misuse of prescribed opioids has been observed, and whether there is a personal or family history of substance abuse or mental health problems. Using the table below, you can determine whether a patient is in the high-, moderate-, or low-intensity monitoring group. For moderate- and high-risk patients, more frequent monitoring is needed, and it is standard practice to use UDSs. The monitoring frequency shown in the following table is quite conservative. Many providers require more office visits for patients receiving chronic opioid prescriptions.

HIGH RISK

High-intensity monitoring (3+ visits per year)	Recommended steps
Dose: More than 100mg MED per day, or more than 40mg per day for methadone Or elevated opioid misuse/safety risk: › Opioid misuse or substance abuse › Losing prescriptions or borrowing opioids › Demanding opioids or getting opioids from multiple prescribers and pharmacies › Recurring emergency department visits	› Increase frequency of follow-up and monitoring to assess stability and to look for misuse or opioid-related problems. › At least two UDSs per year. › Pill counts at all visits.

MODERATE RISK

Moderate-intensity monitoring (2+ visits per year)	Recommended steps
Dose: 41–100mg MED per day Intermediate opioid misuse/safety risk: › Personal or family history of alcohol or drug abuse or mental health issues	› Increase frequency of monitoring if there is opioid misuse or opioid-related problems. › At least one UDS per year.

LOW RISK

Low-intensity monitoring (1+ visit per year)	Recommended steps
Dose: Less than 40mg MED per day Low opioid misuse/safety risk: › Compliant with treatment agreement › No personal or family history of alcohol or drug abuse › No mental health diagnoses	› Safe to begin or continue opioids. › Recommend UDS and pill counts. › Maintain vigilance for adverse medical and psychosocial effects. › Re-evaluate if risk factors of aberrant drug use are observed.

STOP! REASSESS.

Prescribing opioids in the following situations can be dangerous.

USE CAUTION

Re-evaluate your treatment plan and/or seek help from specialists if you:

- Prescribe more than 120mg MED per day without obvious functional improvement
- Prescribe opioids with benzodiazepines, carisoprodol, or alcohol
- Prescribe more than 40mg of methadone per day
- Or if your patient shows signs of significant misuse or illicit drug use.

TAPERING

Opioid Taper/Discontinuation

Opioid therapy should be tapered down or discontinued if any of the following situations occur:

A. The medication fails to show significant analgesia despite incremental dose increases.

B. MED is in excess of 120mg. or methadone dose is in excess of 40mg, without clear sustained improvement in pain and function.

C. Trials of different opioids at equivalent doses fail to provide adequate analgesia.

D. Significant physical risk factors are present (sleep apnea, prolonged QT, pulmonary disease, etc.).

E. Side effects of medication are interfering with quality of life.

F. Patient request.

G. Evidence of misuse, abuse, diversion, or other behavioral/psychological dysfunction.

H. Other violations of opioid agreement.

Opioids should be weaned, rather than abruptly stopped, after chronic use (30 days or greater). When opioids are being sold, injected, used in a dangerous or clearly illegal fashion, immediate discontinuation should be undertaken for patient safety and compliance with the law. Referral to a medication-assisted treatment program (methadone or buprenorphine) may be a safer and more appropriate treatment consideration under these circumstances.

Some providers have found the following dialogue useful when explaining the process to patients:

> *"Medical knowledge changes over time, and just as we have discovered that some of our recommendations today concerning the treatment of cancer or heart disease are different from 10 years ago, the same is true of the treatment of chronic pain. We now know that it can be dangerous to take large amounts of opioids every day. We have also learned that pain relief with high doses may not be any better than with lower doses of pain killers."*

General Considerations

- Some short-term increase in pain is to be expected during the tapering process. This is usually transient, and after achieving a reduced baseline dose, the patient is likely to experience decreased medication-related side effects and a reduced risk of unintentional overdose, without an increase in pain. Many times, opioids may be completely discontinued with no increase in pain, but improved function and quality of life.
- The slower the taper, the less the short-term discomfort. Educating the patient about the risks of their current regimen and what to expect as they taper off the medications is often/can be helpful.
- Some highly motivated patients prefer a rapid taper (weeks versus months). Patient preference needs to be considered in designing a tapering schedule.

- Psychosocial support is an essential component of successful medication withdrawal for patients who have been on long-term opioid therapy. Discussions about weaning are often associated with fear and anxiety about the recurrence or worsening of pain and/or the development of other withdrawal symptoms. Reassure the patient that supportive adjunctive treatment of withdrawal will be provided as needed, and may be quite helpful, but set expectations that this will not include replacement medications such as other opioids or benzodiazepines. Certain medications that treat autonomic responses, medications such as clonidine, loperamide, or hydroxyzine may be useful short-term adjuncts.
- Patient empowerment is key to success. Involve patients in the planning from the beginning. Elicit suggestions from them for healthful activities that can replace reliance on medications.
- Certain therapies, CBT and Living Well With Chronic Illness workshops, for example, can be quite helpful in supporting patients through the tapering process and beyond.
- The last part of the dosage reduction is the most difficult for the patient. This is a phenomenon that is true for many psychoactive drugs. The prescriber and the patient should anticipate this, and utilize supports that are meaningful to the patient. In motivated patients, a slow-down of the tapering process may be necessary toward the end. Liquid forms of medication can be helpful for more precise dosing and can be obtained from a compounding pharmacy.

Early Symptoms of Opioid Withdrawal

- Agitation
- Anxiety
- Muscle aches
- Increased tearing
- Insomnia
- Runny nose
- Sweating
- Yawning

Late Symptoms of Withdrawal

- Abdominal cramping
- Diarrhea
- Dilated pupils
- Goose bumps
- Nausea
- Vomiting

Initial Steps

1 Calculate the MED, review the ORT and patient progress in treatment, including UDS, PDMP, and any signs of aberrant behavior. Use that review to inform the patient concerning the appropriateness of tapering. Involve the patient in the creation of his or her new care plan.

2 Sometimes, giving the patient some time to assimilate this new information may be appropriate. Starting the taper at the follow-up visit may help to build trust.

3 Patients at risk for aberrant behaviors during the tapering process (suicidality, illicit drug use, loss of impulse control) will need referral to a behavioral health specialist prior to the initiation of the taper. It is helpful to work in parallel with such behavioral specialists during the tapering process for those patients.

4 Document your plan and the reasons for the taper in the chart note, and provide appropriate information to your patient.

5 Medication tapering may be a very stressful experience for patients. Close monitoring for aberrant behaviors is critical during this period to assure patient compliance and safety. Misuse of medications, use of illicit drugs, and "doctor shopping" may necessitate a change in approach, requiring a switch from a tapering strategy to substance abuse treatment (residential care or medication-assisted treatment, such as buprenorphine).

Slow-Taper Protocol

1 Long-acting opioids: Decrease total daily dose by 5–10% of initial dose per week.

2 Short-acting opioids: Decrease total daily dose by 5–15% per week.

3 These regimens may need to be slowed toward the end of the tapering process (see General Considerations above). Often, once 25–50% of the total dose is reached, the rate of taper can be slowed to 5% per week.

You and your patient should know the signs and symptoms of opioid withdrawal. Some of those symptoms may be present during this process, and can be controlled by support medication, psychosocial supports, or slowing the tapering process.

Remain engaged with the patient through the taper and provide psychosocial support as needed. Peer-to-Peer, Living Well With Chronic Pain workshops, group visits, CBT, and other counseling modalities may be quite helpful.

4 Consider the following adjuvants as needed:

- Antidepressants to manage irritability, sleep disturbance (e.g. Trazodone)
- Hydroxazine for insomnia and anxiety
- Anti-epileptics for neuropathic pain
- Clonidine for autonomic withdrawal symptoms such as rhinorrhea, diarrhea, sweating, tachycardia, hypertension
- NSAIDS for myalgia (e.g., Ibuprofen)
- Anti-diarrheal agents for diarrhea

Special Considerations for Methadone

Methadone withdrawal symptoms take longer to manifest due to the very long and unpredictable metabolism of the drug. Patients may be overconfident early in the tapering process, only to experience severe withdrawal over time. The same principles of opioid tapering are true for methadone; although, a more drawn-out taper may be necessary. Understanding the unique metabolic characteristics of methadone will be helpful for the patient and provider to achieve a successful dosage reduction.

Benzodiazepine Taper/Discontinuation

Benzodiazepines are potentially addictive drugs that can produce physical dependence, amnesia, emotional blunting, psychomotor retardation, and synergistic respiratory depression when combined with opioids. Anxiety, although initially ameliorated by benzodiazepines taken short term, often returns to near baseline levels with chronic use. Patients may be reluctant to taper off of these medications, fearing the exacerbation of anxiety that usually accompanies the dose reduction process.

Unlike opioids, abrupt withdrawal from high doses of benzodiazepines can result in seizures and death. The detoxification resembles alcohol withdrawal in terms of symptomatology and risk. Some patients will need medically supervised residential treatment to successfully discontinue benzodiazepines.

Withdrawal: The longer the treatment, the higher the dosage, the shorter the half-life, or the faster the taper, then the more likely the patient will have withdrawal symptoms. Even small doses of benzodiazepines taken chronically may produce uncomfortable symptoms if discontinued abruptly.

Common Benzodiazepine Withdrawal Symptoms

Anxiety	Restlessness	Agitation	Fatigue/Lethargy
Nausea	Loss of Appetite	Diaphoresis	Insomnia
Faintness/Dizziness	Tremor	Tinnitus	Increased Acuity to Stimuli
Muscle Cramps/Twitches	Poor Coordination	Difficulty Concentrating	Paresthesia
Perceptual Distortions	Depersonalization	Confusion	

General Considerations

- Some short-term increase in anxiety is to be expected during the tapering process. This is usually transient, and after achieving a reduced baseline dose, the patient is likely to experience decreased medication-related side effects without an increase in anxiety. Many times, benzodiazepines may be completely discontinued with no increase in symptoms, but improved function and quality of life.
- The slower the taper, the less the short-term discomfort. Educating the patient about the risks of their current regimen and what to expect as they taper off the medications is often/can be helpful.
- Some highly motivated patients prefer a rapid taper (weeks versus months). Patient preference needs to be considered in designing a tapering schedule.
- Psychosocial support is an essential component of successful medication withdrawal for patients who have been on long-term benzodiazepine therapy. Discussions about weaning are often associated with fear and anxiety about the recurrence or worsening of anxiety and/or the development of other withdrawal symptoms.

Reassure each patient that supportive adjunctive treatment of withdrawal will be provided as needed, and may be quite helpful, but set expectations that this will not include dangerous replacement medications. Certain non-habit forming medications that treat insomnia specifically (such as Trazodone or Hydroxyzine) might be useful.

- Patient empowerment is key to success. Involve them in the planning from the beginning. Elicit suggestions from patients for healthful activities that can replace reliance on medications.
- Certain therapies, CBT and trauma-focused care, for example, can be quite helpful in supporting patients through the tapering process and beyond.
- The last part of the dosage reduction is the most difficult for patients. This is a phenomenon that is true for many psychoactive drugs. Prescribers and patients should anticipate this, and utilize supports that are meaningful to patients. In motivated patients, a slow-down of the tapering process may be necessary toward the end. Liquid forms of medication can be helpful for more precise dosing and can be obtained from a compounding pharmacy.

Discontinuation Strategies

Here are two strategies that can be used to taper off of benzodiazepines:

1. Switching to a long-acting benzodiazepine (or phenobarbital) and taper (slow taper).
2. Simultaneous treatment with an anti-epileptic drug during taper (allows for a more rapid taper).

Special Circumstances

Consider inpatient/medical residential treatment in patients with significant substance abuse history, history of benzodiazepine overdose, seizure disorder, or illicit benzodiazepine use. Modified CIWA evaluation or MSSA (withdrawal scoring systems), can be used in such circumstances to determine the total 24-hour dose needed to begin the taper and provide safe medical monitoring of the taper process.

Slow-Taper Method

See Ashton Manual (www.benzo.org.uk/manual) for more detailed instruction on this method of reduction.

1. Calculate the dose equivalence of the current benzodiazepine into clonazepam, diazepam, or phenobarbital long-acting drug: (www.benzo.org.uk/bzequiv.htm). Provide behavioral support to the patient during the tapering process above (see General Considerations concerning opioid tapering).
2. Switch the patient from the short-acting drug to the longer-acting drug. Be conservative in estimating the long acting dose since variation in metabolism may create safety issues. Consider a reduction of 25–50% of the calculated dose for initiation of tapering.
3. See the patient for a return visit a few days after initiating the taper to be sure your dose equivalency is appropriate.
4. Reduce the total dose of the long-acting agent by 5–10% per week in divided doses.
5. Consider slowing the taper to 5% or less per week when the dose has been reduced to 25–50% of the starting dose.
6. Consider adjunctive agents to help with symptoms: trazodone, buspirone, antidepressants, hydroxyzine, clonidine, neuroleptics, and alpha blocking agents, have all been found useful.

BENZODIAZEPINE EQUIVALENCY CHART

Drug	Action Onset	Peak Onset (hrs)	Half-life (hrs)	Eliminator	Dose Equivalent
Long-Acting					
Chlordiazepoxide (Librium)	Int	2–4	5–30 (parent); 3–100 (metab)	Oxidation	10mg
Diazepam (Valium)	Rapid	1	20–50 (parent); 3–100 (metab)	Oxidation	10mg
Flurazepam (Dalmane)	Rapid	0.5–2	47–100 (metab)	Oxidation	30mg
Intermediate-Acting					
Alprazolam (Xanax)	Int	0.7–1.6	6–20 (parent)	Oxidation	0.5mg
Clonazepam (Klonopin)	Int	1–4	18–39 (parent)	Oxidation	0.5mg
Lorazepam (Ativan)	Int	1–1.5	10–20 (parent)	Conjugation	1mg
Oxazepam (Serax)	Slow	2–3	3–21 (parent)	Conjugation	15mg
Temazepam (Restoril)	Slow	0.75–1.5	10–20 (parent)	Conjugation	30mg
Short-Acting					
Triazolam (Halcion)	Int	0.75–2	1.6–5.5 (parent)	Oxidation	0.5mg

Onset of Action: Rapid = within 15 min; Intermediate = 15–30 min; Slow = 30–60 min.

Rapid-Taper Method

1. Pre-medicate 2 weeks prior to taper with valproate 500mg BID or carbamazepine 200mg every AM and 400mg every HS. Plan to continue this medication for 4 weeks post-benzodiazepines. Follow all the usual safeguards (lab testing and blood levels) when prescribing these medications.
2. Utilize concomitant behavioral supports.
3. Discontinue the current benzodiazepine treatment and switch to diazepam 2mg BID x 2 days, followed by 2mg every day x 2 days, then stop. For high doses, may begin with 5mg BID x 2 days and then continue as described.
4. Use adjuvant medications as mentioned above for rebound anxiety and other symptoms.

SPECIAL ISSUES

Special Issues and Populations

Patients with Cancer and Other Painful, Terminal Conditions (Palliative Care)

Many of the recommendations in these guidelines are not necessary or appropriate for patients dying from painful, progressive conditions. The goal for treatment of CCNP is to improve function. The goal of treatment for cancer pain, however, is to improve comfort. Escalating doses and high MEDs are not unusual in these circumstances. Care must still be taken to ensure that your medication is going to your patient, but the risk/benefit balance is not the same as it would be in a patient with the expectation of years of productive life.

Treatment of Acute Pain

Unlike chronic pain which has a large non-nociceptive component, acute pain is primarily driven by tissue injury. Adequate analgesia is the goal of acute pain treatment, but should be time limited. Experienced clinicians can judge the average length of time that an acute injury should require opioids, and a step-down approach to nonopioid analgesics is recommended after that time. The WHO analgesic ladder is a helpful guideline, and can readily be found at various Internet sites.

Opioid Use During Pregnancy

Opioid withdrawal during pregnancy is to be avoided. Keep in mind that pregnant women often feel guilty about their drug use and may under-identify the amounts being used. In these cases, the risk of withdrawal may be greater than the woman acknowledges. All women should be screened during pregnancy with UDSs as well as questionnaires such as 5Ps Screening (to assess substance abuse during pregnancy). If there is any question about opioid dependency, a professional evaluation should be undertaken. Methadone and buprenorphine are the preferred treatment options for opioid dependency during pregnancy. Be sure to ask patients about other substance abuse (such as benzodiazepines) that may require specific treatment modalities.

Metabolic changes may occur during pregnancy, so women on methadone treatment regimens may find they need a higher dose, and/or a split dose, to maintain sobriety during pregnancy.

Neonatal Abstinence Syndrome (NAS) is common after delivery when a woman is on methadone maintenance during pregnancy. Buprenorphine is associated with reduced risk of NAS, but has a somewhat lower acceptance rate for pregnant women. The use of medications during pregnancy must be individualized for each woman in terms of efficacy and safety.

Managing Patients in the Emergency Department

The Oregon Chapter of the American College of Emergency Physicians has created a set of guidelines regarding the use of opioids in a hospital emergency department (ED). Emergency medical providers (EMPs) should be supported and should not be subject to adverse consideration when respectfully adhering to these guidelines.

1 Only one medical professional should provide all opioids to treat a patient's chronic pain, to the extent possible.

2 The administration of intravenous and intramuscular opioids in the ED for the relief of acute exacerbations of chronic pain is discouraged.

3 EMPs should not provide replacement prescriptions for controlled substances that were lost, destroyed, or stolen.

4 EMPs should not provide replacement doses of methadone for patients in a methadone treatment program.

5 Long-acting or controlled-release opioids (e.g., oxycodone [OxyContin], fentanyl patches, and methadone) should not be prescribed by EMPs.

6 EMPs are encouraged to access the online Oregon PDMP.

7 EMPs should exercise caution when considering prescribing opioids for patients who present to the ED without a government-issued photo ID.

8 Primary care and pain-management physicians should make patient pain agreements accessible to local EDs and work to include a plan for pain treatment in the ED.

9 EDs should coordinate the care of patients who frequently visit the ED, using an ED care coordination program, to the extent possible.

10 EDs should maintain a list of clinics that provide primary care for patients of all payer types and should refer patients with chronic pain to primary care.

11 EDs should perform screening, brief interventions, and treatment referrals for patients with suspected prescription opiate abuse.

12 The administration of meperidine (Demerol) in the ED is discouraged.

13 For exacerbations of chronic pain, the EMP should contact the patient's primary opioid prescriber or pharmacy, if possible. If prescribing, the EMP should prescribe only enough pills to last until the patient is reasonably able to follow up with his or her primary opioid prescriber.

14 Prescriptions for opioid pain medication from the ED for acute injuries, such as fractured bones, should be in an amount that will last until the patient is reasonably able to receive follow-up care for the injury. In most cases, this should not exceed 30 tablets.

15 ED patients should be asked about past or current substance abuse prior to the EMP prescribing opioid medication for acute pain. Opiates should be prescribed with great caution in the context of substance abuse.

16 EMPs are required by law to evaluate an ED patient who reports pain to determine whether an emergency medical condition is present. If an emergency medical condition is present, the EMP is required to stabilize the patient's condition. The law allows the EMP to use his or her clinical judgment when treating pain and does not require the use of opioids.

Medication-Assisted Treatment (MAT)

- Methadone and buprenorphine/Suboxone are provided under direct medical supervision at federally sanctioned treatment programs. MAT programs operate under strict governmental oversight allowing higher doses than would be considered safe in a providers office setting.
- Buprenorphine/Suboxone is offered by a number of specially trained physicians. Training may be acquired online at www.buprenorphine.samhsa.gov/training. General information can be obtained at www.buppractice.com.
- Naltrexone by injection can be prescribed by providers without special licensure requirements.

Managing Patients on Opioids and Benzodiazepines

Managing New Patients Who Are Already on Opioids

These patients present a unique challenge as well as a unique opportunity. All of the guidelines described earlier apply to these patients, with an emphasis on evaluating prior records before prescribing. You should determine the reason why the patient left the previous practice and confirm relevant facts with the previous provider. The PDMP and a UDS will also be helpful to determine the risk of abuse or misuse. In any event, you should rarely prescribe opioids for such a patient or any other patient on the first visit. This should be part of your office policy, and your receptionist should alert patients to this when appointments are made.

Prescribing opioids for chronic pain is a long-term therapeutic commitment, so be sure you are following the right course of action at the outset.

Concomitant Benzodiazepine (All Sedative Hypnotics) and Opioid Use

Most experts advise against concomitant use of benzodiazepines (BZPs) and opioids because of the synergistic effect of those drugs, resulting in respiratory depression. In addition, the anterograde amnesia that is inevitable with benzodiazepines can lead to inadvertent overdose for predisposed individuals. Whatever the reason, 50 percent of Jackson County opioid overdoses have been associated with concomitant benzodiazepine use. It is strongly recommended that the prescriber check for BZP use by UDS as well as observe for impairment or sedation. Intensive therapy, often requiring inpatient treatment, may be necessary to achieve cessation. Many patients who are dependent on benzodiazepines have a difficult time abstaining from these drugs. Other sedative hypnotic substances (such as alcohol, barbiturates, and carisoprodol) have similar risks.

Concomitant Marijuana and Opioid Use

Medical marijuana is legal in Oregon and many other states. It is still illegal, however, under federal law. Marijuana is clearly a mind-altering drug, and though it may provide mild to moderate pain relief, it does have associated risks and side effects, such as altered response times, perceptual changes, and mood changes. In some circumstances, marijuana use may be associated with other illicit or risky drug use.

Some providers do not prescribe chronic opioids when marijuana is used (the patient has to choose which treatment modality to use). Others decide not to include THC in their UDS so as not to create a conflict with their patients. Others believe that marijuana may provide appropriate additional pain relief. Most providers in southern Oregon have chosen not to prescribe opioids for CCNP in patients who also use marijuana. (See Tapering section.)

Medications of Special Merit

Sleeping pills ("Z" drugs)

The "Z" drugs (zolpidem/Ambien, zaleplon/Sonata, eszopiclone/Lunesta) are indicated for the short term treatment of insomnia. These medications are not benzodiazepines (benzos) but they do act on the same receptors as benzos, and yet have a somewhat different risk profile (reduced seizure risk with withdrawal for example). Many of the adverse effects of benzos are true for the "Z" drugs as well: drowsiness, memory impairment, reduced coordination, depression, and sleep disturbances. Like benzodiazepines, there is an increase in all of these effects with elderly and pediatric patients. There is an increased risk of impairment and overdose when these drugs are combined with other CNS depressants like alcohol, benzos, or opioids.

It is easy to become dependent on these medications, and it can be difficult to return to normal unaided sleep when discontinuing use. There are safer medical alternatives as well as non-pharmacological options that can be explored.

When considering prescribing "Z" drugs:

- Avoid use in patients already on benzodiazepines, opioids, or stimulants.
- Use the lowest dose possible:
  - Avoid prescribing these for children and adolescents
  - Use cautiously and at the lowest doses in the elderly
- Prescribe for only short intervals

Tramadol (Ultram)

This is an opiate-like analgesic, used to treat moderate to severe pain. Many of the risks associated with opioids (respiratory depression, synergy with sedative-hypnotics) are true for tramadol. In addition, there is the risk of precipitating a seizure with this drug. Despite the fact that this is a non-scheduled drug, it can cause physical and psychological dependency with numerous reports of abuse. Here is a direct quote from the DEA:

> *Tramadol hydrochloride may induce psychic and physical dependence of the morphine-type (μ-opioid). Dependence and abuse, including drug-seeking behavior and taking illicit actions to obtain the drug are not limited to those patients with prior history of opioid dependence. The risk in patients with substance abuse has been observed to be higher. Tramadol hydrochloride is associated with craving and tolerance development. Withdrawal symptoms may occur if tramadol hydrochloride is discontinued abruptly.*

We recommend that tramadol be treated as other true opioids when evaluating risks and benefits of opioid treatment.

Carisoprodol (SOMA)

A muscle relaxant with properties and risks similar to benzodiazepines, with similar habit forming properties. Although not previously scheduled, it is now a schedule IV drug, and should be used cautiously, especially in combinations with opioids. It has been removed from the market a number of countries worldwide, and the EU recommends it not be used for the treatment of low back pain. For the purposes of these guidelines consider carisoprodol the equivalent of benzodiazepines.

Recommended Opioid Policy for Dentists

Pain management is routinely required for some dental procedures. Patients must receive respectful care and appropriate management of dental pain. Most often, dental pain management is for acute or episodic situations, requiring short-term prescribing. For many conditions, ibuprofen, acetaminophen, or a combination of the two will suffice for dental pain. In other circumstances, a very small amount of narcotic medications followed by OTCs will provide appropriate pain relief.

General Guidelines

1 Prescribe opioids cautiously to those with a substance abuse history.

2 Ask if patients are getting medications from other doctors, and use the PDMP prior to prescribing opioids whenever possible.

3 Do not prescribe opioids to patients in substance abuse treatment programs without consulting the program's medical staff.

4 Do not offer prescriptions with refills. Use caution if replacing prescriptions that were lost, destroyed, or stolen.

5 Prescribing over the phone is discouraged, especially with patients you have not met, except in rare cases involving known invasive surgery.

6 The use of non-combination opioids is discouraged.

7 If prescribing opioids, prescribe pills only in small dosages, which in most cases should not exceed 16 tablets.

8 When prescribing an antibiotic with the opioids, stipulate that the narcotic must be filled with the antibiotics at the pharmacy.

9 Inform patients how to secure medication against diversion and how to dispose of leftover medication.

10 Narcotics should not be prescribed more than seven days after the last appointment. It is strongly recommended that the patient be assessed in the clinic prior to providing narcotic (same or different narcotic) refills.

11 A second refill (same or different narcotic) request should require that the patient be assessed in the dental clinic and only be provided once a supporting diagnosis to continue with narcotic pain management is established.

12 Third refills are strongly discouraged (except in unusual clinical circumstances that are well documented, such as osteonecrosis management); consider need for chronic pain management by physician.

13 Prolonged pain management (while awaiting specialty care) should be managed by and/or coordinated with the patient's primary care provider.

DIFFICULT CONVERSATIONS

Questions to Use with Patients

Consider questions like these when evaluating patients being considered for Chronic Opioid Treatment (COT) or monitoring patients already receiving COT.

Assessment/Monitoring Questions

In the past month:

- In general, how would you say your health has been? (On a scale of poor, fair, good, very good, or excellent.)
- How much has pain interfered with your daily activities?
- Use a scale from 0 to 10, where 0 is "no interference" and 10 is "unable to do any activities."
- On average, how would you rate your pain?
- Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be."

Assessing Goals for Pain Management

- Other than reducing pain, what is the most important goal (or goals) you hope to achieve to improve your quality of life?
- To what extent have you reached this goal (or these goals)? (0-100%.)

Assessing Medication Effects and Expectations

- How well has the opioid pain medicine worked to relieve your pain?
- Have you been bothered by any side effects?
- How long do you expect to continue using this medicine?

Assessing Patient Problems and Concerns

Problems with Opioids	Concerns about Opioids
Have opioid pain medicines caused you to: Lose interest in your usual activities? Have trouble concentrating or remembering? Feel slowed down, sluggish, or sedated? Feel depressed, down, or anxious? Have difficulty thinking clearly? Have side effects that interfered with work, family, or social responsibilities? Be sleepy or less alert when driving, operating machinery, or doing things when you needed to be alert?	Have you been preoccupied with or thought constantly about using opioid pain medicine? Have you felt you could not control how much or how often you used the medicine? Have you needed to use a higher dose of the medicine to get the same effect? Have you worried that you might be dependent on or addicted to the medicine? Have you wanted to stop using the medicine or to cut down on the amount that you use? Has the medicine caused you to have problems with family, friends, or co-workers? Have family members or friends thought you might be dependent on or addicted to this medicine?

Source: Group Health, Chronic Opioid Therapy for Chronic Non-Cancer Pain Guideline, 2010.

Assessing Patient Psychological Well-Being

Over the last two weeks, how often have you been bothered by:

- Little interest or pleasure in doing things?
- Feeling down, depressed, or hopeless? (Not at all, several days, more than half the days, nearly every day.)

Recommendations for Approaching and/or Responding to Potentially Challenging Patient Interactions

It is understandable and predictable for patients to express concern when they are presented with the information that they may need to reduce or eliminate opioids for the treatment of their pain. Sometimes, their reactions become more desperate as the conversation persists. Consider:

Instead of feeling "responsible" for your patient's pain and suffering, do all you can do to remain "response-able" and show your patient you care about his or her health.

Common Patient Responses to the Request to Change Their Treatment Regimen

I First-line negotiations:

- "You are telling me to _____ (exercise, go to therapy, etc.), and I am telling you that without the pills I can't even get out of bed."
- "You know this means I won't be able to go to work. Is that what you want for me, to lose my job?"
- "Taking these pills is the only way I can manage to take care of my children. You do understand that you are taking their mother/father away from them?

II Second-line negotiations:

- "Are you saying you are just going to let me suffer?"
- "You have no idea how much pain I am in. You are not in my body."
- "This isn't fair. You promised you wouldn't reduce my medications, and you are going back on your word."

III Final desperation negotiations/threats:

- "Do you want me to go get drugs from the street?"
- "Well, I am just going to go to the ER."
- "I will be finding nother provider, who believes me and cares!"

Such patient reactions can be very challenging for healthcare providers to manage. This area of medicine is often highly anxiety-provoking, and providers are often not sure what is the right thing to do. It is even possible for highly confident providers to begin to second guess themselves when it comes to making decisions that patients won't like, but are in their safest and best interest.

Suggestions on How to Compassionately Manage Patients Who Are Confronting These Situations

I. Before going into the patient room

1. Pause and consider what value this challenging conversation will be in the service of: Perhaps it is related to your commitment to practice safe medicine, "Primum Non Nocere," to follow "best practices", to be in alignment with your colleagues, community, and/or practice in this area?
2. Be clear on the outcome you hope to reach. If possible, come up with at least three choices you can live with.
3. Decide if you will "hold the line" with your goal. Flexibility is valuable as long as it adheres to safety principles.
4. If the patient senses any hesitation and/or ambivalence from the provider, the patient is likely to move into "negotiation," which is lengthy and frustrating for all involved.

II. While in the room with the patient

1. Elicit patient perspective on how their chronic pain care is going.
2. Share your concerns, framed around safety (consider having a prepared and practiced, concise description of the new and safe opioid prescribing guidelines for CCNP).
3. Ask the patient to relay back understanding and clarify misconceptions.
4. Identify a shared goal, if possible, and/or agree to disagree on course of treatment.
5. Set limits/Clarify boundaries. Focus on what you are willing to do, rather than on what you refuse to do.

III. Helpful hints

1. Speak slowly and keep it simple. Brief explanations are usually preferred, at least for initial conversations. Avoid the temptation to overexplain or get into rationalizing/negotiating/arguing with the patient about anything.
2. If your intent is to take something away (e.g., a taper or remove a medication), consider what you will offer your patient. It may be as simple as, "I will continue to be your healthcare provider as you move through these changes." You may want to have some preprinted non-opioid treatment suggestions to give to the patient at the end of the visit. In particular, behavioral strategies such as CBT or peer-directed counseling can be very effective adjunctive treatments. It is common for patients to state that they have tried all such treatments to no avail and are not interested. The patient can have this response, and you can give the patient the information at the same time.
3. When a patient becomes highly emotional (angry, desperate, tearful, etc.) it is unreasonable that you will be able to talk the patient into being okay with the changes you are proposing. Be prepared to leave the visit with the patient who is not agreeing to the changes and/or continuing to be highly emotional. As the medical provider, it is your charge to make the changes in the name of safe medicine.
4. Suggest early on that no changes need to be made that day, allowing the patient to adjust to information and consider what supports they may need in order to embark upon the treatment changes.
5. It is highly recommended that you schedule a follow-up appointment before the patient leaves the office. The patient may state they plan to find another provider but it is still recommended that an appointment be set and that a member of the medical team call the patient the following day to check in on the patient and remind them of his or her follow-up appointment.

6 Don't be defensive, as it escalates emotion. Instead, make a statement about the patient's experience, e.g., "The look on your face tells me you are afraid. Is that the right emotion?"

7 Share control. It models collaboration and empowers patients to make changes. This is why offering three options is a good place to start, as it gives the patient control over which option to choose.

8 Focus on function not pain. This permits progress despite ongoing pain.

9 Although it may seem obvious, it is very helpful to state how much you care for your patient and that you have confidence in his or her capacity to make the changes being proposed (even if you don't have high confidence right now, it will increase the more you make these changes and see the resilience of your patient).

Examples of What You Might Want to Say to Your Patients

I. Deal with the patient's emotions by making the following types of statements:

Reflection: "You seem _____ (upset, anxious, fearful, scared), by what I have said."

Validation: "It is understandable that you feel _____ in regard to me not prescribing narcotics when that is the main reason you came in."

"This is a lot of information; it would be understandable if you were experiencing _____ (anger, fear, betrayal, anxiety, hopelessness). As your provider, it is important for me to practice within safe guidelines. Therefore, some treatment adjustments need to be made."

"I hear that you are in real pain and you have every right to _____ (find a new provider, go to the ER, get your Rx from the streets, neighbor, etc.). I hope that you will continue to let us care for you."

You don't have to agree to express understanding.

Support: "I'm sure it has been difficult to keep going to your provider and repeatedly have these tug-o-wars about a prescription"

"I am certain I do not want you to suffer. I care about your health a great deal. I am confident that you are capable of making the adjustments I have outlined."

Or, for example, instead of speaking, hand the crying patient a tissue.

II. Identify the Impasse

"It seems as though we have reached an impasse."

"You and I have very different views on how to best manage your pain."

"At this point, maybe we can agree to disagree. Why don't you take some time to consider the three options wehave discussed, and next week when you come in we will start with the adjustments."

III. Clarify boundaries

What you will do: "I'd like to be your provider and continue to help you with your pain, despite our disagreement."

"I certainly do not want you to _____ (stay in bed, not go to work, neglect children), and due to the safety reasons I have outlined, it is important for us move forward with treatment adjustments."

What you won't do: "Prescribing more of this medicine is something that is not in your best, long-term interest. It is something I feel uncomfortable with and cannot do."

"Unfortunately, I will not be able to _____ (raise the dose, give you a prescription, etc.). I would like you to consider the non-narcotic treatment options we discussed. I hear you have tried them in the past with no success, but I am asking you to consider trying them again."

IV. Manage your reactions

When you say "no," you may:

- Question your judgment, and if you are doing the right thing
- Feel you have failed as a provider
- Feel your behavior is unethical
- Feel mean, unsupportive, and uncaring

Consider looking at your patient's behavior through the lens of "physical dependence":

- It is normal for patients to have heightened emotional reactions, fear of the pain and other physical symptoms when they face opioid withdrawal.
- It is the role of the provider to take charge and safely guide the patient's treatment.

V. Learn to soothe yourself

Breathe. Self-talk. Talk to a colleague who shares your philosophy of pain management.

Gather strength from your core beliefs.

Let your values and core principles of practicing good and safe medicine guide your practice. This will ease your way as you embark on these challenging conversations with your patients.

Potentially Challenging Conversations

As OPG guidelines are implemented, potentially challenging patient conversations may arise.

1 Introducing the new guidelines to new and existing patients.

a "After having reviewed your medical record and gathering some further information, let me start by telling you about some of the things we can offer you (non-opioid treatments)."

b "For safety reasons, I rarely prescribe controlled substances on the first visit (or on the first appointment when a patient has a new request for controlled substances).

c "I would like to offer you some new information we have about treating complex, chronic pain with opioids. Would that be okay with you?" (If patient refuses, suggest that you do so on the next visit. Let the patient have some control over this scary situation for them.)

d. After evaluating a patient and finding some risk of opioid misuse: "Your level of risk limits our treatment choices. We still have some good options and I would like to share some of the things we can offer you for your chronic pain. Would now be a good time?"

2 Compassionate refusal of opioid prescriptions to new patients and existing patients requesting an increase in dose.

a. "Would you be interested in learning some new information about using opioids for chronic complex pain?"

b. "Due to recent information on the safety and effectiveness of using opioids for treating chronic pain, unfortunately, I am not able to offer that medication at this time."

3 The need to reduce or stop opioids (with the intent of keeping the patient in the practice):

a. "I have just shared with you a lot of information. It would be understandable if you were having a strong reaction…(pause)… can you tell me what you are the most concerned about right now?" (You may be surprised by the answer: Don't assume you know.)

b. "It has come to my attention that these medications (or these doses of medications) are not a safe choice for you at this time. Would this be a good time to discuss ways we could work together to begin reducing your dose safely?"

Further Resources

Below are links to websites that offer ideas on how to effectively talk to your patients on this topic:

www.scopeofpain.com/tolls-resources

www.agencymeddirectors.wa.gov/guidelines.asp

www.cdc.gov/primarycare/materials/opioidabuse/index.html

www.supportprop.org/index.html

APPENDICES

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OPIOID RISK TOOL (ORT)

MARK EACH BOX THAT APPLIES	Female	Male
Family history of substance abuse		
Alcohol	☐ 1	☐ 3
Illegal drugs	☐ 2	☐ 3
Prescription drugs	☐ 4	☐ 4
Personal history of substance abuse		
Alcohol	☐ 3	☐ 3
Illegal drugs	☐ 4	☐ 4
Prescription drugs	☐ 5	☐ 5
Age between 16 and 45 years	☐ 1	☐ 1
History of preadolescent sexual abuse	☐ 3	☐ 0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	☐ 2	☐ 2
Depression	☐ 1	☐ 1
Scoring Totals		

ADMINISTRATION

› On initial visit

› Prior to opioid therapy

SCORING (RISK)

0–3 = low

4–7 = moderate

≥8 = high

PHQ-4: THE FOUR-ITEM PATIENT HEALTH QUESTIONNAIREFOR ANXIETY AND DEPRESSION

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous, anxious or on edge	0	1	2	3
Not being able to stop or control worrying	0	1	2	3
Feeling down, depressed or hopeless	0	1	2	3
Little interest or pleasure in doing things	0	1	2	3
TOTALS				

Total score is determined by adding together the scores of each of the 4 items.
Scores are rated as normal (0-2), mild (3-5), moderate (6-8), and severe (9-12).
Total score ≥3 for first 2 questions suggests anxiety.
Total score ≥3 for last 2 questions suggests depression.

Reprinted with permission from Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. Psychosomatics. 2009;50(6):613-21. From *Principles of Neuropathic Pain Assessment and Management*, November 2011.

S T O P B A N G

Screening for Obstructive Sleep Apnea

Ask your patient to answer the following questions to determine if he or she is at risk of obstructive sleep apnea.

S (snore)	Have you been told that you snore?	YES	NO
T (tired)	Are you often tired during the day?	YES	NO
O (obstruction)	Do you know if you stop breathing, or has anyone witnessed you stop breathing while you are asleep?	YES	NO
P (pressure)	Do you have high blood pressure, or are you on medication to control high blood pressure?	YES	NO

If the patient answered *yes* to two or more questions on the STOP portion, he or she is at risk of obstructive sleep apnea.

To find out if the patient is at moderate to severe risk of obstructive sleep apnea, he or she should complete the BANG questions below.

B (BMI)	Is your body mass index greater than 28?	YES	NO
A (age)	Are you 50 years old or older?	YES	NO
N (neck)	Are you a male with a neck circumference greater than 17 inches, or a female with a neck circumference greater than 16 inches.	YES	NO
G (gender)	Are you a male?	YES	NO

The more questions the patient answers yes to, the greater his or her risk of having moderate to severe obstructive sleep apnea.

URINE DRUG SCREENINGS (UDS) FAQ

Using UDS to Monitor Opioid Therapy for Complex Chronic Non-Cancer Pain

The purpose of drug testing is to identify aberrant behavior, undisclosed drug use and/or abuse, and to verify compliance with treatment. If a decision has been made to prescribe opioids for chronic non-cancer pain, the prescriber should get a baseline UDS prior to prescribing and periodically thereafter. The frequency of such testing can be determined by risk stratification based upon screening tools already mentioned in this document (page 19 and Appendix A). Risk determination may change over time as you get to know the patient better, so clinical judgment is critical in determining an appropriate testing schedule. Often explaining the need for routine UDS can lead to a beneficial discussion between provider and patient concerning risky concomitant substance use.

Prior to drug testing, the prescriber should inform the patient of the reason for testing, frequency of testing and consequences of unexpected results. This gives the patient an opportunity to disclose drug use and allows the prescriber to modify the drug screen for the individual circumstances and more accurately interpret the results.

Q Drug screening implies that I don't trust my patients. How do I get around this?

A A self-report of drug use has limited validity, and monitoring behavior alone can fail to detect problems revealed by UDTs. Creating a UDS policy in advance and applying it consistently to all patients on opioids may help de-stigmatize the testing. Inform patients that drug testing is a routine procedure for all patients starting or maintained on opioid therapy and it is an important tool for monitoring the safety of opioid therapy. Possible language for explaining to patient includes:

- Ensures my capacity to provide treatment for your pain while balancing the need for safety."
- Provides critical information needed to assess the success of your therapy."
- Prescription medications are a common form of treatment for chronic pain. However, each person reacts differently to them. UDS enables us to identify individual risks related to your medications and avoid problems."
- Our clinic uses 'universal precautions' in opioid prescribing, which includes UDS. This is the same as wearing gloves on all patients when drawing blood."

Q Can I tell whether my patient has taken the dose of opioid(s) I prescribed?

A No. It is very difficult to correlate urine drug concentration with a patient's dose. UDS can detect the parent drug and/or its metabolite(s) and demonstrate recent use of prescribed drugs and illegal substances. However, it CANNOT determine the amount of drug used and when the last dose was taken, nor can it identify the source of the drug.

Q My patient says he is a "high metabolizer" and that is why the expected drug is not found in the urine. Is this possible?

A A small percentage of persons are ultrarapid metabolizers. They metabolize specific drugs more rapidly than typical patients. It would be rare to take an opioid as prescribed and have a totally negative UDS. It is important that you use testing that is specific to the medication of interest and with cutoff thresholds that are extremely low.

Q How do I deal with marijuana?

A This is a complex issue. Marijuana is currently classified as a Schedule I drug by the DEA. For that reason, many providers will not prescribe opioids to patients using cannabis. Other providers reference State "Medical Marijuana" laws (http://apps.leg.wa.gov/RCW/default.aspx?cite=69.51A&full=true) and feel comfortable prescribing opioids to cannabis users. Some providers adopt a "don't ask, don't tell" policy, and request the lab to remove marijuana from the UDS so that positive results are not seen. Do your homework and create an office policy. Then disclose this policy to your patients.

Q Would short-acting opioids show up in UDS?

A Urine testing typically has a 1- to 3-day window of detection for most drugs depending on dose and individual differences in drug metabolism. Short-acting opioids can be detected if the lab removes the cutoff concentration so that the presence of lower concentrations is detected. If the laboratory uses LC/MS/MS, then it will have a lower limit of detection (LOD) with less interference.

Q Why confirm results?

A Immunoassays used in drug screening can cross-react with other drugs and vary in sensitivity and specificity. Thus, confirmation with a more accurate method may be required for clinical decision making. Confirmatory drug testing (GC/MS or LC/MS/MS) of the original specimen is recommended for unexpected results, or in cases where patients are known to be high risk. However, on occasion, even confirmatory testing requires expert assistance for interpretation. Consider consultation with the lab before discussing/confronting the patient with unexpected test results and discontinuing opioid therapy.

Q Should I use temperature and adulteration strips?

A It depends. Drug testing for clinical compliance, unlike employment testing, does not require a strict "chain-of-custody" However, if tampering is a concern, the specimen should be monitored for temperature and/or adulterants. Normal human urine should have a temperature between 90°F – 100°F, pH between 4.5 – 8.5 and creatinine >20 mg/dL. Be aware that there are multiple websites and devices devoted to getting a "clean" urine drug screen.

Q Should I perform a drug screen on every visit for patients using opioids for chronic pain?

A No. Random screening based on the frequency recommended in the guideline should suffice for most patients. Those patients who you feel require drug screening on every visit, are perhaps not candidates for chronic opioid therapy.

Risk Category	UDS Frequency	Recommended Drug Panel to Test
Low Risk by ORT (1 or more/year)	Periodic (e.g. up to 1/year)	Drug you are prescribing if not listed Amphetamines Opiates Cocaine Benzodiazepines Alcohol Barbiturates Oxycodone Methadone Fentanyl Marijuana Testing for all drug classes may not be necessary, depending on clinical situation.
Moderate Risk by ORT (2 or more/year)	Regular (e.g. up to 2/year)	
High Risk by ORT (3 or more/year) or opioid doses >120 mg MED/d	Frequent (e.g. up to 2+/year)	
Aberrant Behavior (lost prescriptions, multiple requests for early refills, opioids from multiple providers, unauthorized dose escalation, apparent intoxication, etc.)	At time of visit (Address aberrant behaviors in person, not by telephone)	

Consideration

Typically, the initial (screening) drug test uses an immunoassay method to identify the presence of a drug (presumptive positive). Because of cross reactivity and different sensitivity and specificity between immunoassays, a second confirmatory test is required unless result is expected or the patient has disclosed drug use. Confirmatory drug tests use gas chromatography/mass spectrometry or liquid chromatography/tandem mass spectrometry (GC/MS or LC/MS/MS) to verify a presumptive positive result.

Contact the laboratory director, toxicologist or a certified Medical Review Officer (MRO) in your area for questions about drug testing or result.

If a point of care (POC) test is used, contact technical support from the manufacturer for questions.

UDS Results

Interpreting UDS results can be challenging, especially when the parent drug can be metabolized to other commonly prescribed drugs. The table on the next page may aid prescribers when interpreting UDS results. The following UDS results should be viewed as a "red flag," requiring confirmation and intervention:

- Negative for opioid(s) you prescribed
- Positive for drug (benzodiazepines, opioids, etc) you did NOT prescribe or have knowledge of
- Positive for amphetamine or methamphetamine
- Positive for alcohol
- Positive for cocaine or metabolites

If a confirmatory drug test substantiates a "red flag" result AND is positive for prescribed opioid(s):

- Prescriber should consider a controlled taper and a referral to an addiction specialist or drug treatment program depending on the circumstances.
- Prescriber should consider extraneous circumstance such as duration of action of the drug and timing of last dose. Consultation with your laboratory's pharmacologist may be useful. Discontinuing prescribing and substance abuse referral should be considered. Prescriber should stop prescribing opioid(s) and consider a referral to an addiction specialist or drug treatment program depending on the circumstances.

PRESCRIPTION DRUG MONITORING PROGRAM (PDMP)

Health Information Designs Inc.

Oregon Query Report

Date: 02/06/13
Page#: 1

Patient Rx History Report

PURPLE LARA

Search Criteria: Last Name 'purple' and First Name 'lara' and D.O.B. = '06/17/32' and Address = '' and Request Period = '06/01/11' to '02/06/13' - 1 out of 1 Recipients Selected.

Patients that match search criteria

00000234 PURPLE LARA, DOB 06/17/32; 111-9090 COMMODO ST, DONALD OR 97020

Fill Date	Product, Str, Form	Qty	Pt ID	Prescriber	Written	RX#	Pharm
06/30/2011	LORAZEPAM 0.5 MG TABLET	3.000	00000234	0006	02/28/2011	4004882	0001
06/30/2011	ACETAMINOPHEN-COD #3 TABLET	90.000	00000234	0007	04/15/2011	4005028	0001
06/30/2011	ALPRAZOLAM 0.25 MG TABLET	90.000	00000234	0008	06/16/2011	4005208	0001
06/30/2011	ZOLPIDEM TARTRATE 5 MG TABLET	36.000	00000234	0006	[illegible]/28/2011	4004882	0001
06/30/2011	HYDROCODON-ACETAMINOPH 7.5-500	360.000	00000234	0009	[illegible]/30/2011	4005247	0001
06/29/2011	HYDROCODON-ACETAMINOPH 7.5-750	180.000	00000234	0001	04/1[illegible]/2011	4005015	0001
06/29/2011	ZOLPIDEM TARTRATE 10 MG TABLET	135.000	00000234	000[illegible]	06/[illegible]8/2011	4005244	0001
06/28/2011	HYDROCODON-ACETAMINOPHEN 5-500	120.000	00000234	000[illegible]	[illegible]/19/2011	4005128	0001
06/27/2011	ZOLPIDEM TARTRATE 10 MG TABLET	90.000	00000234	[illegible]02	04/16/2011	4005027	0001
06/25/2011	ZOLPIDEM TARTRATE 10 MG TABLET	90.000	00000234	000[illegible]	04/16/2011	4005027	0001
06/24/2011	HYDROCODON-ACETAMINOPH 7.5-750	180.000	00000234	0001	06/23/2011	4005229	0001

Prescribers for prescriptions listed

0001 KNOPF, GREGORY M MD; GRESHAM TROUTDALE FAM. MED. CTR., [illegible]00 SW 257TH AVENUE, PO BOX 730, TROUTDALE OR 97060
0002 LOVATO, KIMBERLY K; 641 SE MILLER AVE, DALLAS OR [illegible]338
0003 BEAMAN, DOUGLAS NEAL MD; 501 NORTH GRAHAM, SUITE 2[illegible] PORTLAND OR 97227
0004 THOMAS, STEPHEN JOHN MD; 17600 SW ALEXANDER [illegible] ALOHA OR 97006
0005 HILL, TIMOTHY A MD; CENTER FOR ORTHOPEDIC, [illegible]200 [illegible] NEW ROAD, SUITE 200, BEND OR 97701
0006 VRANNA, LEE E MD; 1135 WHISKEYTOWN [illegible]RT, REDDING [illegible] 96001
0007 COLLINS, DAVID MCAVLEY MD; SHERIDAN MEDICAL C[illegible]TER, 222 S.E. JEFFERSON, SHERIDAN OR 97378
0008 MA, HAIYUN E (MSN); JUNCTION CITY [illegible]DICAL [illegible]LINIC, 355 WEST THIRD AVE., JUNCTION CITY OR 97448
0009 SHORTZ, ROGER WILLIAM MD; 3065 RICH[illegible] PARKWAY, SUITE 102, RICHMOND CA 94806

Pharmacies that dispensed prescriptions listed

0001 AMERIPHARM, INC; DBA MEDVANTX PHARMACY SERVICES, 2503 E 54TH ST. N, SIOUX FALLS SD 57104,

Patients that match search criteria

00000234 PURPLE LARA, DOB 06/17/32; 111-9090 COMMODO ST, DONALD OR 97020

Report Disclaimers:

The Oregon PDMP makes no claims, promises, or guarantees about the accuracy, completeness, or adequacy of the contents of this report, and expressly disclaims liability for errors and omissions in the contents of this report. The records herein are based on information submitted by pharmacies. Records in this report should be verified with the patient before any clinical decisions are made or actions are taken. Access to the record of an individual who is not a patient under the care of the person accessing the record is not permitted by law.

Sample

PATIENT TREATMENT AGREEMENTS

Sample 1. Controlled Substance Agreement

Why an agreement? The medication we are prescribing has the potential to provide much benefit, but it also can do harm to you or others. Misuse of pain medications is becoming a large problem in our community. We are doing our part to ensure that our prescriptions are taken as directed. We also want to protect you and inform you concerning the uses and abuses of this medication.

What are the Benefits of opiate treatment? Opiates, also called opioids, provide relief from pain and a sense of well-being. They can allow you to perform activities that you might otherwise find limiting due to pain.

What are the risks of opioid treatment? Opioids produce physical dependency with prolonged use. That means that you may experience discomfort if you discontinue these medications abruptly after taking them for over a few weeks. Some individuals have a hard time remaining medication free after being on long term opioids for that reason.

Opioids may decrease your ability to breathe deeply. This is especially true when they are combined with other sedating drugs like alcohol and some tranquilizers. This can lead to accidental overdose deaths.

Less serious side effects may include: constipation, decrease in sexual interest and performance, weight gain, sleepiness, urination difficulties, and itchiness. As with any medication, there is the rare possibility of a severe allergic reaction.

Some people are at risk of abusing these medications and may feel compelled to take them for their pleasurable effect. Therefore we are obliged to provide safeguards to protect you from these potential risks.

What are those safeguards? Our clinic has the following regulations for all patients taking long-term opioids; we will not prescribe these medications for chronic use without first:

› Obtaining all pertinent medical records
› Obtaining a urine drug screening (UDS)
› Reviewing your medical condition and past history
› Having a signed agreement between a clinician and yourself outlining the expectations of both parties.

What can I expect from the clinic? Our clinic agrees to provide you with appropriate doses of medication in a timely fashion and on an ongoing basis as long as there are no contraindications. You will be treated respectfully and professionally.

What does the clinic expect from me? The clinic expects all patients will agree to the following:

› Agree to have only one prescriber of opioids and use only one pharmacy.
› Bring their pill bottles to every clinic visit.
› Have a valid phone number available to our staff, and to respond within 24 hours to the clinic if asked.
› Agree to random urine drug screenings and random pill counts.
› Agree to a chemical dependency or other specialist consultation should your provider feel that would be appropriate.
› Allow open communication between this clinic and other providers concerning the use of these medications.
› Advise other treatment providers of the medication you are taking and to inform this clinic of any health care emergencies requiring pain or anxiety treatment.
› Agree to treat our staff respectfully and courteously.

Suggestions for safely handling your prescription: These medications can be dangerous if combined with other sedating substances. These medications are sought after by drug abusers. Therefore we ask that you follow these suggestions to provide safety for you and your medications:

- Keep all medicines in a safe, preferably locked container, out of sight and out of the reach of children.
- Never share these medicines with others. Never take other people's pain medications.
- Avoid drinking alcohol while taking these medicines.
- Never combine these medications with other opioids or benzodiazepines (tranquilizers like Ativan, Xanax,Valium or Klonopin) unless advised to by your provider.
- Never use illicit drugs while using these medications.
- Be aware that opioids may affect your judgment and driving skills, particularly when your dose is increasing.

How will I obtain my refills? The clinic's policy on refills is:

- Refill prescriptions will only be written at a clinic visit. Therefore refills will not take place over the phone, through the mail, or by calling the pharmacist.
- All dosage changes will occur at the next clinic visit.
- Lost or stolen medications may not be refilled until the next scheduled visit.

Will this medication relieve my pain? It is unrealistic to expect opioids to relieve all discomfort. We hope to reduce your pain so that you can regain function; that is to allow you to enjoy activities that you participated in prior to the onset of your pain. We will continue to ask that you participate in activities that improve your ability to perform daily activities. We may, in the course of your treatment, ask you to exercise, attend classes, or see a specialist of our choosing.

What are the consequences of not following these agreements? Your clinician has agreed to provide you with these medications as long as necessary, but also has the obligation to protect you and the community from abuse of these substances. In the event of suspected misuse, your provider may insist on a referral to a specialist in the assessment and treatment of drug dependency, or may immediately discontinue prescribing. Lack of improvement in function or to achieve adequate pain control may also necessitate the discontinuing of opioid medications.

I will receive my prescriptions at the following pharmacy only:

Name and phone: _____

I agree to allow the following health care facilities to share information (including any pertinent mental health, drug or alcohol history or conditions) with my provider, and to allow my health care provider to freely share pertinent health care information with these facilities for the purpose of coordinating my medical care.

Facility: _____

Facility: _____

Facility: _____

Facility: _____

By signing below I am agreeing to abide by the conditions of this agreement.

Patient's signature: _____ **Date** _____

Person obtaining the consent: _____ **Date** _____

Sample 2. Patient/Clinic Agreement for the use of Controlled Substances

Your provider has prescribed _____ for _____ (diagnosis).
To continue receiving this medication from your provider, you are expected to follow the policies below. If you do not follow them, your provider may decide to stop prescribing the medication for you.

1 You are expected to take the medication as directed by your clinician, and to make your medication last until the next scheduled appointment. We expect our patients to be responsible for their prescriptions. You should never give any of your medications to someone else. We will not fill requests for lost or stolen prescriptions or medications.

2 Refills for controlled substances will only be done by appointment at the clinic. We will not fill requests for controlled substances by phone, after hours, or on weekends. We expect our patients to plan ahead to upcoming vacations, weekends and holidays and make a timely appointment if a prescription will need to be filled early.

3 By signing below you agree to submit urine or blood as requested by your provider for random drug screens. You also agree to have a working phone number where clinic staff can reach you within 24 hours. That number is _____. You agree to update the clinic anytime you move or change your phone number.

4 You agree to bring your pill bottles to each regular visit.

5 Any patient who receives controlled substances from La Clinica on an ongoing basis is expected to receive these prescriptions only from our organization. If you receive additional medicines for an unanticipated injury or condition, and these are not prescribed by a La Clinica provider, you are required to call the clinic the next business day, advise us of the situation and release records of the encounter to La Clinica.

6 While taking narcotics or other controlled substances you are expected to refrain from misusing or abusing other drugs which could alter consciousness, impair judgment, or cause addiction, including, alcohol, marijuana, methamphetamine, or other illegal drugs. If you in any way use these medications to harm yourself, you will no longer receive them at this clinic.

7 You may be required to seek treatments or consultations you have to pay for yourself.

8 In addition to taking pain relief medication, you are expected to comply with your clinician's other recommendations for improving your pain relief, or ability to function.

9 We require you to use only one pharmacy for your refills. Your pharmacy is _____. If you decide to change pharmacies you must advise us immediately.

10 You authorize, by your signature below, any employee of La Clinica to call any other health care provider, including Emergency Department staff and pharmacies, to obtain information regarding the prescription of any substance.

Your signature acknowledges you have received a copy of this agreement.

Patient Signature _____ Date _____

Print Name _____ Medical Record Number _____

The use of narcotics poses risks to patients. By prescribing _____ to you, we expect the following improvements:

_____ Increased ability to exercise

_____ Lose weight

_____ Increased ability to participate in family activities

_____ Able to go shopping

_____ Increased ability to do housework

_____ Able to return to work

OR _____

Alternatives to taking _____ include: _____

In addition to taking _____ to reduce your chronic pain, you are expected to:

_____

Your allergies are: _____

The following is not necessarily a complete list of the side effects of pain medicines, but common side effects include:

_____

BRAIN Sleepiness, difficulty thinking, confusion, slow reflexes. It is possible to be convicted of driving under the influence (DUI) if you drive while using prescribed medication.

LUNG Difficulty breathing or slowed breath rate to the point you stop breathing.

STOMACH Nausea, vomiting. Constipation can be severe.

SKIN Itching, rash.

GENITO-URINARY Difficulty urinating. These drugs reduce interest in and ability to perform sexual activities.

ALLERGY Potential for allergic reaction.

TOLERANCE With long term use, an increasing amount of the same drug may be needed to achieve the same effect.

PHYSICAL DEPENDENCE/WITHDRAWAL: Physical dependence develops within 3-4 weeks when taking these drugs. If they are stopped abruptly, symptoms of withdrawal may occur. Withdrawal can be extremely difficult and last a long time. Use of all controlled substances needs to be slowly tapered off under the direction of your prescriber.

ADDICTION: This refers to the abnormal behavior directed toward acquiring or using drugs in a non-medically necessary manner. People with a history of alcohol or drug abuse are at increased risk.

Avoid medications or substances which increase drowsiness or limit the ability to think clearly, react quickly, or which decrease your rate of breathing. Talk to your provider before taking any of these medications, even if you can buy them over the counter.

I understand these risks and agree to accept them. I will let my prescriber know of any problems or side effects I am having with this medication.

Name (print) _____ Signature _____ Date _____

Sample 3. Patient Treatment Agreement

I, _____ (patient receiving chronic pain medications), agree to correctly use pain medications prescribed for me as part of my treatment for chronic pain. I understand that these medications may not get rid of my pain but may decrease the pain and increase the level of activity that I am able to do each day. I understand that the Pain Management Clinic will deal with my chronic pain and will not deal with any of my other medical conditions.

I understand that (name) will be my pain management provider and the only provider who will be ordering medications for my chronic pain.

I understand that I have the following responsibilities (initial each item you agree to):

_____ I will only take medications at the amount and frequency prescribed.

_____ I will not increase or change how I take my medications without the approval of my pain management provider.

_____ I will not ask for refills earlier than agreed. I will arrange for refills ONLY during regular office hours. I will make the necessary arrangements before holidays and weekends.

_____ I will get all pain medications only at one pharmacy. I will let my pain management provider know if I change pharmacies. **Pharmacy** _____ **Phone Number** _____

_____ I will allow my pain management provider to provide a copy of this agreement to my pharmacy.

_____ I will not ask for any pain medications or controlled substances from other providers and will let my pain management provider know of all medications I am taking, including non-legal drugs.

_____ I understand that other physicians should not change doses of my pain medications made by another provider.

_____ I will notify the Pain Management Clinic of any changes to my pain medications made by another provider.

_____ I will let my other health care providers know that I am taking these pain medications and that I have a pain management agreement.

_____ In event of an emergency, I will give this same information to emergency department providers.

_____ I will allow my pain management provider to discuss all my medical conditions and treatment details with pharmacists, physicians, or other health care providers who provide my health care for purposes of care coordination.

_____ I will inform my pain management provider of any new medications or medical conditions.

_____ I will protect my prescriptions and medications. I understand that lost or misplaced prescriptions will not be replaced.

_____ I will keep medications only for my own use and will not share them with others. I will keep all medications away from children.

In addition, I will do the following (initial each box):

_____ I must make an appointment with a drug and alcohol counselor and bring proof of following my treatment plan. Contact number is 1-800-562-1240).

_____ I must take a drug test test _____ (frequency).

_____ I agree to pill counts to prove I am using my medications correctly.

_____ If I fail a drug test, I will take the drug test _____ (frequency).

_____ If I fail a drug test, I will be referred to Medicaid's Patient Review and Coordination Program that restricts me to certain providers, such as a primary doctor. (http://maa.dshs.wa.gov/PRR)

_____ If I sell my narcotics, my name will be referred to the DSHS fraud unit.

_____ If I fail all of the above, I will be discharged from your care with no notice.

Should any of the above not show good faith efforts and my providers feel they can no longer prescribe my pain medications in a safe and effective way, I may be notified and discharged from their care.

I agree to use only the following providers. I will notify my physician of any changes in my health care and/or changes in my providers.

Provider: _____ **Clinic:** _____ **Phone:** _____

Provider: _____ **Clinic:** _____ **Phone:** _____

Patient Signature: _____ **Provider Signature:** _____

MATERIAL RISK NOTICE

This will confirm that you, _____, have been diagnosed with the following condition(s) causing you chronic intractable pain: _____.

I have recommended treating your condition with the following controlled substances: _____.

In addition to significant reduction in your pain, your personal goals from therapy are: _____.

Alternatives to this therapy are: _____.

Additional therapies that may be necessary to assist you in reaching your goals are: _____.

Notice of Risk: The use of controlled substances may be associated with certain risks such as, but not limited to:

Central Nervous System: Sleepiness, decreased mental ability, and confusion. Avoid alcohol while taking these medications and use care when driving and operating machinery. Your ability to make decisions may be impaired.

Cardiovascular: Irregular heart rhythm from mild to severe.

Respiratory: Depression (slowing) of respiration and the possibility of inducing bronchospasm (wheezing) causing difficulty in catching your breath or shortness of breath in susceptible individuals.

Gastrointestinal: Constipation is common and may be severe. Nausea and vomiting may occur as well.
Dermatological: Itching and rash. Endocrine: Decreased testosterone (male) and other sex hormones (females); dysfunctional sexual activity.

Urinary: Urinary retention (difficulty urinating).

Pregnancy: Newborn may be dependent on opioids and suffer withdrawal symptoms after birth.

Drug Interactions: With or altering the effect of other medications cannot be reliably predicted.

Tolerance: Increasing doses of drug may be needed over time to achieve the same (pain relieving) effect. Physical dependence and withdrawal: Physical dependence develops within 3-4 weeks in most patients receiving daily doses of these drugs. If your medications are abruptly stopped, symptoms of withdrawal may occur. These include nausea, vomiting, sweating, generalized malaise (flu-like symptoms), abdominal cramps, palpitations (abnormal heartbeats). All controlled substances (narcotics) need to be slowly weaned (tapered off) under the direction of your physician.

Addiction (Abuse): This refers to abnormal behavior directed towards acquiring or using drugs in a non-medically supervised manner. Patients with a history of alcohol and/or drug abuse are at increased risk for developing addiction.

Allergic reactions: Are possible with any medication. This usually occurs early after initiation of the medication. Most side effects are transient and can be controlled by continued therapy or the use of other medications.

This confirms that we discussed and you understand the above. I asked you if you wanted a more detailed explanation of the proposed treatment, the alternatives and the material risks, and you (Initial one):
_____ was satisfied with that explanation and desired no further information.
_____ requested and received, in substantial detail, further explanation of the treatment, alternatives and material risks.

_____ DATE _____

PATIENT SIGNATURE

Explained by me and signed in my presence.

_____ DATE _____

PHYSICIAN SIGNATURE

MEDICAL RISKS OF LONG-TERM OPIOID USE

Medical risk	How common?	Description and information
Respiratory depression		
Opioid overdose	< 1% per year	• Caused by severely slowed breathing, which you may not notice • Severe cases are treated in the hospital • Can cause death
Breathing problems during sleep	25%	• Can cause or worsen sleep apnea • You may not notice breathing problems
Falls, fractures		
Falls causing hip & pelvis fractures	1%-2% per year	
Gastrointestinal		
Constipation	30%-40%	• It helps to use stool-softeners or medicines that stimulate bowel movements
Serious intestinal blockage	<1% per year	• Caused by severe constipation • Severe cases are treated in the hospital
Hormonal effects		
Hypogonadism, impotence, infertility, osteoporosis	25%-75%	• Hypogonadism=lowered sex hormones, which can worsen sexual function • Osteoporosis can make you more likely to fracture
Cognitive and neurophysiologic effects		
Sedation	15%	• Can cause difficulty driving and thinking clearly
Disruption of sleep	25%	
Hyperalgesia	Not known	• Hyperalgesia = being more sensitive to pain
Psychosocial		
Depression, anxiety, deactivation, apathy	30%-40%	• Can cause loss of interest in usual activities, which can lead to depression. Depression can worsen pain, just as pain can worsen depression.
Addiction, misuse and diversion	5%-30%	• Misuse or overdose can occur if others—including children and teens—gain access to the medicine. • Your pharmacist can tell you how to dispose of unused medicines safely.
Other		
Dry mouth that may cause tooth decay	25%	• Brush your teeth and rinse your mouth often • Chew sugarless gum and drink water or sugarfree, non-carbonated fluids
Mycolonus	Not known	Myoclonus = muscle twitching

Source: Group Health, Chronic Opioid Therapy for Chronic Non-Cancer Pain Guideline, 2010.

GRADED PAIN AND FUNCTION SCALE

Pain Intensity and Interference

In the last month, on average, how would you rate your pain? Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be"? (That is, your usual pain at times you were in pain.)

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

In the last month, how much has paininterfered with your daily activities? Use a scale from 0 to 10, where 0 is "no interference" and 10 is "unable to carry on any activities"?

No Interference										**Unable to carry on any activities**
0	1	2	3	4	5	6	7	8	9	**10**

OSWESTRY LOW BACK PAIN DISABILITY QUESTIONNAIRE

The Oswestry Disability Index (also known as the Oswestry Low Back Pain Disability Questionnaire) is an extremely important tool that researchers and disability evaluators use to measure a patient's permanent functional disability. The test is considered the "gold standard" of low back functional outcome tools.[1]

SCORING INSTRUCTIONS

For each section the total possible score is 5: If the first statement is marked, the section score = 0; if the last statement is marked, it = 5. If all 10 sections are completed, the score is calculated as follows:

Example: 16 (total scored)
50 (total possible score) x 100 = 32%

If one section is missed or not applicable, the score is calculated:

16 (total scored)
45 (total possible score) x 100 = 35.5%

Minimum detectable change (90% confidence): 10% points (Change of less than this may be attributable to error in the measurement.)

INTERPRETATION OF SCORES

0% to 20%: minimal disability	The patient can cope with most living activities. Usually no treatment is indicated apart from advice on lifting, sitting and exercise.
21%-40%: moderate disability	The patient experiences more pain and difficulty with sitting, lifting and standing. Travel and social life are more difficult, and they may be disabled from work. Personal care, sexual activity and sleeping are not grossly affected, and the patient can usually be managed by conservative means.
41%-60%: severe disability	Pain remains the main problem in this group, but activities of daily living are affected. These patients require a detailed investigation.
61%-80%: crippled	Back pain impinges on all aspects of the patient's life. Positive intervention is required.
81%-100%	These patients are either bed-bound or exaggerating their symptoms.

INSTRUCTIONS

The following questionnaire has been designed to give us information as to how your back or leg pain is affecting your ability to manage in everyday life. Please answer by checking ONE box in each section for the statement which best applies to you. We realize you may consider that two or more statements in any one section apply, but please check only the box that indicates the statement which most clearly describes your problem.

1. Fairbank JC, Pynsent PB. The Oswestry Disability Index. Spine 2000 Nov 15;25(22):2940-52; discussion 52.

SECTION 1—PAIN INTENSITY

- ☐ I have no pain at the moment.
- ☐ The pain is very mild at the moment.
- ☐ The pain is moderate at the moment.
- ☐ The pain is fairly severe at the moment.
- ☐ The pain is very severe at the moment.
- ☐ The pain is the worst imaginable at the moment.

SECTION 2—PERSONAL CARE (WASHING, DRESSING, ETC.)

- ☐ I can look after myself normally without causing extra pain.
- ☐ I can look after myself normally but it causes extra pain.
- ☐ It is painful to look after myself and I am slow and careful.
- ☐ I need some help but manage most of my personal care.
- ☐ I need help every day in most aspects of self-care.
- ☐ I do not get dressed, I wash with difficulty and stay in bed.

SECTION 3—LIFTING

- ☐ I can lift heavy weights without extra pain.
- ☐ I can lift heavy weights but it gives extra pain.
- ☐ Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently placed, eg. on a table.
- ☐ Pain prevents me from lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned.
- ☐ I can lift very light weights.
- ☐ I cannot lift or carry anything at all.

SECTION 4—WALKING

- ☐ Pain does not prevent me walking any distance.
- ☐ Pain prevents me from walking more than 1 mile.
- ☐ Pain prevents me from walking more than ½ mile.
- ☐ Pain prevents me from walking more than 100 yards.
- ☐ I can only walk using a stick or crutches I am in bed most of the time.

SECTION 5—SITTING

- ☐ I can sit in any chair as long as I like.
- ☐ I can only sit in my favorite chair as long as I like.
- ☐ Pain prevents me sitting more than one hour.
- ☐ Pain prevents me from sitting more than 30 minutes.
- ☐ Pain prevents me from sitting more than 10 minutes.
- ☐ Pain prevents me from sitting at all.

SECTION 6—STANDING

- ☐ I can stand as long as I want without extra pain.
- ☐ I can stand as long as I want but it gives me extra pain.
- ☐ Pain prevents me from standing for more than 1 hour.
- ☐ Pain prevents me from standing for more than 3 minutes.
- ☐ Pain prevents me from standing for more than 10 minutes.
- ☐ Pain prevents me from standing at all.

SECTION 7—SLEEPING

- ☐ My sleep is never disturbed by pain.
- ☐ My sleep is occasionally disturbed by pain.
- ☐ Because of pain I have less than 6 hours sleep.
- ☐ Because of pain I have less than 4 hours sleep.
- ☐ Because of pain I have less than 2 hours sleep.
- ☐ Pain prevents me from sleeping at all.

SECTION 8—SEX LIFE (IF APPLICABLE)

- ☐ My sex life is normal and causes no extra pain.
- ☐ My sex life is normal but causes some extra pain.
- ☐ My sex life is nearly normal but is very painful.
- ☐ My sex life is severely restricted by pain.
- ☐ My sex life is nearly absent because of pain.
- ☐ Pain prevents any sex life at all.

SECTION 9—SOCIAL LIFE

- ☐ My social life is normal and gives me no extra pain.
- ☐ My social life is normal but increases the degree of pain.
- ☐ Pain has no significant effect on my social life apart from limiting my more energetic interests (e.g., sports).
- ☐ Pain has restricted my social life and I do not go out as often.
- ☐ Pain has restricted my social life to my home.
- ☐ I have no social life because of pain.

SECTION 10—TRAVELLING

- ☐ I can travel anywhere without pain.
- ☐ I can travel anywhere but it gives me extra pain.
- ☐ Pain is bad but I manage journeys over two hours.
- ☐ Pain restricts me to journeys of less than one hour.
- ☐ Pain restricts me to short necessary journeys under 30 minutes.
- ☐ Pain prevents me from travelling except to receive treatment.

ADDITIONAL ASSESSMENT TOOLS

Specific Psychosocial Assessment	Tools to Evaluate
Substance abuse history	ORT, CAGE, Audit, Dast. SOAPP-R
Psychiatric/Mental health history	PHQ, PMQ, DIRE, GAD-7, PCL-C
ADLs/self-care	Oswestry, SF-36 or 12, pain log/diary, ACPS QOL
Self-perception of disability	DIRE, COMM, SF-36 or 12
SI/SA history	Roland-Morris Low-Back Pain and Disability Questionnaire

ORT Opioid Risk Tool. Very simple, evidence-based and widely used.

CAGE Four-item self-test for identifying usage patterns that may reflect problems with alcohol.

PHQ Patient Health Questionnaire, a 2-, 4-, or 9-item depression scale; tool for assisting in diagnosing depression.

DIRE Diagnosis, intractability, risk, efficacy tool that assesses the risk of opioid abuse and the suitability of candidates for long-term opioid therapy.

COMM Current Opioid Misuse Measure. A 17-item self-assessment to identify patients with chronic pain who are taking opioids and have indicators of current aberrant drug-related behaviors.

SBIRT Screening, brief intervention, and referral to treatment. An effective, evidence-based method to intervene in alcohol and drug misuse.

OSWESTRY The Oswestry Low-Back Pain Disability Questionnaire, a tool that researchers and disability evaluators use to measure a patient's permanent functional disability. The test is considered the gold standard of low back functional outcome tools.

SOAPP-R The Screener and Opioid Assessment for Patients with Pain-Revised. Predicts possible opioid abuse in chronic pain.

CHRONIC PAIN TREATMENT CHECKLIST

This checklist may be useful as a means to ensure compliance with these guidelines.

- [ ] Hx and Px with assessment of baseline function and pain.
- [ ] Review all relevant prior records.
- [ ] Has there been a prior unsuccessful attempt to treat with non-opioid modalities?
- [ ] Is the diagnosis appropriate for opioid treatment?
- [ ] Psychosocial and risk assessment: risk of medication abuse (ORT), psychiatric co-morbidity PHQ-4 or other validated tools, evidence of existing abuse (PDMP).
- [ ] Are there co-prescribed drug interaction risks? Benzodiazepines are generally contraindicated.
- [ ] Sleep risk assessment (S T O P B A N G or equivalent).
- [ ] UDS: Any unexpected results?
- [ ] Have you checked the PDMP for prescriptions of which you were unaware?
- [ ] Create a treatment plan that emphasizes patient self-management.
- [ ] Are there appropriate referrals?
- [ ] Have you explored all reasonable non-opioid treatment options: medical, behavioral, physiotherapy, and lifestyle changes?
- [ ] Have you considered partnering with a substance abuse treatment program?
- [ ] Check women of child-bearing age for pregnancy.

If prescribing opioids, proceed with caution:

- [ ] Obtain a signed Material Risk Notice.
- [ ] Establish treatment goals with periodic review of goals over time.
- [ ] Monitor compliance (UDSs, pill counts, PDMP, call-backs).
- [ ] Monitor improvement in pain and function, including overall well-being.
- [ ] Obtain consultation as needed: mental health, substance abuse, pain management, specialty care, pregnant women.
- [ ] Have you considered partnering with a behavioral health specialist (CBT counselor, peer-to-peer coordinator, Living Well with Chronic Disease facilitator, substance abuse counselor)?

METABOLISM DATA FOR COMMON MEDICATIONS

Drugs or Drug Classes	Detection Time in Urine*	Urine Drug Screening to Order	Expected Results	Consideration
Opioids or "opiates" – Natural (from opium)				
Codeine (Tylenol #2/3/4)	1-3 days	Opiates Immunoassay + GC/MS or LC/MS/MS Opiates	Opiates Immunoassay – positive GC/MS or LC/MS/MS – codeine, possibly morphine & hydrocodone	Immunoassays for "opiates" are responsive for morphine and codeine but do not distinguish which is present. Confirmatory testing is required to reliably identify drug(s) present. Since codeine is metabolized to morphine and small quantities to hydrocodone, these drugs may be found in the urine. Also, morphine may metabolize to produce a small amount (<10%) of hydromorphone.
Morphine (Avinza, Embeda, MS Contin, Kadian)	1-3 days		Opiates Immunoassay –positive GC/MS or LC/MS/MS – morphine, possibly hydromorphone	
Opioids – Semisynthetic (derived from opium				
Hydrocodone (Lorcet, Lortab, Norco, Vicodin)	1-3 days	Opiates Immunoassay + GC/MS or LC/MS/MS Opiates	Opiates Immunoassay –positive GC/MS or LC/MS/MS – hydrocodone, possibly hydromorphone	"Opiates" immunoassays may also detect semisynthetic opioids depending on their cross-reactivity pattern. However, a negative result does not exclude use of semisynthetic opioids. Confirmatory testing (GC/MS or LC/MS/MS) is required to verify compliance with the prescribed semisynthetic opioid(s). Since hydrocodone is metabolized in small amounts to hydromorphone, both may be found in the urine. Likewise, oxycodone is metabolized to oxymorphone, so these may both be present in the urine of oxycodone users. However, the reverse is not true. In other words, hydromorphone and oxymorphone use does not result in positive screens for hydrocodone and oxycodone, respectively.
Hydromorphone (Dilaudid, Exalgo)	1-3 days	Opiates Immunoassay + GC/MS or LC/MS/MS Opiates	Opiates Immunoassay –positive GC/MS or LC/MS/MS –hydromorphone	
Oxycodone (Roxicet, OxyContin)	1-3 days	Oxycodone Immunoassay + GC/MS or LC/MS/MS Opiates	Opiates Immunoassay –positive GC/MS or LC/MS/MS – oxycodone possibly oxymorphone	
Oxymorphone (Opana)	1-3 days	Opiates or Oxycodone Immunoassay + GC/MS or LC/MS/MS Opiates	Opiates or Oxycodone Immunoassay –positive GC/MS or LC/MS/MS – oxymorphone	
Opioids – Synthetic (man-made)				
Fentanyl	1-3 days	GC/MS or LC/MS/MS Fentanyl	GC/MS or LC/MS/MS – fentanyl & norfentanyl	Current "opiates" immunoassays do not detect synthetic opioids. Thus confirmatory testing (GC/MS or LC/MS/MS) is needed to identify these drugs. If the purpose is to document compliance with treatment, the laboratory can be instructed to remove the cutoff concentration so that the presence of lower concentrations can be identified.
Meperidine (Demerol)	1-3 days	GC/MS or LC/MS/MS Meperidine	GC/MS or LC/MS/MS – normeperidine, possibly meperidine	

Drugs or Drug Classes	Detection Time in Urine*	Urine Drug Screening to Order	Expected Results	Consideration
Opioids – Synthetic (man-made) - continued				
Methadone (Methadose)	3-7 days	Methadone Immunoassay + GC/MS or LC/MS/MS Methadone	Methadone Immunoassay – positive GC/MS or LC/MS/MS – methadone & EDDP	
Propoxyphene (Darvon, Darvocet)	1-3 days	Propoxyphene Immunoassay + GC/MS or LC/MS/MS Propoxyphene	Propoxyphene Immunoassay – positive GC/MS or LC/MS/MS – propoxyphene & norpropoxyphene	
Others				
Alcohol	Up to 8 hours	Alcohol	Alcohol – see Consideration	Additional testing for alcohol metabolites, ethyl glucuronide (EtG) or ethyl sulfate.
Amphetamines	2-3 days	Amphetamines, Methamphetamines or MDMA Immunoassay + GC/MS or LC/MS/MS Amphetamines	Amphetamines, methamphetamines or MDMA Immunoassay – see Consideration GC/MS or LC/MS/MS – amphetamine, methamphetamine or MDMA	Amphetamines immunoassays are highly cross-reactive so results should be interpreted cautiously, and may require consultation with the lab. They may detect other sympathomimetic amines, such as ephedrine, pseudoephedrine or selegiline. Confirmatory testing can identify which amphetamine is present.
Barbiturates	1-3 days w/short-acting; up to 30 days w/long acting	Barbiturates Immunoassay	Barbiturates Immunoassay – see Consideration	The clearance half-life of intermediate-acting barbiturates averages 24 hours. It takes about 5 to 7 half-lives to clear 98% of a drug dose. Thus, the presence of anintermediated-acting barbiturate indicates exposure within 5-7 days.
Benzodiazepines	1-3 days w/short-acting; up to 30 days w/long acting	Benzodiazepines Immunoassay	Benzodiazepines Immunoassay – see Consideration GC/MS or LC/MS/MS – alprazolam, diazepam, clonazepam, lorazepam, etc.	Immunoassays for benzodiazepines have a 28% overall false negative rate and vary in cross-reactivity. Certain benzodiazepines (clonazepam and alprazolam) have limited detectability by most available immunoassays. Confirmatory testing is needed when use is expected or suspected.
Cocaine or benzoylecgonine	2-4 days	Cocaine Metabolites Immunoassay	Cocaine Metabolites Immunoassay – see Consideration	Cocaine immunoassays do not cross-react with other topical anesthetics that end in "caine" (e.g. lidocaine) and are highly specific for cocaine use.
Marijuana	2-4 days; up to 30 days w/ chronic heavy use	Cannabinoids (THC) Immunoassay	Cannabinoids Immunoassay – see Consideration GC/MS or LC/MS/MS – THC	THC may be an indicator of the patient's risk category. Prescribers should have an office policy, discuss with the patients reason for use and adjust monitoring plan accordingly.

*Agency Medical Directors Group, Interagency guideline on Opioid dosing for Chronic Non-cancer Pain, 2010.

BEHAVIORAL HEALTH RISKS SCREENING TOOL

SOUTHERN OREGON Perinatal Task Force

For Pregnant Women and Women of Childbearing Age

Patient/Client Name _____ Date _____

Screener Name _____ Date _____

Reviewed by Qualified Provider _____ Date _____

Women and their children's health can be affected by emotional problems, alcohol, tobacco, other drug use and violence. Women and their children's health are also affected when these same problems are present in people who are close to them. Alcohol includes beer, wine, wine coolers, liquor and spirits. Tobacco products include cigarettes, cigars, snuff and chewing tobacco.

1. Have you smoked any cigarettes or used any tobacco products in the past three months?	TOBACCO		☐ YES		☐ NO
2. Did any of your parents have a problem with alcohol or other drug use?	PARENTS	☐ YES			☐ NO
3. Do any of your friends have a problem with alcohol or other drug use?	PEERS	☐ YES			☐ NO
4. Does your partner have a problem with alcohol or other drug use?	PARTNER		☐ YES		☐ NO
5. In the past, have you had difficulties in your life due to alcohol or other drugs, including prescription medications?	PAST		☐ YES		☐ NO
6. Check YES if she agrees with any of these statements. – In the past month, have you drunk any alcohol or used other drugs? – How many days per month do you drink? _____ – How many drinks on any given day? _____ – How often did you have 4 or more drinks per day in the last month? _____	PRESENT		☐ YES		☐ NO
7. Over the last few weeks, has worry, anxiety, depression, or sadness made it difficult for you to do your work, get along with other people, or take care of things at home?	EMOTIONAL HEALTH				☐ YES ☐ NO
8. Are you feeling at all unsafe in any way in your relationship with your current partner?	VIOLENCE			☐ YES	☐ NO

Review risk.

Refer to tobacco cessation program or addictions and recovery programs.

Refer to domestic violence prevention.

Refer to mental health program.

Develop a follow-up plan with patient.

PROVIDER USE ONLY

Brief Intervention/Brief Treatment	Y	N	NA
Did you **State** your medical concern?	☐	☐	☐
Did you **Advise** to abstain or reduce use?	☐	☐	☐
Did you **Check** patient's reaction?	☐	☐	☐
Did you **Refer** for further assessment?	☐	☐	☐
Did you **Provide** written information?	☐	☐	☐

Moderate drinking for non-pregnant women is one drink per day. Women who are pregnant or planning to become pregnant should not use alcohol, tobacco, illicit drugs or prescription medication other than as prescribed.

Developed by the Institute for Health and Recovery (IHR), Massachusetts, February, 2007. Adapted by the Southern Oregon Perinatal Task Force in partnership with AllCare Health Plan, Oregon, May 2013.

COMPARISON OF CURRENT OPIOID GUIDELINES

www.woema.org

LEADERSHIP WOEMA EDUCATION SERVICE

Clinical Issue	ACOEM Guidelines	American Pain Society Guidelines	Canadian Pain Guidelines	Colorado Guidelines	California MTUS Guidelines	Washington Guidelines
Screen all patients for opioid risks, using a questionnaire?	Yes, all patients; SOAPP is suggested	Yes. Questionnaire "likely" to help; suggest SOAPP, PADT, or COMM	Consider using questionnaire; suggest Opioid Risk Tool (ORT)	No recommendation	CAGE, SOAPP, Opioid Risk Tool (ORT), others suggested	PQ9, CAGE-AID
Initiate opioids only after treatment failure?	Yes	No. Start chronic opioids when benefits are likely to outweigh risks	Physician should document "comprehensive knowledge of the patient's pain condition"	Yes	Yes	N/A
Urine drug screen on all patients on chronic opioids?	Yes	Urine drug screens recommended "periodically" in patients at high risk for drug abuse. "Consider" urine drug screens in low risk patients	No recommendation for routine urine drug testing; physician should screen by history for aberrant behaviors	Yes	Consider	Yes
Urine drug screen only for high risk with acute pain?	Yes	Recommended	No recommendation for routine urine drug screenings	Yes	Consider	Yes
Frequency of urine drug screen?	2 to 4 times a year, random	Could be as often as weekly in "very high risk" patients; no other recommendation for frequency	No recommendation for routine urine drug screening at all	At least annually	Random	Frequency of urine drug screening depends on both MED and ORT risk score (range from 1 to 4 times a year)
Pain agreements for ALL patients on chronic narcotics?	Yes	Recommend written informed consent when starting chronic opioids. Sample "Pain Agreement"	Consider in patients at high risk for abuse; norecommendation for routine use of pain agreements	Yes	Optional	Yes
Pain agreements for "high risk" patients?	Yes	No recommendation; sample "Pain Agreement" included in Appendix	No recommendation for routine use of pain agreements	Yes	Optional	N/A
Discontinue/wean opioids if no functional improvement	Yes	Yes	No recommendation	No recommendation	Yes	Yes
Increase dose of meds if additional functional improvement obtained?	Yes	Yes	Yes	No recommendation	Yes	
Maximum morphine-equivalent dose before additional screening?	N/A	200 MEQ (morphine equianalgesic dose)	200 MEQ (morphine equianalgesic dose)	N/A	N/A	120 MEQ (morphine equianalgesic dose)
Consultation with pain specialist recommended?	Yes. PRN	Primary care physician should continue to manage. Consider consult, at clinician's judgment	No	Required	Yes, as per Washington	Yes, suggested if >100 MEQ, but required if > than 120 MEQ
Attempt periodic wean of opioids if functional improvement?	Yes	No recommendation	No recommendation	No recommendation	Yes	
Attempt periodic wean of meds for ALL patients on chronic opioids?	Yearly	Yes	No recommendation	No recommendation	N/A	
Psychiatry consult recommended?	Yes, especially during wean	Consider, at clinician's judgment	Referral to pain management specialist recommended for certain high risk conditions	Yes	Yes	Yes. Must have psych eval if combining narcotics with benzodiazepines, sedatives, etc.
PT recommended?	Yes, especially during drug wean and to establish HEP.	No recommendation	No recommendation		Yes	N/A
Physician to consult PDMP (Prescription Drug Monitoring Program) regularly	N/A	N/A	N/A	Yes	N/A	N/A
Other clinical advice			Discontinue or taper benzodiazepines before initiating chronic opioids	Requires the physician to prepare a written Treatment Plan. Supplemental Fee Schedule for extra documentation		Urine drug screen-first use immunoassay (less expensive); if needed after a positive result, confirmatory test (GC/MS or other)
Advice about driving?		No evidence to suggest that chronic opioid use impairs driving; warn patients not to drive if they "feel impaired"	Advise not to drive until opioid dose stabilized			

WOEMA wishes to thank the following members who compiled this poster: Paul Papanek, MD, MPH, FACOEM, Scott Levy, MD, MPH, FACOEM, and Steven Feinberg, MD.

PATIENT AND COMMUNITY RESOURCES

	Inpatient care, residential	Populations served	Chronic pain services	Sliding scale	Payment options
Adapt Josephine County-Recovery Services					
418 NW 6th St., Grants Pass, OR 97526 541-474-1033 Fax: 541-474-0770 www.adaptoregon.org	✓	Adults and adolescents	✓	✓	OHP, commercial insurance
The Addictions Recovery Center					
111 Genesee St., Medford, OR 97504 541-779-1282 Fax: 541-779-2081 www.addictionsrecovery.org	✓	Adults and children	✓	✓	OHP, commercial insurance
Allied Health-Recovery Services					
777 Murphy Road, Medford, OR 97504 541-772-2763 Fax: 541-734-3164		Adults	✓ (for those with addiction only. Methadone and Suboxone.)	✓	OHP, commercial insurance
Choices Josephine County-Recovery Services					
109 Manzanita Ave Grants Pass, OR 97526 541-479-8847 Fax: 541-471-2679		Adults and adolescents	✓		OHP
Jackson County Mental Health					
1005 E Main St., Medford, OR 97503 541-774-8201 www.co.jackson.or.us	✓	Adults and families	✓	✓	OHP
Kolpia-Recovery Services *(offices in Medford and Talent)*					
10 S Bartlett St, Ste 204 Medford, OR 97503 541-227-6729 Fax: 541-482-0964 www.kolpiacounseling.com		Adults and adolescents	✓ (including Suboxone)		OHP, commercial insurance
On Track-Recovery Services *(offices in Medford, Grants Pass, White City, and Ashland)*					
221 W Main St., Medford, OR 97501 541-772-1777 Fax: 541-734-2410 www.ontrackrecovery.org	✓	Adults and children	✓	✓	OHP, Medicare, commercial insurance
Options for Southern Oregon, Inc.					
1215 SW G St., Grants Pass, OR 97526 541-476-2373 Fax 541-476-1526 www.optionsonline.org	✓	Adults and families		✓	OHP
Phoenix Counseling Center-Recovery Services					
153 S Main St., Phoenix, OR 97520 541-535-4133 Fax: 541-535-5458 www.phoenixcounseling.org		Adults and adolescents	✓	✓	OHP, commercial insurance

LINKS

Group Health: Principles for More Selective and Cautious Opioid Prescribing
www.ghinnovates.org/?p=3573

University of Washington: Pain Medicine Provider Toolkit
http://depts.washington.edu/anesth/education/pain/index.shtml

Center for Disease Control
www.cdc.gov/primarycare/materials/opoidabuse/index.html

Washington State Agency Medical Directors
www.agencymeddirectors.wa.gov

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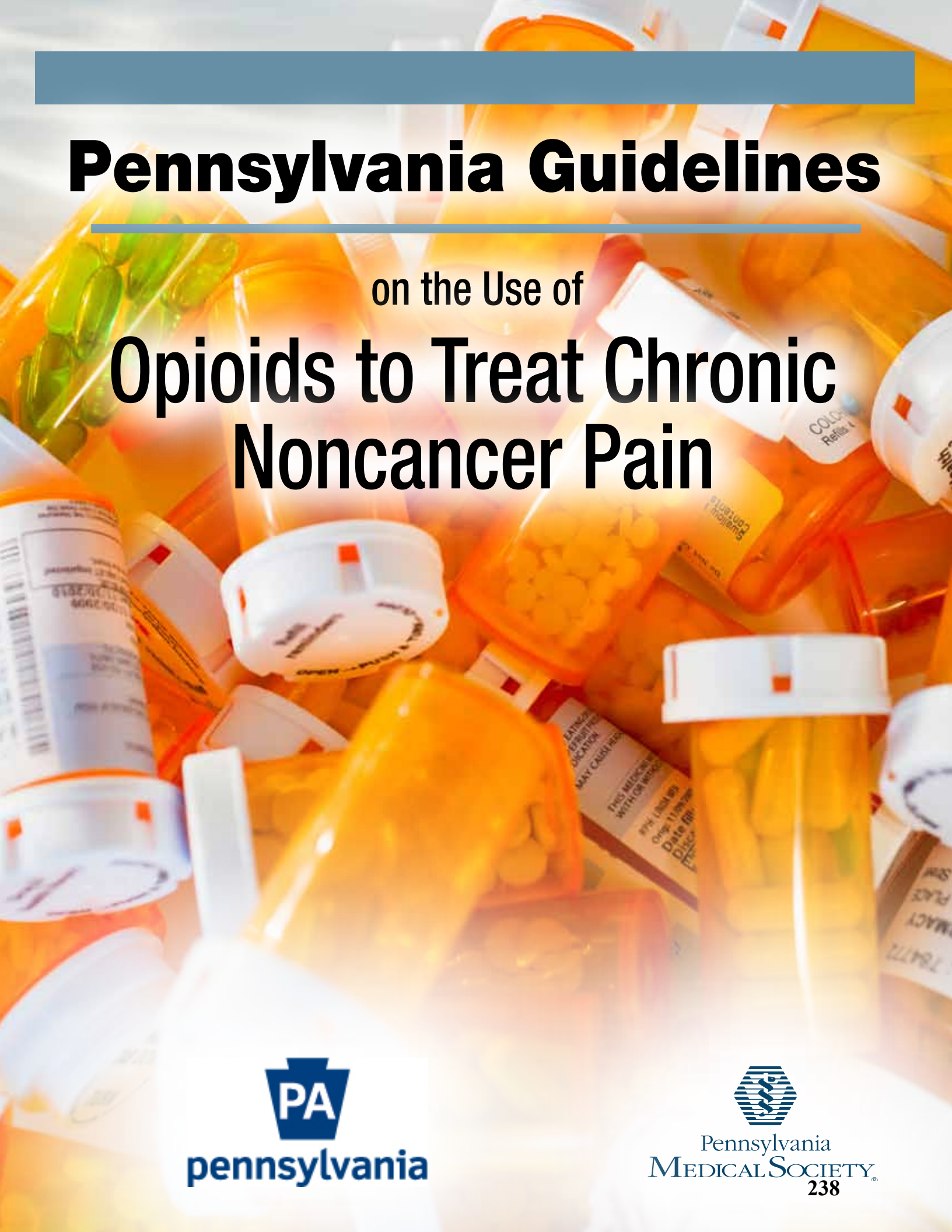
Pennsylvania Guidelines

on the Use of

Opioids to Treat Chronic Noncancer Pain



pennsylvania

Pennsylvania Medical Society

Pennsylvania Guidelines on the Use of Opioids to Treat Chronic Noncancer Pain

Chronic pain is a major health problem in the United States, occurring with a point-prevalence of about one-third of the US population.[1] More women than men experience chronic pain, and the prevalence of chronic pain increases with age. The impact of pain on individuals and society is substantial. In a recent survey, individuals reporting frequent or persistent pain within the last 3 months reported that their pain often caused problems with sleep and mood, and 32% reported not being able to work.[2] The economic impact of chronic pain in the United States is staggering. A recent Institute of Medicine report estimated the annual cost in the United States was $560 to over $600 billion, including healthcare costs ($261-300 billion) and lost productivity ($297-336 billion).[3]

Chronic pain is best treated using an interdisciplinary, multi-model approach. The treatment team often includes the patient and his or her family, the primary care provider, a physical therapist, a behavioral health provider and one or more specialists. Patient outcomes are optimized when several treatments are used in a coordinated manner. These treatments may include activating physical therapy, cognitive-behavioral therapy, proper use of medications, and interventions when indicated. Reliance on only one medication or treatment modality can lead to inadequate pain control and increased risk of harm.

Chronic opioid therapy is a common treatment option for chronic pain, and its use has increased substantially over the last 15 years, in spite of limited evidence of safety and long-term efficacy in the general patient population. Prescription drug abuse has increased significantly over the last 15 years, and this increase has been attributed in part to the increased use of opioids to treat chronic noncancer pain.[4] About 6.1 million Americans abused or misused prescription drugs in 2011. Drug poisoning deaths, the vast majority of which involve prescription drugs, surpassed traffic-related accidents as the leading cause of injury-related deaths in the United States in 2009.[5] Prescription opioids are now responsible for over 16,000 deaths and 475,000 Emergency Department visits a year in the United States.

These guidelines address the use of opioids for the treatment of chronic noncancer pain. These guidelines do not address the use of opioids for acute pain, nor do they address the use of opioids for the treatment of pain at the end-of-life. These guidelines are intended to help health care providers improve patient outcomes when providing this treatment, including avoiding potential adverse outcomes associated with the use of opioids to treat pain. These guidelines are intended to supplement and not replace the individual prescriber's clinical judgment. Additional detailed information may be obtained from recently published evidence based guidelines.[6-8]

Opioid analgesics may be necessary for the relief of pain, but improper use of opioids poses a threat to the individual and to society. Providers have a responsibility to diagnose and treat pain using sound clinical judgment, and such treatment may include the prescribing of opioids. Providers also have a responsibility to minimize the potential for the abuse and diversion of opioids. Therefore, providers should use proper safeguards to minimize the potential for abuse and diversion of opioids.

These guidelines suggest that health care providers incorporate the following key practices into their care of the patient receiving opioids for the treatment of chronic noncancer pain:

- Before initiating chronic opioid therapy, clinicians should conduct and document a history, including documentation and verification of current medications, and a physical examination. Appropriate testing should be completed before starting chronic opioid therapy. The initial evaluation should include documentation of the patient's psychiatric status and substance use history. Clinicians should consider using a valid

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screening tool to determine the patient's risk for aberrant drug-related behavior.

- Opioids should rarely be used as a sole treatment modality. Rather, opioids should be considered as a treatment option within the context of multimodality therapy. Providers should recognize that high risk patients, including those with significant psychiatric co-morbidities, may require specialty care, and that chronic opioid therapy may not be possible absent needed specialty care.
- Patients at risk for obstructive sleep apnea (OSA) are at increased risk for harm with the use of chronic opioid therapy. Providers should consider the use of a screening tool for OSA, refer patients for proper evaluation and treatment when indicated, and seek to ensure patients with OSA are compliant with treatment.

- When starting chronic opioid therapy, the provider should discuss the risks and potential benefits associated with treatment, so that the patient can make an informed decision regarding treatment. Reasonable goals and expectations for treatment should be agreed upon, and the patient should understand the process for how the care will be provided, including proper storage and disposal of controlled substances. Providers should proactively review the necessity of periodic compliance checks that may include urine or saliva drug testing and pill counts. Providers may wish to document this discussion through the use of an opioid treatment agreement.
- Initial treatment with opioids should be considered by clinicians and patients as a therapeutic trial to determine whether chronic opioid therapy is appropriate. Both clinicians and patients should understand that chronic opioid therapy will not be effective for all patients, either due to lack of efficacy or the development of unacceptable adverse events, including aberrant drug-related behavior.
- Patient's opioid selection, initial dosing, and dose adjustments should be individualized according to the patient's health status, previous exposure to opioids, response to treatment (including attainment of established treatment goals), and predicted or observed adverse events.
  - Caution should be used in patients also taking benzodiazepines, as the use of benzodiazepines in addition to chronic opioid therapy increases the risk of serious adverse events.
  - Caution should be used with the administration of methadone, as the administration of methadone for the treatment of chronic pain is associated with increased risk of harm. Providers should be aware of the special pharmacokinetics of methadone and the need for careful dosing and monitoring.
  - Caution should be used with the administration of chronic opioids in women of childbearing age, as chronic opioid therapy during pregnancy increases risk of harm to the newborn. Opioids should be administered with caution in breastfeeding women, as some opioids may be transferred to the baby in breast milk.
  - When chronic opioid therapy is used for an elderly patient, clinicians should consider starting at a lower dose, titrating slowly, using a longer dosing interval, and monitoring more frequently.
  - Patients with co-existing psychiatric disorder(s) may be at increased risk of harm related to chronic opioid therapy. Therefore, clinicians should carefully weight the risk of harm against the potential for benefit when considering chronic opioid therapy, and if chronic opioids are used, consider careful dose selection, frequent monitoring and consultation where feasible.
  - It is not appropriate to refer patients receiving chronic opioid therapy to the emergency department to obtain prescriptions for opioids.
  - When a dose of chronic opioid therapy is increased, the clinician is advised to provide counseling the patient on the risk of cognitive impairment that can adversely affect the patient's ability to drive or safely do other activities. The risk of cognitive impairment is increased when opioids are taken with other centrally acting sedatives, including alcohol and benzodiazepines.
- Total daily opioid doses above 100 mg / day of oral morphine or its equivalent is not associated with improved pain control, but is associated with

a significant increase in risk of harm. Therefore, clinicians should carefully consider if doses above 100 mg / day of oral morphine or its equivalent are indicated. Consultation for specialty care may be appropriate for patients receiving high daily doses of opioids.

- Clinicians should reassess patients on chronic opioid therapy periodically and as warranted by changing circumstances. Monitoring should include documentation of response to therapy (pain intensity; physical and mental functioning, including activities of daily living; and assessment of progress toward achieving therapeutic goals), presence of adverse events, and adherence to prescribed therapies.
- Clinicians should carefully monitor patients for aberrant drug-related behaviors. Monitoring may include periodic review of available information regarding the prescribing of opioids and other controlled substances to the patient through available databases, urine or saliva drug screening or pill counts. Consideration should be given to routine periodic urine drug screening as a monitoring tool.
- Clinicians should consider increasing the frequency of ongoing monitoring, as well as referral for specialty care, including psychological, psychiatric and addiction experts for patients identified to be at high risk for aberrant drug-related behavior.
- In patients who have engaged in aberrant drug-related behaviors, clinicians should carefully determine if the risks associated with chronic opioid therapy outweigh documented benefit. Clinicians should consider restructuring therapy (frequency or intensity of monitoring), referral for assistance in management, or discontinuation of chronic opioid therapy. Appropriate referral for addiction evaluation and treatment should be provided.
- Clinicians should discontinue chronic opioid therapy in patients who engage in repeated aberrant drug-related behaviors or drug abuse-diversion, experience no progress toward meeting therapeutic goals, or experience intolerable adverse effects.
- Clinicians should be aware of and understand current federal and state laws, regulatory guidelines, and policy statements that govern the use of chronic opioid therapy for chronic non-cancer pain.

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ANA
AMERICAN NURSES ASSOCIATION

Nursing's Role in Addressing Nation's Opioid Crisis

Opioid drug-related overdose has risen steadily over the past two decades, becoming one of the leading causes of death in the United States. The American Nurses Association (ANA) recognizes the central role nurses can play in addressing this crisis and has set out to develop resources aimed at promoting a comprehensive approach.

As health care providers practicing on the front lines of the opioid epidemic, registered nurses are qualified and well positioned to play a leading role in assessing, diagnosing, and managing patients battling addiction.

Stemming the tide of opioid addiction and overdose deaths in the U.S. demands a comprehensive approach. ANA recognizes the significance of this public health crisis and is committed to helping nursing stand as a leading provider in the fight against opioid dependence, overdose, and death.

Expanded Access to Medication-Assisted Treatment

Expanding access to medication-assisted treatment (MAT) is a critical step in addressing the growing opioid epidemic, comprehensively. ANA has sought to amend the Drug Addiction Treatment Act of 2000 (DATA 2000) in order to allow Advance Practice Registered Nurses (APRNs) with appropriate training to prescribe buprenorphine. Expansion of the DATA 2000 waiver program to include the four APRN roles would safely and significantly increase access to medication-assisted treatment (MAT) for patients who need it most.

Prescriber Education & Training

ANA believes the current crisis calls for additional support and focus on prescriber education -- advanced practice registered nurse (APRNs) education already prepares practitioners to effectively and safely prescribe opioids, Taking steps to ensure that health care professionals who prescribe opioids are properly trained and educated in opioid prescribing is a critical and necessary investment.

In collaboration with the White House, ANA proudly joined forces with 40 other provider groups in a pledge to train more than 540,000 opioid prescribers over the next two years.

Deterrent Formulations

ANA urges greater investments in the scientific and clinical research needed to advance the development, assessment, and deployment of abuse-deterrent technologies. Issues surrounding abuse and misuse of prescription opioids must be balanced with the real and legitimate needs of those seeking treatment for pain. Developing abuse deterrent formulations (ADFs) is an important tool in preventing abuse. The US Food and Drug Administration (FDA) considers the development of these products a high public health priority.

American Nurses Association Department of Government Affairs
8515 Georgia Avenue, Suite 400 | Silver Spring, MD 20910 | T 301.628.5094 | F 301.628.5348 | www.RNaction.org | RNaction@ana.org

The Role of Prescription Drug Monitoring Programs (PDMPs)

ANA supports the increased utilization of PDMPs and will be working with our constituent/state nurses association to increase awareness of PDMPs and the number of APRN prescribers who are registered.

Prescription drug monitoring programs (PDMPs) play an important role in preventing inappropriate access to prescription opioids. While interventions to improve safe and appropriate prescribing must be employed to curb dangerous practices, it is important that any such improvements don't serve to limit access to appropriate pain management for patients that need it.

Increase Access to Opioid Antagonist - Naloxone

ANA supports increasing access to Naloxone for first responders, family, friends, and caregivers of those who are known to be chronic users of opioids. Naloxone is a critical tool in preventing overdose by opioids such as heroin, morphine, and oxycodone. ANA believes that the development of civil liability protections for those trained in administration of Naloxone should coincide with any efforts to increase access and that third party payers, including Medicaid and Medicare, should cover this life saving measure.

American Nurses Association Department of Government Affairs
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June 3, 2016

Division of Dockets Management (HFA 305)
Food and Drug Administration
5630 Fishers Lane
Rm. 1061
Rockville, MD 20852

RE: FDA–2016–N–0820, Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee; Notice of Meeting

To Whom It May Concern:

The American Association of Nurse Anesthetists (AANA) welcomes the opportunity to submit comments on the ER/LA Opioid Analgesics REMS Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. The AANA shares the US Food and Drug Administration's (FDA's) concern about the increase in opioid drug use, abuse and deaths and is committed to collaboratively working toward a common solution to help curb the opioid epidemic in the US.

Background of AANA and CRNAs

The AANA is the professional association representing more than 49,000 Certified Registered Nurse Anesthetists (CRNAs) and student registered nurse anesthetists in the United States. More than 90 percent of the nation's nurse anesthetists are members of the AANA. CRNAs are advanced practice registered nurses who personally administer more than 40 million anesthetics to patients each year in the United States. CRNAs provide anesthesia for a wide variety of surgical cases and in some states are the sole anesthesia providers in nearly 100 percent of rural hospitals, affording these medical facilities obstetrical, surgical, trauma stabilization, and pain management capabilities. CRNAs work in every setting in which anesthesia is delivered including hospital surgical suites and obstetrical delivery rooms, ambulatory surgical centers, pain management facilities, and the offices of dentists, podiatrists, and all types of specialty surgeons.

Recommendations

The AANA makes the following recommendations regarding the ER/LA Opioid Analgesics REMS Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics:

- **Patient engagement should be a central component of pain management.**

  Patient-centered care offers the patient greater transparency, understanding, and engagement in their care. Using a shared decision making model facilitates collaborative care through planning and discussion of risks and benefits of the pain management plan, encourages the patient to express his or her preferences and values, and jointly establishes realistic goals for the patient's well-being and quality of life. In the treatment of pain, patients and their caregivers should understand the etiology of pain, treatment plans and goals, treatment options and alternatives, as well as consequence to non-adherence to the pain management plan. For chronic pain management, particularly if opioids are prescribed in the treatment, the clinician should enter into a pain management treatment agreement with the patient.

- **Acute and chronic pain management involves a multidisciplinary approach; therefore education should extend to all members of the multidisciplinary team and be aligned with national guidelines.**

  The AANA supports provider education regarding alternative non-pharmacologic and pharmacologic modalities for pain management that minimize the use of opioids. Many clinicians across numerous specialties, such as primary care, anesthesia, addiction, pain, emergency, and palliative care, are involved in the management of acute and chronic pain. Interprofessional education should be evidence-based and align with national guidelines, such as the Centers for Disease Control and Prevention (CDC) *Guideline for Prescribing Opioids for Chronic Pain*. The AANA has many resources related to acute and chronic pain management which can be applied to patient care settings, such as *Chronic Pain Management Guidelines* and *Regional Anesthesia for Surgical Procedures and Acute Pain Management, Practice Considerations*, and the AANA would be happy to serve as a resource on this effort.

- **A multimodal approach to pain management should be considered as part of the patient-specific treatment plan and can lessen the need for opioid use.**

  For surgical pain, a preemptive, often multimodal, approach to acute pain management integrating regional anesthesia techniques has been shown to be advantageous in a wide array of surgical specialties. Preemptive analgesia may improve the patient's postoperative acute pain experience, minimize the transition to a chronic pain state and have a positive, long-term effect. The use of an enhanced recovery after surgery (ERAS) protocol, to include multimodal pain management, may reduce the patients' stress response to surgery, minimize use of opioids, and accelerate the return to normal daily function.

  Chronic pain management may also incorporate a multimodal treatment approach. Non-pharmacologic treatment modalities may decrease pain and when appropriate should be considered as part of the plan of care. When a pharmacologic approach, including opioid medications, is used, the treatment should be tailored to the patient's level of pain, functionality, and response.

- **REMS should incorporate immediate release (IR) opioid medications.**

  AANA recommends that the ER/LA Opioid Analgesics REMS be expanded to include IR opioids. IR opioids may be prescribed postoperatively and have the potential for addiction. Consistent, standardized clinician education and patient monitoring for the treatment of acute pain using IR opioids may mitigate opioid addiction or transition to ER/LA opioid formulations.

- **Engage with professional organizations, such as the AANA, to support all stakeholders' needs in the development of any standardized REMS resources and tools.**

  Many physician and nursing organizations, patient advocacy groups, and governmental agencies share the common concern of increased opioid use, abuse, and deaths in the US. The AANA recommends that the FDA collaborate with all interested parties, including the AANA and relevant professional education, certification, and accrediting bodies, in the further refinement of the current ER/LA opioid REMS and any future resource or recommendation development (e.g., IR

opioid medications). Many clinicians, including CRNAs, regularly manage patients who suffer from acute and chronic pain. Engagement with various stakeholder groups will increase awareness of FDA's educational tools and resources and foster commitment to the common goal of more judicious use of opioids among all clinicians on the multidisciplinary patient care team.

We thank you for the opportunity to comment and further partner with the FDA on this important issue. Please do not hesitate to contact Lynn Reede, DNP, MBA, CRNA, FNAP, Senior Director, Professional Practice, at (847) 655-1136 or lreede@aana.com if you have any questions or comments.

Sincerely,

Juan F. Quintana, DNP, MHS, CRNA
AANA President

cc: Wanda O. Wilson, PhD, MSN, CRNA, AANA Executive Director/Chief Executive Officer
Lynn Reede, DNP, MBA, CRNA, FNAP, AANA Senior Director, Professional Practice

American Association of Nurse Anesthetists
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Remediation for Opioid Over-Prescribing by APRNs

National Council of State Boards of Nursing
Norfolk, Virginia, June 2016
Randall S. Hudspeth, PhD, APRN-CNS/CNP, FRE, FAANP

Objectives

1. To define overprescribing.
2. To discuss common instances when a BON engages to investigate APRNs involving opioid related issues.
3. To discuss issues to be considered in practice remediation following a discipline decision being made.
4. To review currently available methodologies and resources for over-prescribing remediation.

Defining Over Prescribing

Generally agreed to in the literature to be…

Prescribing opioids in (1) greater amounts and/or (2) on more occasions than is considered therapeutically necessary.

Opioid Prescribing Prevalence

By Provider Type

Analysis of total 2013 claims, most opioids were prescribed by:

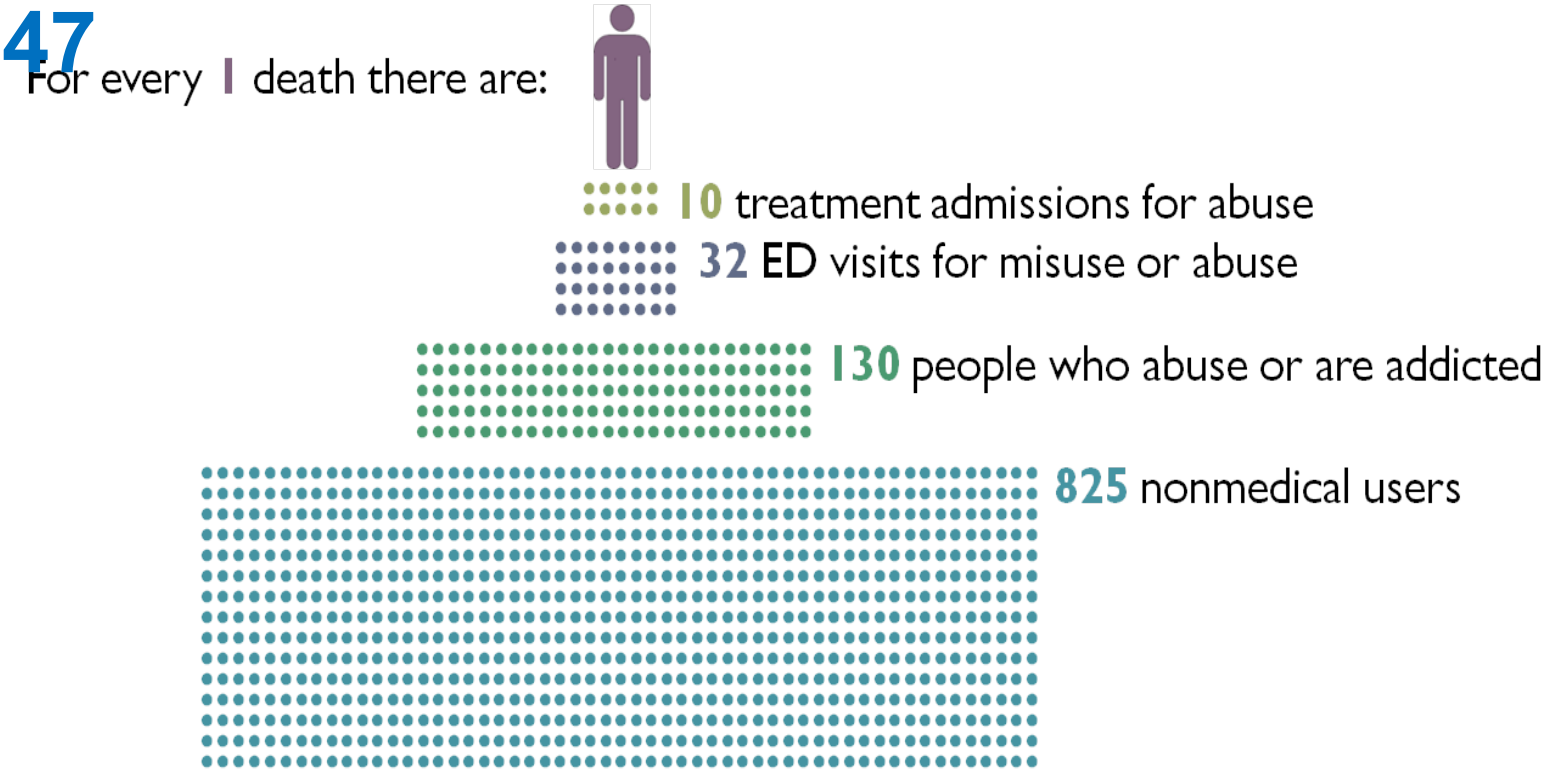
- **physicians in family practice (15.3 million prescriptions)**
- **physicians in internal medicine (12.8 million)**
- **nurse practitioners (4.1 million)**
- **physician assistants (3.1 million).**

Research identified the top 10% of opioid prescribers accounted for 57% of all opioid prescriptions.
For all Medicare drug data: the top 10% of all prescribers accounted for 63% of all prescriptions.

Reference: *JAMA Intern Med*. Published online December 14, 2015

Deaths Quadrupled since 2000

2014 DIED FROM OPIOID OVERDOSE = 28,647



Reference: CDC, available at: http://www.cdc.gov/drugoverdose/data/statedeaths.html

When are Regulatory Boards Most Commonly Involved?

1. When there is a complaint against an APRN regarding prescribing practices, patient care outcomes, or refusing to treat patients.

2. When there is a problem of diversion by the APRN.

3. When an APRN who is in a recovery program develops a condition that requires that they take a short term pain medication.

Trends and Issues Monitoring Opioid Over Prescribing

1. More complaints and issues are being addressed than in past years.
2. Inter-disciplinary Boards are inconsistent with managing prescribing related discipline.
3. More regulatory policies, national standards , assessment and ***monitoring tools*** are in place for use today.
4. **After a disciplinary decision is made, resources assisting the APRN to bring their practice back into compliance with standards and safety are difficult to find, access, utilize and implement.**
5. Often times, regulators charged to monitor remediation lack knowledge about the standards and safe practice themselves.

Risk Assessment Tools: Examples

Tool	# of items	Administered By
Patients considered for long-term opioid therapy:		
ORT Opioid Risk Tool	5	patient
SOAPP® Screener & Opioid Assessment for Patients w/ Pain	24, 14, & 5	patient
DIRE Diagnosis, Intractability, Risk, & Efficacy Score	7	clinician
Characterize misuse once opioid treatments begins:		
PMQ Pain Medication Questionnaire	26	patient
COMM Current Opioid Misuse Measure	17	patient
PDUQ Prescription Drug Use Questionnaire	40	clinician
Not specific to pain populations:		
CAGE-AID Cut Down, Annoyed, Guilty, Eye-Opener Tool, Adjusted to Include Drugs	4	clinician
RAFFT Relax, Alone, Friends, Family, Trouble	5	patient
DAST Drug Abuse Screening Test	28	patient
SBIRT Screening, Brief Intervention, & Referral to Treatment	Varies	clinician

Opioid Risk Tool (ORT)

Mark each box that applies	Female	Male
1. Family Hx of substance abuse		
Alcohol	☐ 1	☐ 3
Illegal drugs	☐ 2	☐ 3
Prescription drugs	☐ 4	☐ 4
2. Personal Hx of substance abuse		
Alcohol	☐ 3	☐ 3
Illegal drugs	☐ 4	☐ 4
Prescription drugs	☐ 5	☐ 5
3. Age between 16 & 45 yrs	☐ 1	☐ 1
4. Hx of preadolescent sexual abuse	☐ 3	☐ 0
5. Psychologic disease		
ADD, OCD, bipolar, schizophrenia	☐ 2	☐ 2
Depression	☐ 1	☐ 1

Scoring Totals:

Administer

On initial visit

Prior to opioid therapy

Scoring *(risk)*

0-3: low

4-7: moderate

≥8: high

Webster LR, Webster RM. *Pain Med.* 2005;6:432-42.

Current Prescribing Debate

ANDREW KOLODNY MD
EXEC DIR, PHYSICIANS FOR RESPONSIBLE OPIOID PRESCRIBING

"For the first time, the federal government is communicating clearly that the widespread practice of treating common pain conditions with long-term opioids is inappropriate.
The CDC is making it perfectly clear that medical practice needs to change because we're harming pain patients and fueling a public health crisis."

THOMAS FRIEDEN MD
CDC DIRECTOR

"We know of no other medication routinely used for a nonfatal condition that kills patients so frequently. We hope to see fewer deaths from opiates. That's the bottom line. These are really dangerous medications that carry the risk of addiction and death."

Current Prescribing Debate

CHRIS HANSON
PRESIDENT AMERICAN CANCER SOCIETY

"The move disregards the important role of pain management for cancer survivors who experience severe pain that limits their quality of life. Pain does not end when an individual completes treatment. Most often, cancer patients deal with lasting effects from their disease or treatment including pain for a significant period of time or indefinitely."

INDIVIDUAL PATIENT CONCERNS

- Chronic pain patients not happy…
- Multiple articles on patient concerns
- Example: New Hampshire

Opioid prescription debate: Grappling with pain and the law By MARK HAYWARD New Hampshire Union Leader [examples a NP]

- Reference: http://www.unionleader.com/Opioid-prescription-debate:-Grappling-with-pain-and-the-law#sthash.laF1MG4f.dpuf

Remediation Options Available to a BON Beyond Traditional Discipline

1. Alternative to Discipline programs focused on diversion/ misuse or abuse of controlled substances by impaired nurses can be a model for practice remediation.
2. Minimal organized programs are available nationally.
3. The professional literature has few resources to guide remediation efforts after discipline/license surrender or other negotiated agreements are completed.

BON Considerations in Crafting Practice Remediation Strategies

- Consider using a framework such as "Just Culture" or other decision guidance work to provide clarity to the process.
- Determine competency issues.
  - Is over opioid prescribing the only issue?
  - Competent APRN in a bad situation?
  - Knowledge deficit with negative outcome?
- Consider long term outcomes or remediation and if successes can be replicated with others?

Ethical Issues for BON Consideration in Prescribing Remediation

- Achieving the right balance in oversight of APRN opioid prescribing without dictating practice.
  - Each patient has unique needs and differing pathologies require different modes of treatment.
- Punishment versus professional development.
- Public Protection versus Access to Services.
- Public Protection versus provider development as a role of the BON?

Remediation Strategies

- Practice Controls
  - Prescriptive limitation
    - Required peer review and periodic reporting.
    - Varying levels of supervision or collaborative decisions on all or specific prescribing.
    - Restriction from opioid prescribing.
      - Limitations by category/schedule or full restriction.
    - Length of time for prescribing remediation limitations.

Remediation Strategies

- Education options
  - Practice Standards established by professional organizations.
  - Continuing Education in safe opioid prescribing
    - NP Healthcare Foundation resources at: https://wwww.nphealthcarefoundation.org/ce/
  - Participation in formal programs such as the FDA endorsed "Opioid Prescribing, Safe Practice, Changing Lives"… formerly "REMS."

Education Resources

- National Association Guidelines
  - Federation of State Medical Boards.
  - Pain Societies for professionals.
  - Pain Organizations by diseases for general public and providers.
- CDC Guidelines of March 2016.

- **SCOPE**-Safe and Competent Opioid Prescribing Education

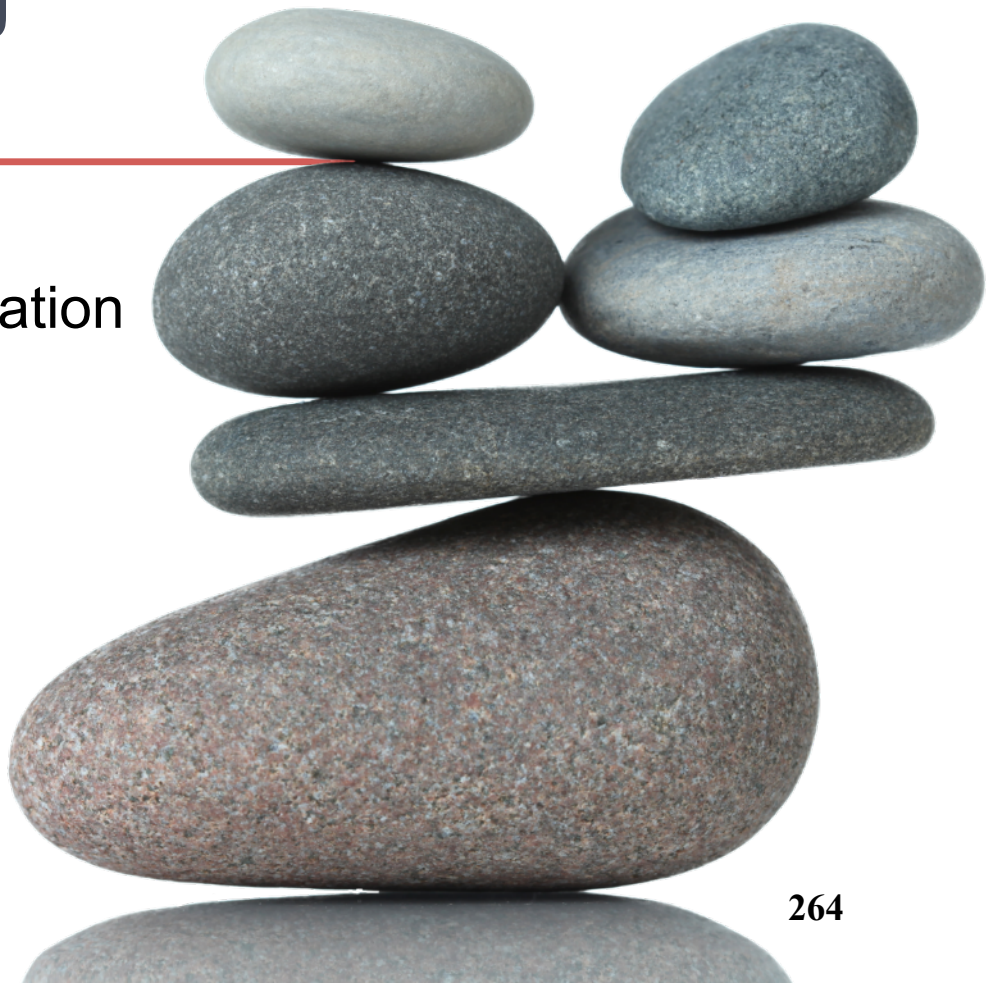
available at:
https://www.scopeofpain.com/

Live conferences
Online training
Printed materials
Toolkits

ER/LA OPIOID REMS:

Achieving Safe Use While Improving Patient Care

Presented by CO*RE
Collaboration for REMS Education
www.core-rems.org



Collaborative for
REMS Education

Organizations

Founding Partners

- American Pain Society (APS)
- American Academy of Hospice and Palliative Medicine (AAHPM)
- American Association of Nurse Practitioners (AANP)
- American Academy of Physician Assistants (AAPA)
- American Osteopathic Association (AOA)
- American Society of Addiction Medicine (ASAM)
- California Academy of Family Physicians (CAFP)
- Healthcare Performance Consulting (HPC)
- Interstate Postgraduate Medical Association (IPMA)
- Nurse Practitioner Healthcare Foundation (NPHF)

Strategic Partners

- Physicians Institute for Excellence in Medicine which coordinates 15 state medical societies
- Medscape
- American Academy of Family Physicians
- American College of Emergency Physicians (***New in 2015***)

AAHPM
American Academy of Hospice and Palliative Medicine

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American Pain Society
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EDUCATION
TREATMENT
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Contemporary Issues Helping to Control Opioid Misuse

- Electronic Prescribing
- Electronic Medical Records
- Use of nationally vetted opioid risk abuse assessment tools
- Screenings—Urine drug tests, depression inventories
- Introduction of Informed Consents for opioid prescribing
- Patient and Provider Agreements
- Prescription Drug Monitoring Programs--PDMP

Possible Future BON Considerations

- Partnering with state Boards Of Pharmacy to publish access rates of PDMPs by APRNs.
- Required CE linked to controlled substance prescribing authority.
- Peer review requirement specific to opioid prescribing and use of nationally vetted pain management and safe prescribing standards.
- Endorse Opioid Prescribing Guidelines similar to Federation of State Medical Boards.

2016 NCSBN DISCIPLINE CASE MANAGEMENT CONFERENCE

Tennessee Board of Nursing

Elizabeth Lund, MSN,RN, Executive Director

06/08/2016

Teamwork to Address Prevention & Detection of Narcotic Overprescribing

Key Points

- Tennessee story
- Stimulate ideas
- Data-driven
- Teamwork, communication, trust

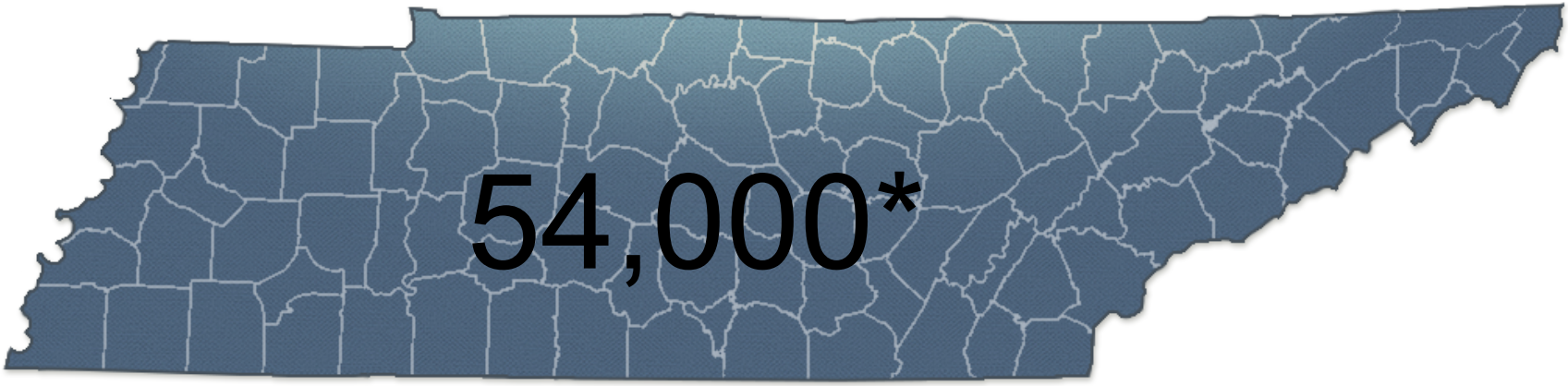
Progress!

Setting the Stage

Tennessee - Umbrella Agency

- 30 Health Related Boards
  - Office of General Counsel
    - Attorneys assigned to boards
- Investigations Division
    - RN investigators
    - Regional offices
- History of working autonomously

Prescribing Licensees



*10,500 (21%)
Advanced Practice Registered Nurses

Problem

- Prescription drug abuse identified as priority

C-II Controlled Substance Utilization by State

A State Comparison: Annual Prescriptions per Capita 2014 CII Products					
Rank	State	Rx per Capita	Rank	State	Rx per Capita
1	Alabama	1.4	27	District of Columbia	0.8
2	**Tennessee**	**1.3**	28	Massachusetts	0.8
3	Louisiana	1.2	29	Virginia	0.8
4	West Virginia	1.2	30	Iowa	0.8
5	Mississippi	1.2	31	Nebraska	0.8
6	Kentucky	1.2	32	Montana	0.8
7	Arkansas	1.2	33	Vermont	0.8
8	South Carolina	1.1	34	Washington	0.8
9	Oklahoma	1.1	35	Connecticut	0.8
10	Michigan	1.0	36	Arizona	0.7
11	Indiana	1.0	37	Maryland	0.7
12	North Carolina	1.0	38	Wyoming	0.7
13	Delaware	1.0	39	North Dakota	0.7
14	Kansas	1.0	40	Colorado	0.7
15	Ohio	1.0	41	South Dakota	0.7
16	Rhode Island	0.9	42	Illinois	0.7
17	Maine	0.9	43	New Mexico	0.7
18	Missouri	0.9	44	Florida	0.7
19	Utah	0.9	45	Minnesota	0.7
20	Oregon	0.9	46	Texas	0.7
21	Georgia	0.9	47	Alaska	0.6
22	Pennsylvania	0.9	48	New Jersey	0.6
23	New Hampshire	0.9	49	New York	0.6
24	Idaho	0.8	50	California	0.5
25	Nevada	0.8	51	Hawaii	0.5
26	Wisconsin	0.8	52	Puerto Rico	N/A
All states = 0.8 annual prescriptions per capita					

2013 USA total CII prescriptions = 257,450,331; TN total = 8,954,973
2014 USA total CII prescriptions = 249,953,231; TN total = 8,668,742

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TN's Prescription Drug Problem

275.5 Million Hydrocodone Pills

51 pills per every Tennessean over age 12

116.6 Million Xanax Pills

22 pills per every Tennessean over age 12

113.5 Million Oxycodone Pills

21 pills per every Tennessean over age 12

Defining Morphine Milligram Equivalents

- MME stands for Morphine Milligram Equivalents.
- Different opioids have different morphine equivalents and are calculated in relation to morphine.

Morphine 1 mg = 1 MME

Hydrocodone 1 mg = 1 MME

Converting Opioids to Morphine Milligram Equivalents

Formula for MME per day:

$$\frac{\text{Strength(in mg) X Morphine Equivalent X Quantity}}{\text{Number of days}}$$

Conversions to Morphine Milligram Equivalents:

Opioid name	Milligrams (mg) of opioid	Equivalent milligrams (mg) of morphine
Buprenorphine (Oral)	1	10
Fentanyl	1	7.2
Hydromorphone	1	4
Methadone	1	3
Oxymorphone	1	3
Oxycodone	1	1.5
Hydrocodone	1	1
Morphine	1	1
Codeine	1	0.15
Tramadol	1	0.1

Example: **80 MME**

=

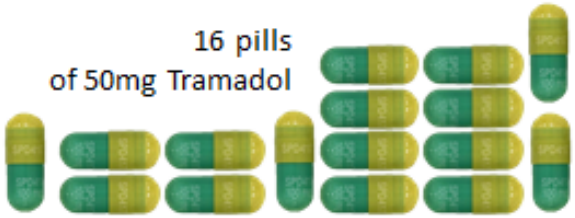
1 pill of 8mg Buprenorphine

=

2.5 pills of 8mg Hydromorphone

=

16 pills of 50mg Tramadol



Top Prescribers

Guidelines recommend

<120 MEDD

- Hydrocodone/ Percocet
  - Hydrocodone 10 mg

    12 pills per day
  - Percocet 10 mg

    8 pill per day

CSMD reveals up to

500 MEDD per patient

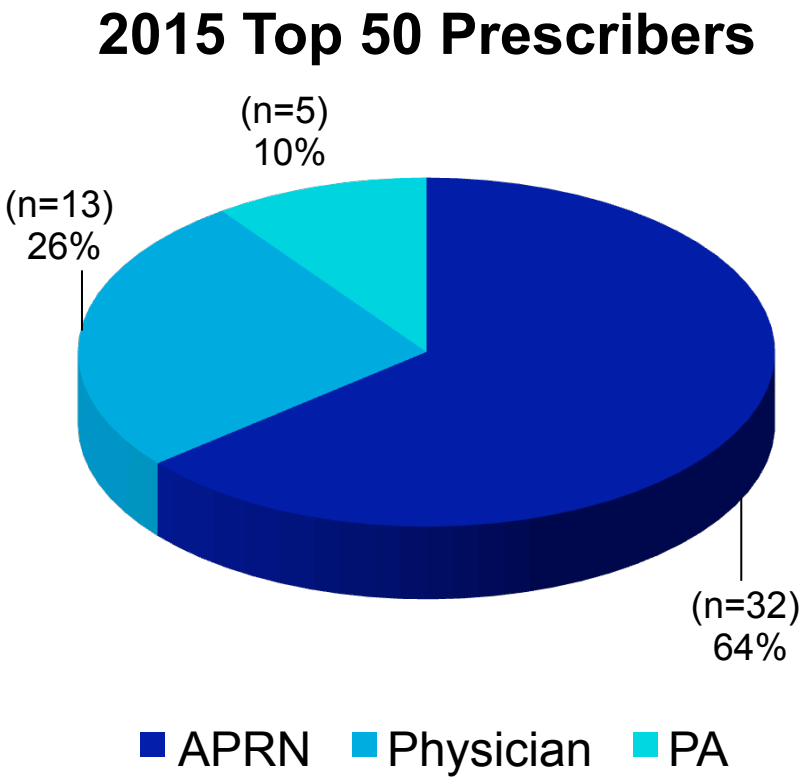
(have seen up to 700)

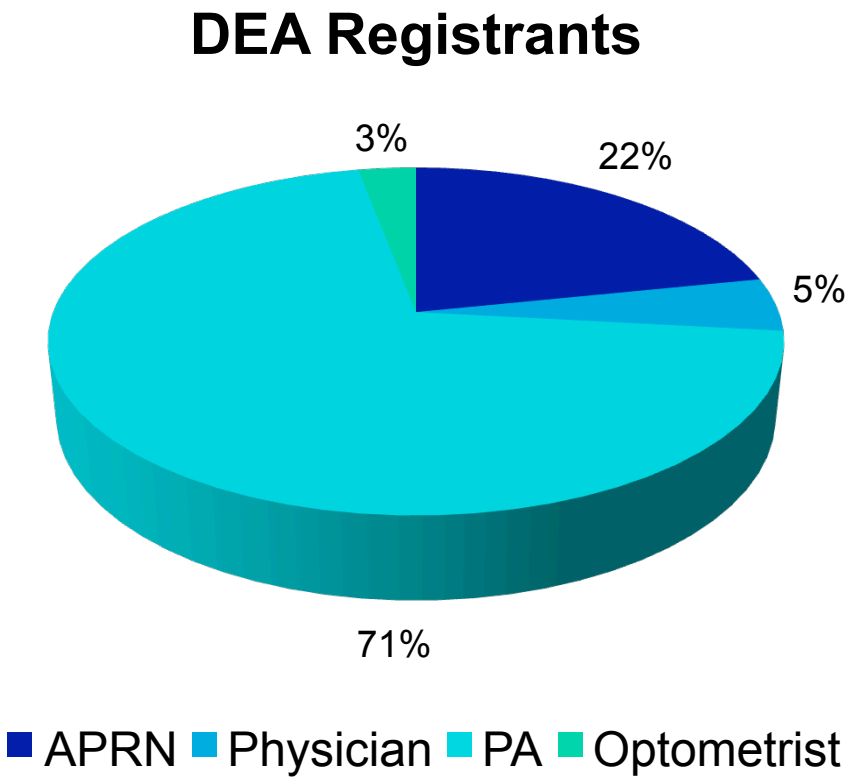
- Hydrocodone/ Percocet
  - Hydr

    50
  - Perc

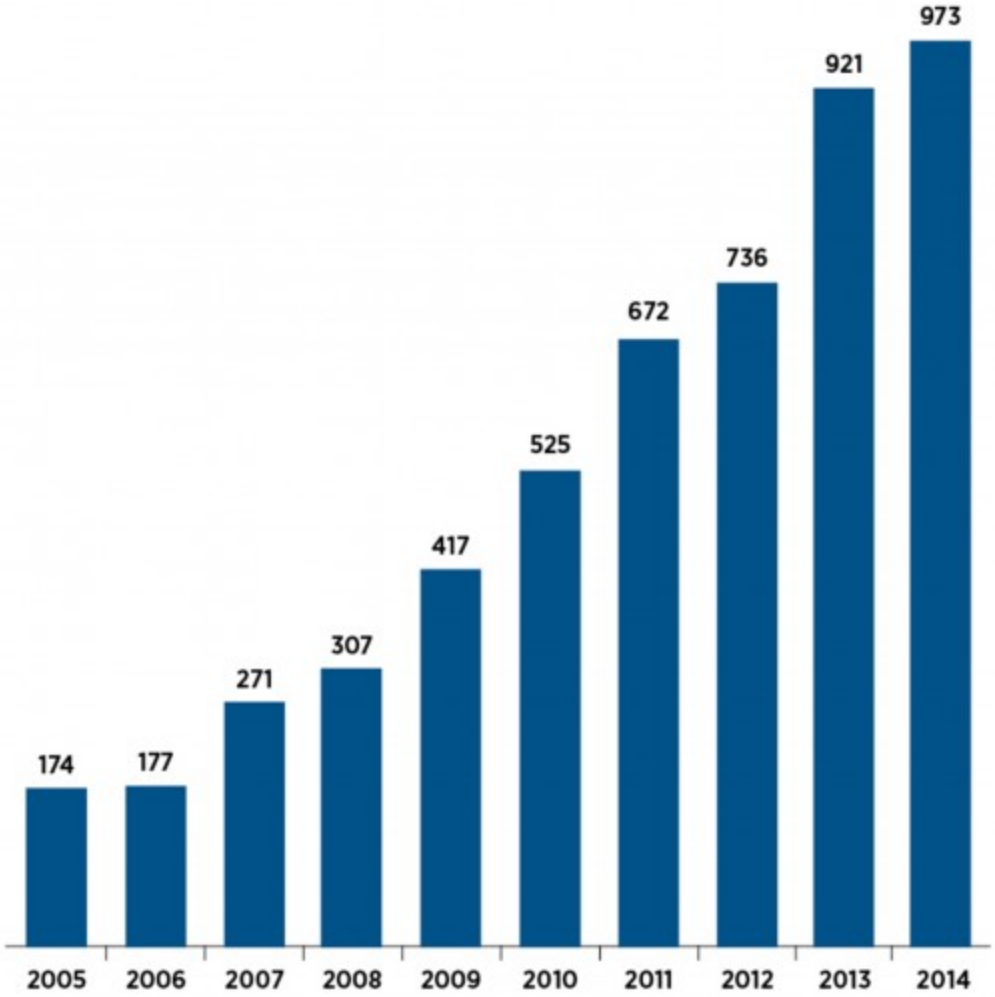
    33

Comparison of Top 50 to Prescribers with DEA



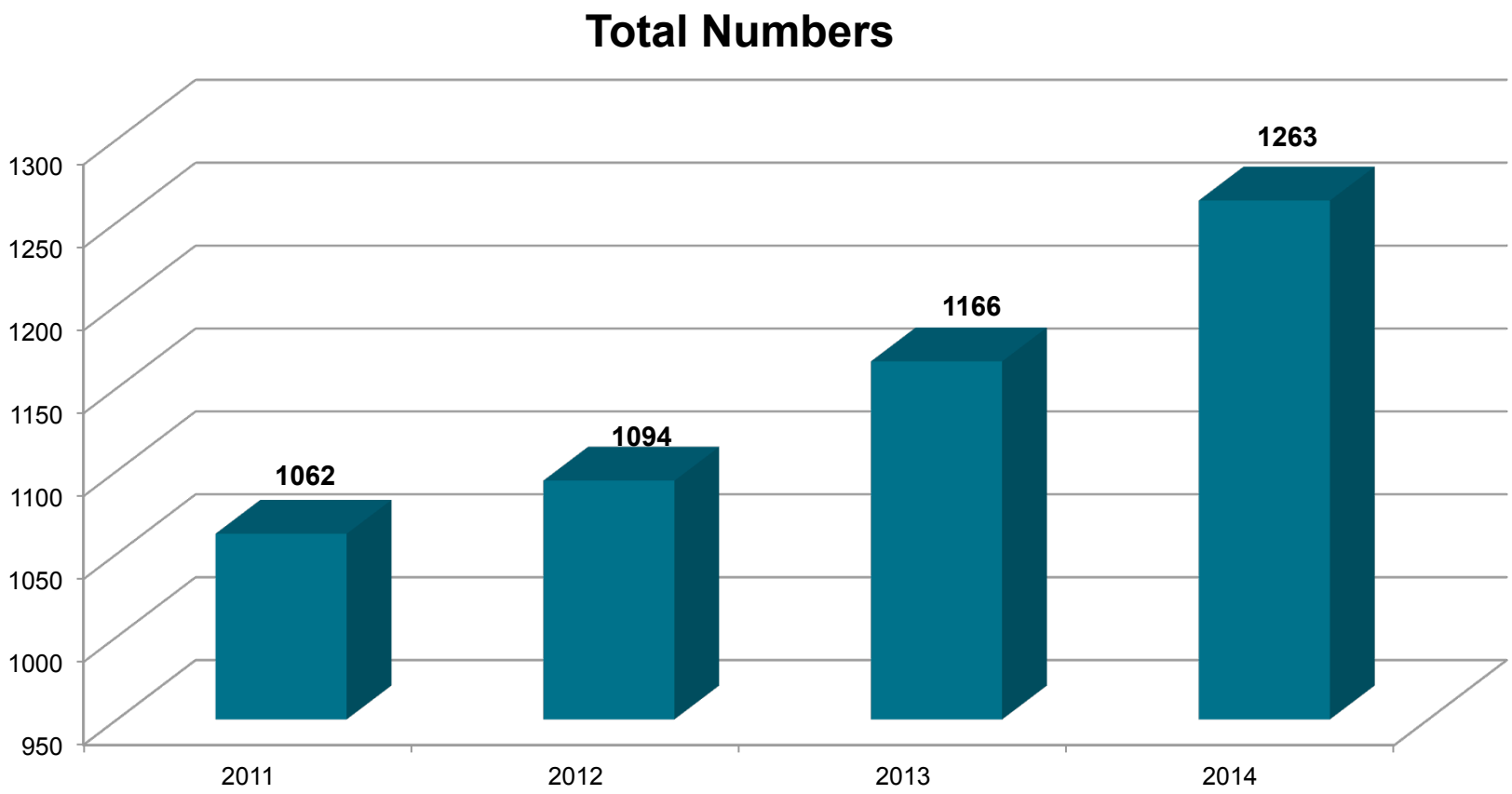


Number of Inpatient Hospitalizations with Any Diagnosis of Neonatal Abstinence Syndrome in Tennessee, 2005-2014



Source: Better Tennessee website:
http://bettertennessee.com/mist/

Drug Overdose Death: 2011-2014



Source: TN Department of Health

Legislative Efforts

Prescription Safety Act of 2012

Controlled Substance Monitoring Database (CSMD)

- Requires registration
- Mandates query before initial prescription of opioid & benzodiazepine
- Must identify method of payment
- Pharmacy must report prescriptions within 7 days

Authorizes agreements with other states for data sharing

Addison Sharp Prescription Regulatory Act of 2013

- Mandates chronic pain treatment guidelines be developed and updated annually
  - Panel of experts
- Approved by the boards
  - Adopted as policy
- Disseminated to licensees
  - Newsletters
  - Symposia
- Requires 2 hours of CE related to controlled substance prescribing to include chronic pain guidelines

“Top 50 Act” of 2013

- Identify top 50 prescribers of controlled substances
- Send letter to prescriber and supervisor
  - Response requested

“Chronic Pain Guidelines Act” of 2014

- Chronic Pain Guidelines written by January 1, 2014
- All prescribers with DEA 2 hours CME every 2 years
- Prescribe 30 days at a time Schedule II-IV
- By January 1, 2014 the commissioner shall develop recommended treatment guidelines for prescribing opioids, benzodiazepines, barbiturates, and carisoprodol. That can be used in the state as guide for caring for

“Naloxone Act” of 2015

- Allows a licensed healthcare practitioner to prescribe naloxone to a person at risk of having an opiate related overdose, or a family member or friend of the at risk individual
- Requires training in administration of naloxone prior to drug being prescribed (Training being prepared by TDH)
- Provides immunity from civil prosecution for both prescribing practitioner and indivic administering naloxone

Teamwork Begins

Controlled Substance Monitoring Data Base Committee

- Created in 2002
- Examine database information to ID and report unusual patterns of prescribing and dispensing controlled substances
- Member representatives from prescribing boards
- Currently BON chair serves on the committee

Environmental Challenges

- Nursing Association introduces full practice authority bill
- Medical Association mobilized
- APRNs in the hot seat
- Denial, Anger and Suspicion
- What we were doing was not effective and nursing was not at the table
- How to turn the tide and contribute to solutions to beat the epidemic?

APRN Competency Audit

- Increased audit
- Notified stakeholders of increased audit
- Quickly identified issues
- Quadrupled the percentage of records audited:
  - notice and formulary
  - current national certification
  - 1 contact hour of continuing education addressing controlled substances prescribing

Audit Changes Made

- Simplified the audit form and instructions
- Simplified the formulary
  - 1 page
  - Check list
- Collected data on compliance
  - Initial
  - Final

Prescription Drug Abuse Task Force

- Purpose
  - Analyze and interpret data
  - Collaborate
  - Discuss legislation
- Team composition
  - Medical
  - Nursing
  - Pharmacy
  - Legal
  - Commissioner's staff
  - CSMD staff

Result: Began to understand one another's culture

BON Contribution to Prescription Drug Abuse Task Force

- Examined data from APRN audits
- Analyzed data found in CSMD
  - Identified top 50 prescribers (information confidential)
- Evaluated board disciplinary action from overprescribing team

Education is Key

- Face-to-face contact hours on prescribing practices and registration in the data base (CSMD) as part of an interdisciplinary team
- Stepped up email push notifications regarding new prescriptive requirements
- Medical Director of Special Projects provides board member education at each quarterly meeting

Team Initiatives

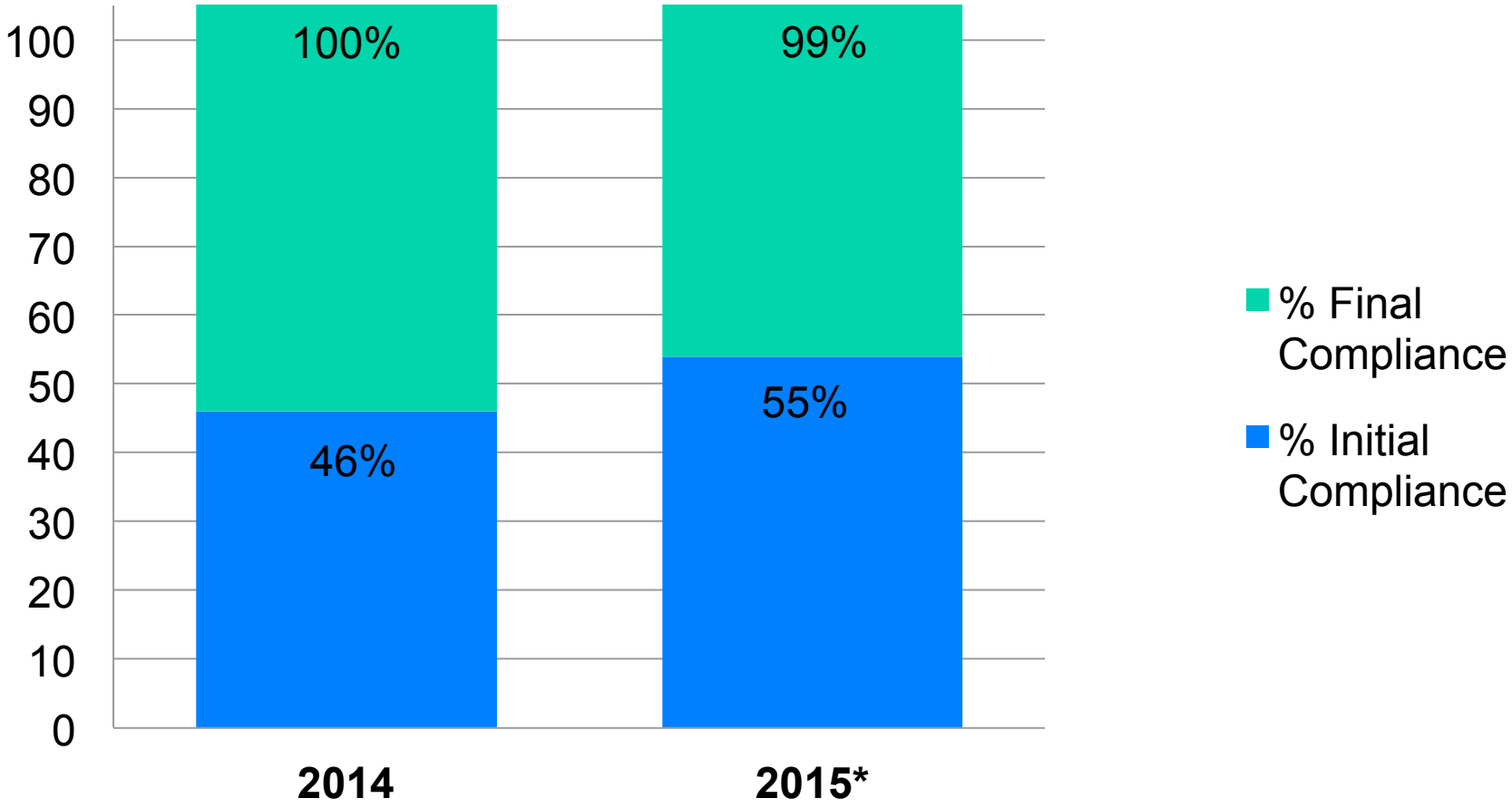
- Endorsed "Tennessee Clinical Practice Guidelines for Outpatient management of Chronic Non-Malignant Pain" (Chronic Pain Guidelines)
- Vet Board released a position to nursing for APRN
- Additionally - Nursing Board
  - Committed to continuing education of board members and staff
  - Hired a full time APRN to work with interdisciplinary overprescribing team

Detection/Education

Because the majority of the top 50 prescribers are APRNs

- Stepped up audits
- Purposeful and random audits
- Education vs enforcement
- Created opportunity to communicate

APRN Audit 2014 - 2015 Compliance



**Final compliance calculated when audit is closed.*

Survey APRN Nursing Education Programs

- Contact hours re overprescribing
- Findings: No consistency
- Prescription Drug Abuse Task Force developed and distributed educational DVD to education programs

Strategic Map

Public Health Approach to the Opioid Abuse Epidemic
Tennessee Department of Health Strategic Map, 2016

Adopted 1/11/16

Reduce Opioid Misuse, Abuse & Overdose

A	B	C	D	E
Improve Primary Prevention	Improve Monitoring and Surveillance	Improve Regulation and Enforcement	Increase Utilization of Treatment (2º Prevention)	Increase Access to Appropriate Pain Management
Improve education for consumers, families & HCWs	Optimize use of the CSMD	Provide prescriber/ dispenser education on regulation & enforcement	Destigmatize & approach addiction as a treatable chronic illness	Require pain management clinic physicians to have specialty certification
Expand use of optimal prescribing guidelines	Link other data sources to the CSMD	Improve collaboration with law enforcement	Expand SBIRT training and use	Develop a model for desirable integrated pain practices
Actively support community coalitions	Improve the high risk patient model	Expedite investigations supporting Board oversight of prescribers	Expand appropriate use of MAT	Increase access for uninsured
Expand efforts to reduce NAS	Develop a high risk prescriber model for individuals and practices	Eliminate "Pill Mills"	Expand treatment alternatives to incarceration	Work with academic partners to improve training of prescribers
Facilitate community interventions, including safe disposal of drugs	Develop a high risk dispenser model	Improve legislation to allow proactive regulation	Partner with Mental Health to expand treatment options for opioid misuse	Describe how patient care is impacted by sudden clinic closure
Reduce harm from needle use	Improve proactive use of clinical monitoring tools		Advocate for Prescription for Success including treatment and care	Expand the availability and use of Naloxone

Expand and Strengthen Key Partnerships and Collaborative Infrastructure

Secure/Realign Resources and Infrastructure to Implement Comprehensive Approaches

Use Data, Evaluation and Research to Inform Interventions and Continuous Improvement

Improve Primary Prevention

- Improve education for consumers, families, and health care workers
  - Focus 12-25 y/o
  - Repurpose meth-lab trailers to opioid education
  - Symposia
- Expand use of optimal prescribing guidelines
  - ED and pain management
- Actively support community coalitions
  - Anti-drug coalitions, other across state

Improve Primary Prevention

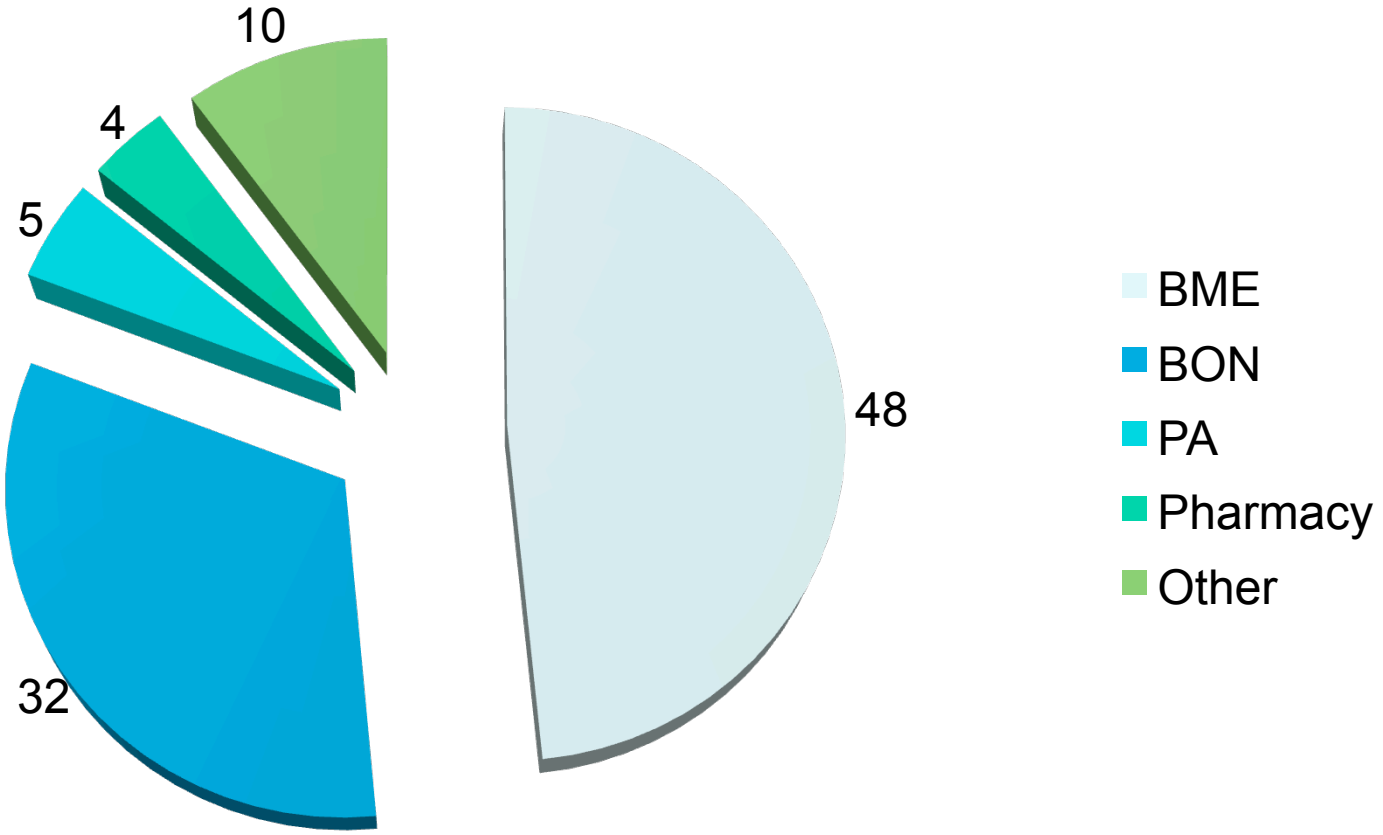
- Expand efforts to reduce NAS
  - New RN position
- Facilitate community interventions, including safe disposal of drugs
  - Public Service Announcements
- Expand the availability and use of naloxone
  - Pharmacist prescribe

Results

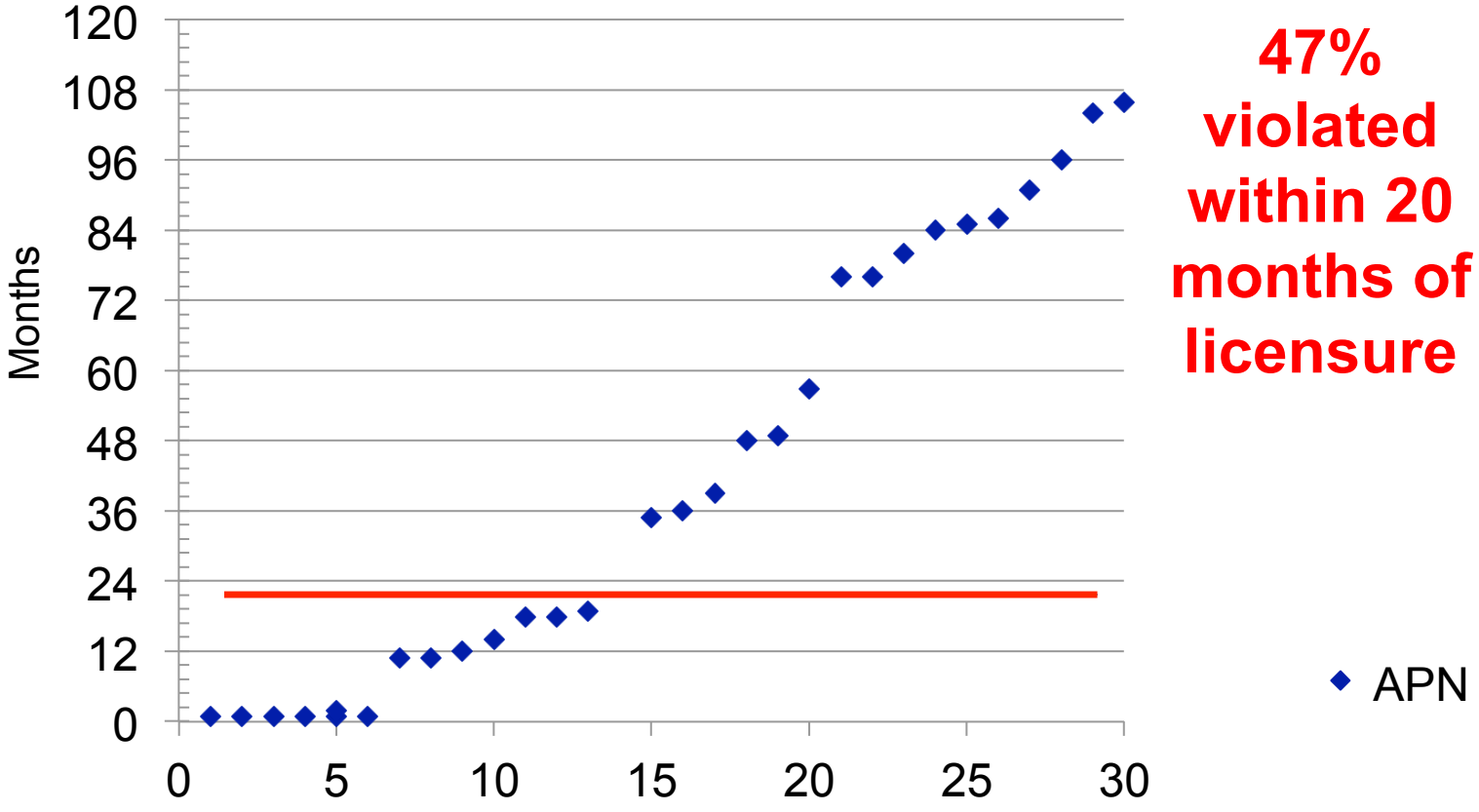
Over Prescribing Disciplinary Actions

N=99

2013-Present

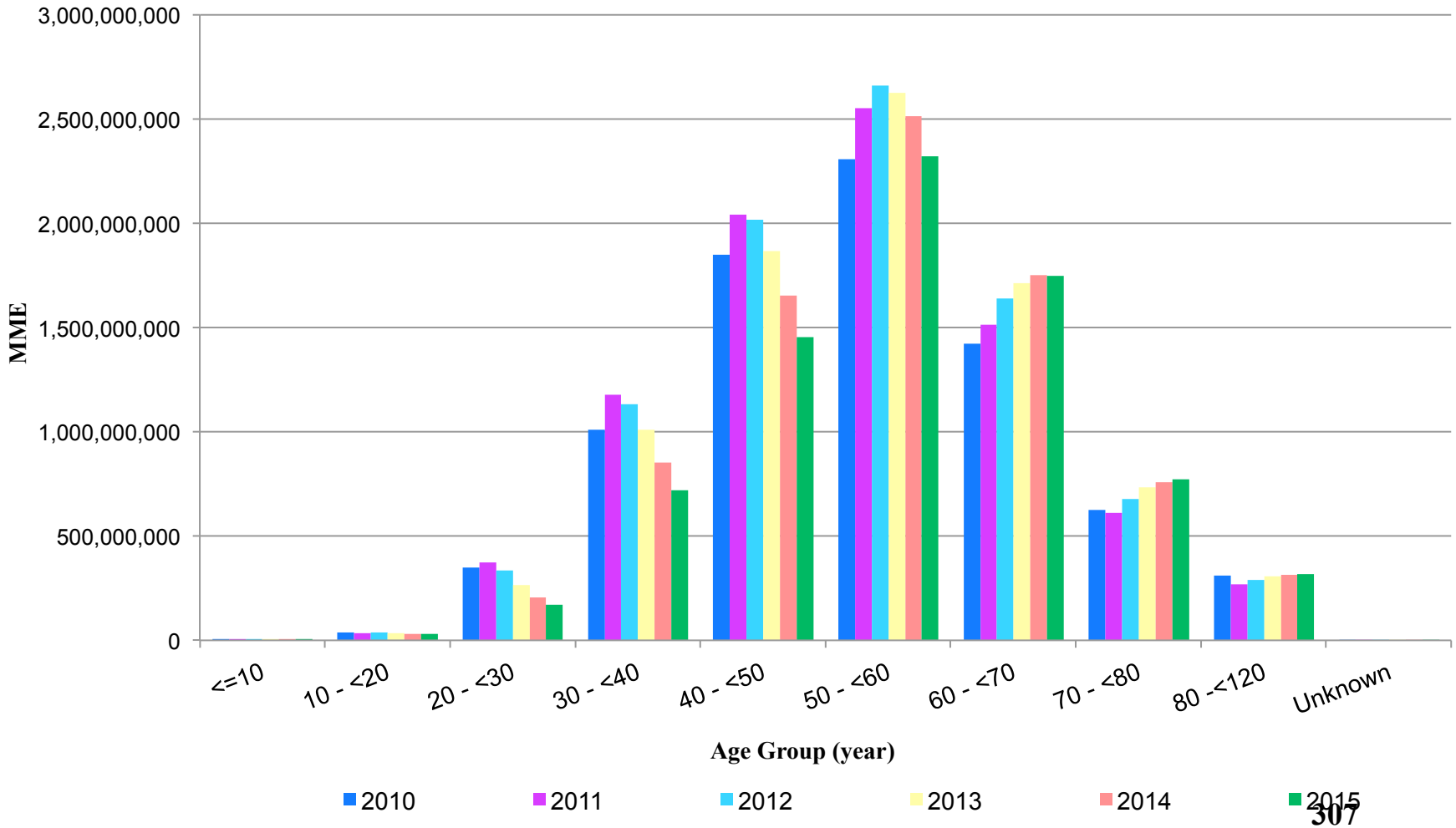


Months licensed prior to violation N=30



April 2013 thru February 2016

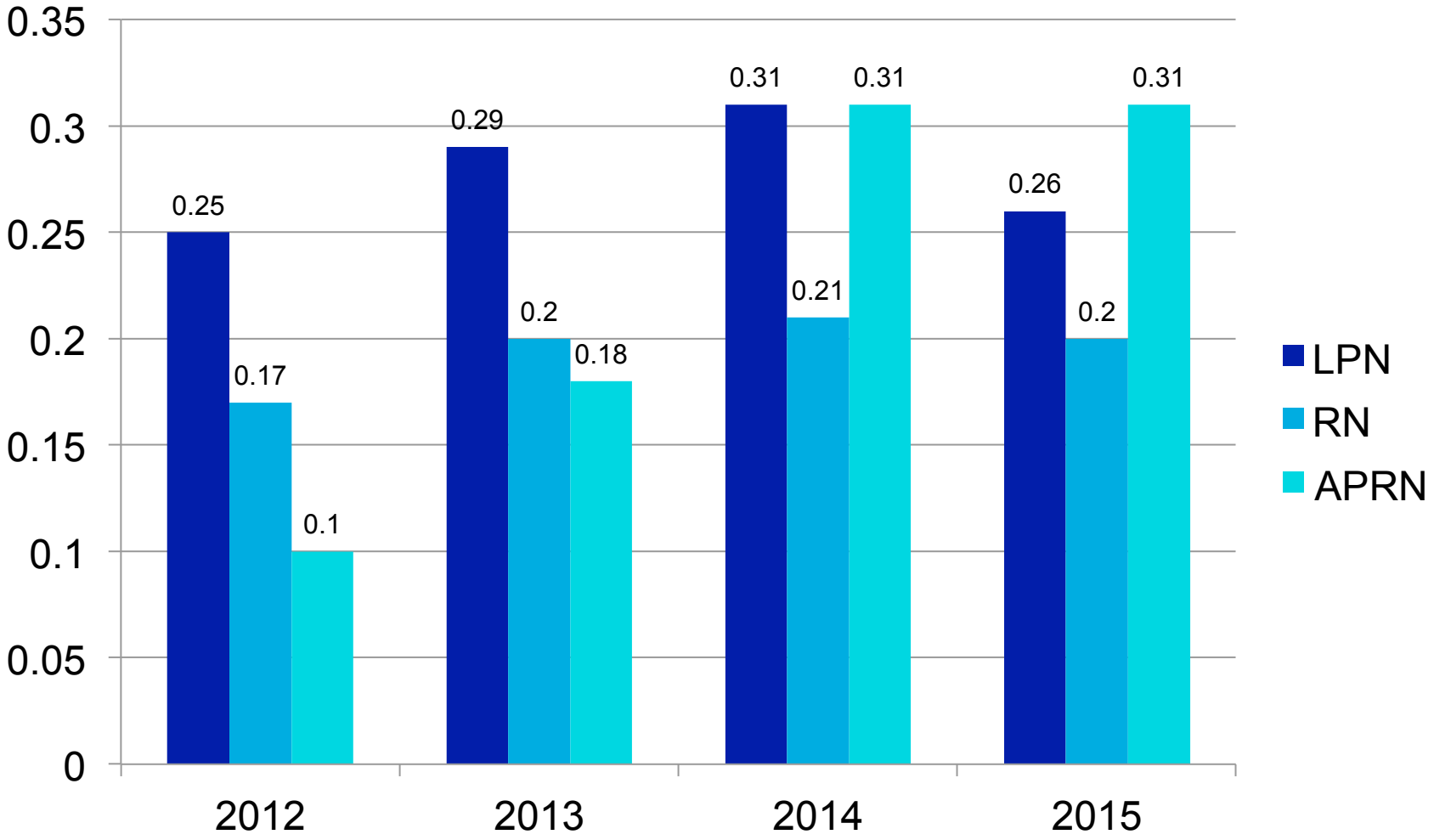
Morphine Milligram Equivalents of Opioids Dispensed to TN Patients by Age



Annual Morphine Milligram Equivalents per Capita for Pain

Year	Amount
2010	1130
2011	1233
2012	1250
2013	1230
2014	1164
2015	901

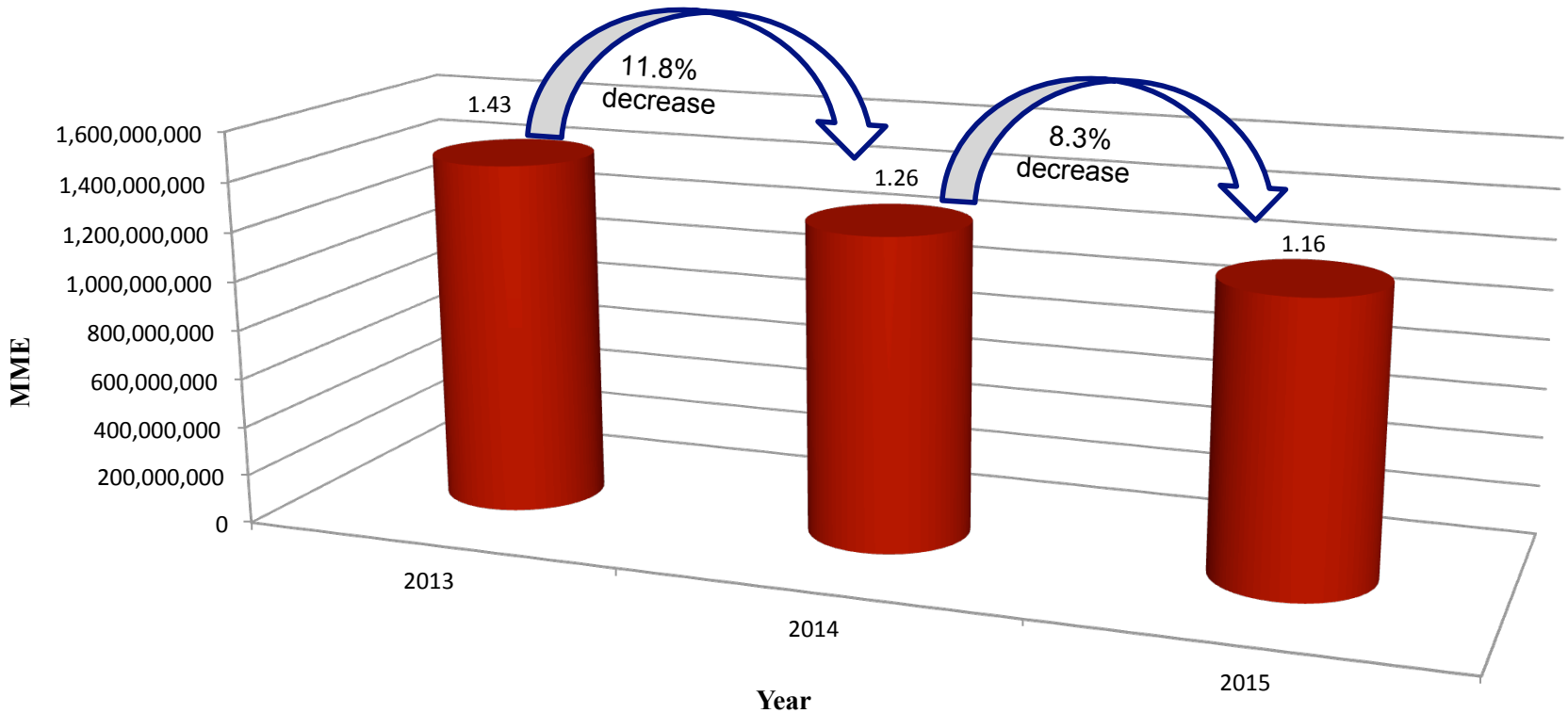
Percent of Licenses Disciplined



Analysis of Top 50

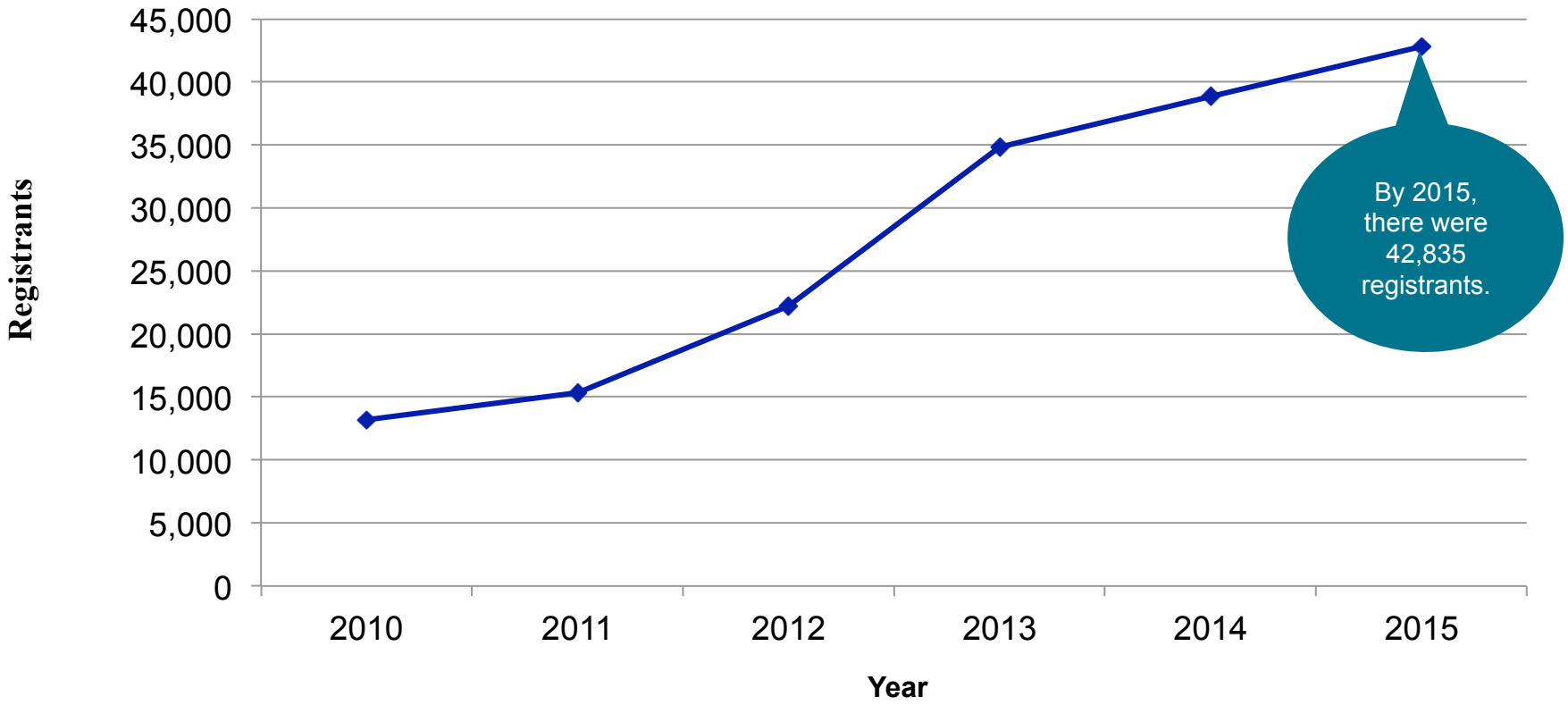
- Education
  - Type of Degree
  - National Certification
- Demographics
  - Age
  - Physical Location
  - Gender
- Role
- Length of Licensure

Morphine Milligram Equivalents Prescribed by Top 50 Prescribers and Dispensed in 2013 - 2015*



*MME in 2013 and 2014 covered 12-month opioid prescriptions written by the top 50 prescribers from April 1 of preceding year to March 31 of current year; MME in 2015 covered opioid prescriptions filled by the patients of the top 50 prescribers during January 1, 2014 to December 31, 2014.

Number of Registrants of the CSMD, 2010-2015



Chronic Pain Guidelines

- Interdisciplinary panel wrote chronic pain guidelines
- BON endorsed “Tennessee Clinical Practice Guidelines for Outpatient Management of Chronic Non-Malignant Pain”—Fall 2014
- Panel reconvened in August 2015 to review/ revise guidelines
  - BON endorsed revisions February 2016

Education/Outreach

- Free symposia providing contact hours on prescribing practices and chronic pain guidelines as part of an interdisciplinary team

- Community stakeholders made the presentations available simultaneously online, archived the content and made the program available online

Board Member Education

- Medical Director of Special Projects provides board member education at each quarterly meeting
- Board supports staff and board member continuing education
- NCSBN “HIVE” a resource comp
  boards of nursing initiatives

Board Actions

- Endorsed Tennessee Chronic Pain Guidelines—Fall 2014, reaffirmed February 2016
- Increased APRN continuing education requirement of two contact hours addressing controlled substances prescribing including Tennessee Chronic Pain Guidelines
- Increased board panels from two to three to expedite hearings
- Supported APRN staff positio

Future

- Continue/grow teams
- Extend efforts to RNs and LPNs in fighting the opioid epidemic
- Expand collaboration with health care facilities
  - Annual HCF training
- Include Education in all forums
  - School site visits
  - Student presentations
  - Facility In-service

Introduction for the FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics

In April 2011, FDA announced the elements of a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of extended-release and long-acting (ER/LA) opioid analgesics outweigh the risks. The REMS supports national efforts to address the prescription drug abuse epidemic.

As part of the REMS, all ER/LA opioid analgesic companies must provide:

- Education for prescribers of these medications, which will be provided through accredited continuing education (CE) activities supported by independent educational grants from ER/LA opioid analgesic companies.

- Information that prescribers can use when counseling patients about the risks and benefits of ER/LA opioid analgesic use.

FDA developed core messages to be communicated to prescribers in the Blueprint for Prescriber Education (FDA Blueprint), published the draft FDA Blueprint for public comment, and considered the public comments when finalizing the FDA Blueprint. This final FDA Blueprint contains the core educational messages. It is approved as part of the ER/LA Opioid Analgesic REMS and will remain posted on the FDA website for use by CE providers to develop the actual CE activity. A list of all REMS-compliant CE activities that are supported by independent educational grants from the ER/LA opioid analgesic companies to accredited CE providers will be posted at www.ER-LA-opioidREMS.com as that information becomes available.

The CE activities provided under the FDA Blueprint will focus on the safe prescribing of ER/LA opioid analgesics and consist of a core content of about three hours. The content is directed to prescribers of ER/LA opioid analgesics, but also may be relevant for other healthcare professionals (e.g., pharmacists). The course work is not intended to be exhaustive nor a substitute for a more comprehensive pain management course.

Accrediting bodies and CE providers will ensure that the CE activities developed under this REMS will be in compliance with the standards for CE of the Accreditation Council for Continuing Medical Education (ACCME) [1,2] or another CE accrediting body as appropriate to the prescribers' medical specialty or healthcare profession.

For additional information from FDA, including more detailed Questions and Answers about the REMS for ER/LA Opioid Analgesics, see http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm163647.htm.

[1] Accreditation Council for Continuing Medical Education. 2016. *Accreditation Requirements. Criteria for CME Providers-Accreditation Criteria*. Accessed on February 22, 2016.
[2] Accreditation Council for Continuing Medical Education. 2016. *Accreditation Requirements. Criteria for CME Providers-Standards for Commercial Support*. Accessed on February 22, 2016.

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics

Why Prescriber Education is Important

Health care professionals who prescribe extended-release (ER) and long-acting (LA) opioid analgesics (hereafter referred to as ER/LA opioid analgesics) are in a key position to balance the benefits of prescribing ER/LA opioid analgesics to treat pain against the risks of serious adverse outcomes including addiction, unintentional overdose, and death. Opioid misuse and abuse, resulting in injury and death, has emerged as a major public health problem.

- Based on the 2010 National Survey on Drug Use and Health, public health experts estimate more than 35 million Americans age 12 and older used an opioid analgesic for non-medical use some time in their life—an increase from about 30 million in 2002.[3]
- In 2009, there were nearly 343,000 emergency department visits involving nonmedical use of opioid analgesics.[4]
- In 2008, nearly 36,500 Americans died from drug poisonings, and of these, nearly 14,800 deaths involved opioid analgesics.[5]
- Improper use of any opioid can result in serious side effects including overdose and death, and this risk can be greater with ER/LA opioid analgesics.

Appropriate prescribing practices and patient education are important steps to help address this public health problem. Health care professionals who prescribe ER/LA opioid analgesics have a responsibility to help ensure the safe and effective use of these drug products. ER/LA opioid analgesics should be prescribed only by health care professionals who are knowledgeable in the use of potent opioids for the management of pain.

The expected results of the prescriber education in this REMS are that the prescribers will:

a. Understand how to assess patients for treatment with ER/LA opioid analgesics.
b. Be familiar with how to initiate therapy, modify dose, and discontinue use of ER/LA opioid analgesics.
c. Be knowledgeable about how to manage ongoing therapy with ER/LA opioid analgesics.
d. Know how to counsel patients and caregivers about the safe use of ER/LA opioid analgesics, including proper storage and disposal.
e. Be familiar with general and product-specific drug information concerning ER/LA opioid analgesics.

I. Assessing Patients for Treatment with ER/LA Opioid Analgesic Therapy

a. Prescribers should consider risks involved with ER/LA opioid analgesics and balance these against potential benefits. Risks include:
    i. Overdose with ER/LA formulations, as most dosage units contain more opioid than immediate-release formulations.

---

[3]Substance Abuse and Mental Health Services Administration. 2011. *Results from the 2010 National Survey on Drug Use and Health: Detailed Table*, Table 7.1.a. Rockville, MD. http://www.samhsa.gov/data/NSDUH/2k10NSDUH/tabs/Sect7peTabs1to45.htm#Tab7.1A. Accessed on February 22, 2016.

[4]Substance Abuse and Mental Health Services Administration. 2011. *Drug Abuse Warning Network, 2009: National Estimates of Drug-Related Emergency Department Visits*, Table 19. Rockville, MD. http://www.samhsa.gov/data/2k11/DAWN/2k9DAWNED/HTML/DAWN2k9ED.htm#Tab19. Accessed on February 22, 2016.

[5]Warner M, Chen LH, Makuc DM, Anderson RN, and Miniño AM. 2011. Drug Poisoning Deaths in the United States, 1980–2008, in U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, *NCHS Data Brief*, *No 81*. December 2011. Hyattsville, MD. http://www.cdc.gov/nchs/data/databriefs/db81.pdf. Accessed on February 22, 2016.

ii. Life-threatening respiratory depression
iii. Abuse by patient or household contacts
iv. Misuse and addiction.
v. Physical dependence and tolerance.
vi. Interactions with other medications and substances (See table in Section VI for product-specific information).
vii. Risk of neonatal opioid withdrawal syndrome with prolonged use during pregnancy.
viii. Inadvertent exposure/ingestion by household contacts, especially children.

b. Prescribers should assess each patient's risk of abuse, including substance use and psychiatric history. Prescribers should:
   i. Obtain a complete history and conduct a complete physical examination. The history should include assessment for a family history of substance abuse and psychiatric disorders, as well as special considerations regarding dose and adverse effects in geriatric patients, pregnant women, and children.
      - A history of substance abuse does not prohibit treatment with ER/LA opioid analgesics but may require additional monitoring and expert consultation.
   ii. Be knowledgeable about risk factors for opioid abuse.
   iii. Understand and appropriately use screening tools for addiction or abuse to help assess potential risks associated with chronic opioid therapy and to help manage patients using ER/LA opioid analgesics (e.g., structured interview tools).
   iv. Adequately document all patient interactions and treatment plans.
c. Prescribers should understand when to appropriately refer high risk patients to pain management specialists.
d. Prescribers should understand opioid tolerance criteria as defined in the product labeling.
   - Prescribers should know which products and which doses are indicated for use only in opioid-tolerant patients. (See table in Section VI for product-specific information).

II. Initiating Therapy, Modifying Dosing, and Discontinuing Use of ER/LA Opioid Analgesics

a. Prescribers should have awareness of federal and state regulations on opioid prescribing.
b. Prescribers should be aware that:
   i. Dose selection is critical, particularly when initiating therapy in opioid non-tolerant patients.
   ii. Some ER/LA opioid analgesics are only appropriate for opioid-tolerant patients. **(**See table in Section VI for product-specific information**)**
   iii. Dosage should be individualized in every case.
   iv. Titration should be based on efficacy and tolerability. (See individual product labeling)
c. Prescribers should be knowledgeable about when and how to supplement pain management with immediate-release analgesics, opioids and non-opioids.
d. Prescribers should be knowledgeable about converting patients from immediate-release to ER/LA opioid products and from one ER/LA opioid product to another ER/LA opioid product.
e. Prescribers should understand the concept of incomplete cross-tolerance when converting patients from one opioid to another.
f. Prescribers should understand the concepts and limitations of equianalgesic dosing and follow patients closely during all periods of dose adjustments.

g. Prescribers should understand the warning signs and symptoms of significant respiratory depression from opioids and monitor patients closely, especially at the time of treatment initiation and dose increases.
h. Prescribers should understand that tapering the opioid dose is necessary to safely discontinue treatment with ER/LA opioid analgesics when therapy is no longer needed.

III. Managing Therapy with ER/LA Opioid Analgesics

a. Prescribers should establish analgesic and functional goals for therapy and periodically evaluate pain control, functional outcomes, side-effect frequency and intensity, and health-related quality of life.
b. Prescribers should be aware of the existence of Patient Prescriber Agreements (PPAs).
    i. PPAs are documents signed by both prescriber and patient at the time an opioid is prescribed.
    ii. PPAs can help ensure patients and caregivers understand the goals of treatment, the risks, and how to use the medications safely.
    iii. PPAs can include commitments to return for follow-up visits, to comply with appropriate monitoring (such as random drug testing), and to safeguard the medication.
c. Prescribers should monitor patient adherence to the treatment plan, especially with regard to misuse and abuse by:
    i. Recognizing, documenting, and addressing aberrant drug-related behavior.
    ii. Utilizing state Prescription Drug Monitoring Programs, where practical, to identify behaviors that may represent abuse.
    iii. Understanding the utility and interpretation of drug testing (e.g., screening and confirmatory tests), and using it as indicated.
    iv. Screening and referring for substance abuse treatment as indicated.
    v. Performing medication reconciliation as indicated.
d. Prescribers should understand how to anticipate and manage adverse events associated with ER/LA opioid analgesics.
e. Prescribers should be aware that there are no adequate and well-controlled studies of ER/LA opioid analgesics in pregnant women. ER/LA opioid analgesics should be used during pregnancy only if the potential benefit justifies the risk to the fetus.
f. Prescribers should be aware of the pregnancy status of their patients. If opioid use is required for a prolonged period in a pregnant woman, prescribers should advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.
g. Prescribers treating patients with ER/LA opioid analgesics should periodically assess benefits and side effects of these drugs, and the continued need for opioid analgesics.
h. Prescribers should understand the need for reevaluation of patient's underlying medical condition if the clinical presentation changes over time.
i. Prescribers should be familiar with referral sources for the treatment of abuse or addiction that may arise from the use of ER/LA opioid analgesics.

IV. Counseling Patients and Caregivers about the Safe Use of ER/LA Opioid Analgesics

a. Prescribers should use the Patient Counseling Document as part of the discussion when prescribing opioid analgesics.

b. Prescribers should explain product-specific information about the prescribed ER/LA opioid analgesic.
c. Prescribers should explain how to take the ER/LA opioid analgesic as prescribed.
d. Prescribers should explain the importance of adherence to dosing regimen, how to handle missed doses, and to contact their prescriber should pain not be controlled.
e. Prescribers should inform patients and caregivers to read the specific ER/LA opioid analgesic Medication Guide they receive from the pharmacy.
f. Prescribers should warn patients and caregivers that under no circumstances should an oral ER/LA opioid analgesic be broken, chewed or crushed. In addition, patches and buccal films should not be cut, torn, or damaged prior to use. Manipulating the ER/LA opioid analgesic described above may lead to rapid release of the ER/LA opioid analgesic causing overdose and death. When a patient cannot swallow a capsule whole, prescribers should refer to the product labeling to determine if it is appropriate to sprinkle the contents of a capsule on applesauce or administer via a feeding tube.
g. Prescribers should caution patients and caregivers that the use of other CNS depressants such as sedative-hypnotics and anxiolytics, alcohol, or illegal drugs with ER/LA opioid analgesics can cause overdose and death. Patients and caregivers should be instructed to only use other CNS depressants, including other opioids, under the instruction of their prescriber.
h. Prescribers should instruct patients and caregivers to tell all of their doctors about all medications the patient is taking.
i. Prescribers should warn patients and caregivers not to abruptly discontinue or reduce the ER/LA opioid analgesic and discuss how to safely taper the dose when discontinuing.
j. Prescribers should caution patients and caregivers that ER/LA opioid analgesics can cause serious side effects that can lead to death, even when used as recommended. Prescribers should counsel patients and caregivers on the risk factors, signs, and symptoms of overdose and opioid-induced respiratory depression, gastrointestinal obstruction, and allergic reactions.
k. Prescribers should counsel patients and caregivers on the most common side effects of ER/LA opioid analgesics, and about the risk of falls, working with heavy machinery, and driving.
l. Patients or caregivers should call their prescriber for information about managing side effects.
m. Prescribers should explain to patients and caregivers that sharing ER/LA opioid analgesics with others may cause them to have serious side effects including death, and that selling or giving away ER/LA opioid analgesics is against the law.
n. Prescribers should counsel patients and caregivers to store ER/LA opioid analgesics in a safe and secure place away from children, family members, household visitors, and pets.
o. Prescribers should warn patients and caregivers that ER/LA opioid analgesics must be protected from theft.
p. Prescribers should counsel patients and caregivers to dispose of any ER/LA opioid analgesics when no longer needed by flushing them down the toilet.
q. Prescribers should counsel patients and caregivers to inform them about side effects.
r. Adverse events should be reported to the FDA at 1-800-FDA-1088 or via http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf.

V. General Drug Information for ER/LA Opioid Analgesic Products

Prescribers should be knowledgeable about general characteristics, toxicities, and drug interactions for ER/LA opioid analgesic products. For example,

a. ER/LA opioid analgesic products are scheduled under the Controlled Substances Act and can be misused and abused.
b. Respiratory depression is the most important serious adverse effect of opioids as it can be immediately life-threatening.
c. Constipation is the most common long-term side effect and should be anticipated.
d. Drug-drug interaction profiles vary among the products. Knowledge of particular opioid-drug interactions, and the underlying pharmacokinetic and pharmacodynamic mechanisms, allows for the safer administration of opioid analgesics.
    i. Central nervous system depressants (alcohol, sedatives, hypnotics, tranquilizers, tricyclic antidepressants) can have a potentiating effect on the sedation and respiratory depression caused by opioids.
    ii. Some ER opioid formulations may rapidly release opioid (dose dump) when exposed to alcohol. Some drug levels may increase without dose dumping when exposed to alcohol. See individual product labeling.
    iii. Using opioids with monoamine oxidase inhibitors (MAOIs) may result in possible increase in respiratory depression. Using certain opioids with MAOIs may cause serotonin syndrome.
    iv. Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone (ADH).
    v. Some opioids (methadone, buprenorphine) can prolong the QTc interval.
    vi. Concomitant drugs that act as inhibitors or inducers of various cytochrome P450 enzymes can result in higher or lower than expected blood levels of some opioids.
    vii. See table in Section VI for product-specific information.
e. Tolerance to sedating and respiratory-depressant effects of opioids is critical to the safe use of ER/LA opioid analgesics.
    i. For ER products, patients must meet the criteria for opioid tolerance, described in the table in Section VI, before using:
        a. certain products,
        b. certain strengths,
        c. certain daily doses, and
        d. in specific indicated patient populations (e.g., pediatric patients).
    ii. See the table in Section VI for product-specific information.
f. ER/LA opioid analgesic tablets must be swallowed whole. ER/LA opioid analgesic capsules should be swallowed intact or when necessary, the pellets from some capsules can be sprinkled on applesauce and swallowed without chewing.
g. For transdermal products, external heat, fever, and exertion can increase absorption of the opioid, leading to fatal overdose. Transdermal products with metal foil backings are not safe for use in MRIs.
h. For buccal film products, the film should not be applied if it is cut, damaged, or changed in any way. Use the entire film.
i. Follow the instructions for conversion in the Dosage and Administration section (2.1) in the *Prescribing Information* of each product when converting patients from one opioid to another.

VI. Specific Drug Information for ER/LA Opioid Analgesic Products

Prescribers should be knowledgeable about specific characteristics of the ER/LA opioid analgesic products they prescribe, including the drug substance, formulation, strength, dosing interval, key instructions, specific information about conversion between products where available, specific drug interactions, use in opioid-tolerant patients, product-specific safety concerns, and relative potency to morphine. The attached table is a reference. For detailed information, prescribers can refer to prescribing information available online via DailyMed at www.dailymed.nlm.nih.gov or Drugs@FDA at www.fda.gov/drugsatfda.

Drug Information Common to the Class of Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Avinza (morphine sulfate ER capsules) **Belbuca** (buprenorphine buccal film) **Butrans** (buprenorphine transdermal system) **Dolophine** (methadone HCl tablets) **Duragesic** (fentanyl transdermal system) **Embeda** (morphine sulfate ER-naltrexone capsules) **Exalgo** (hydromorphone HCl ER tablets) **Hysingla ER** (hydrocodone bitartrate ER tablets) **Kadian** (morphine sulfate ER capsules)	**MorphaBond** (morphine sulfate ER tablets) **MS Contin** (morphine sulfate ER tablets) **Nucynta ER** (tapentadol HCl ER tablets) **Opana ER** (oxymorphone HCl ER tablets) **OxyContin** (oxycodone HCl ER tablets) **Targiniq ER** (oxycodone HCl/naloxone HCl ER tablets) **Xtampza ER** (oxycodone ER capsules) **Zohydro ER** (hydrocodone bitartrate ER capsules)
Dosing Interval	▪ Refer to individual product information.
Key Instructions	▪ Limitations of usage: • Reserve for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. • Not for use as an as-needed analgesic. • Not for mild pain or pain not expected to persist for an extended duration. • Not for use in treating acute pain. ▪ Individually titrate to a dose that provides adequate analgesia and minimizes adverse reactions. ▪ The times required to reach steady-state plasma concentrations are product specific; refer to product information for titration interval. ▪ Continually reevaluate to assess the maintenance of pain control and the emergence of adverse reactions. ▪ During chronic therapy, especially for non-cancer-related pain, periodically reassess the continued need for opioids. ▪ If pain increases, attempt to identify the source, while adjusting the dose. ▪ When an ER/LA opioid analgesic is no longer required, gradually titrate downward to prevent signs and symptoms of withdrawal in the physically-dependent patient. **Do not abruptly discontinue these products.** ▪ Solid oral dosage forms: • Swallow tablets and capsules whole: crushing, chewing, breaking, cutting or dissolving may result in rapid release and absorption of a potentially fatal dose of opioid. • Some capsules can be opened and pellets sprinkled on applesauce for patients who can reliably swallow without chewing and used immediately. See individual product information. • Exposure of some products to alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of opioid. • Dispose of unused product by flushing down the toilet. ▪ Transdermal dosage forms: • Avoid exposure to external heat. Patients with fever must be monitored for signs or symptoms of increased opioid exposure. • Location of application must be rotated. • Prepare skin by clipping, not shaving hair, and washing area only with water. ▪ Buccal film dosage form: • Do not use if the package seal is broken or the film is cut, damaged, or changed in any way. ▪ See individual product information for the following: • Dosage reduction for hepatic or renal impairment.

Drug Information Common to the Class of Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Drug Interactions Common to the Class	▪ Concurrent use with other central nervous system depressants (sedatives, hypnotics, general anesthetics, antiemetics, phenothiazines, other tranquilizers, and alcohol) can increase the risk of respiratory depression, hypotension, profound sedation, or coma. Reduce the initial dose of one or both agents. ▪ Avoid concurrent use of mixed opioid agonist/antagonists (i.e., pentazocine, nalbuphine, and butorphanol) or partial opioid agonists (buprenorphine) in patients who have received or are receiving a course of therapy with a full opioid agonist. In these patients, mixed opioid agonist/antagonists and partial opioid agonists may reduce the analgesic effect and/or may precipitate withdrawal symptoms. ▪ Opioids may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression. ▪ Concurrent use with anticholinergic medication increases the risk of urinary retention and severe constipation, which may lead to paralytic ileus.
Use in Opioid-Tolerant Patients	▪ Adult patients considered opioid-tolerant are those receiving, for one week or longer: o at least 60 mg oral morphine/day o 25 mcg transdermal fentanyl/hour o 30 mg oral oxycodone/day o 8 mg oral hydromorphone/day o 25 mg oral oxymorphone/day ▪ Pediatric patients (11 years and older) considered opioid-tolerant are those who are already receiving and tolerating a minimum daily opioid dose of at least 20 mg oxycodone orally or its equivalent (applicable to OxyContin's pediatric indication only) ▪ See individual product information for which products: • Have strengths or total daily doses only for use in opioid-tolerant patients. • Are only for use in opioid-tolerant patients at all strengths.
Contraindications	▪ Significant respiratory depression ▪ Acute or severe asthma in an unmonitored setting or in the absence of resuscitative equipment ▪ Known or suspected paralytic ileus ▪ Hypersensitivity (e.g., anaphylaxis) ▪ See individual product information for additional contraindications.
Relative Potency To Oral Morphine	▪ **These are intended as general guides.** ▪ Follow conversion instructions in individual product information. ▪ Incomplete cross-tolerance and inter-patient variability require the use of conservative dosing when converting from one opioid to another - halve the calculated comparable dose and titrate the new opioid as needed.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Avinza	Morphine Sulfate ER Capsules, 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, and 120 mg
Dosing Interval	Once a day
Key Instructions	▪ Initial dose in opioid non-tolerant patients is 30 mg. ▪ Titrate in increments of not greater than 30 mg using a minimum of 3 to 4 day intervals. ▪ Swallow capsule whole (do not chew, crush, or dissolve). ▪ May open capsule and sprinkle pellets on applesauce for patients who can reliably swallow without chewing; use immediately. ▪ Maximum daily dose: 1600 mg due to risk of serious renal toxicity by excipient, fumaric acid.
Specific Drug Interactions	▪ Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of morphine. ▪ P-gp inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold.
Use in Opioid-Tolerant Patients	90 mg and 120 mg capsules are for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	None
Belbuca	Buprenorphine Buccal Film, 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg
Dosing Interval	Every 12 hours (or once every 24 hours for initiation in opioid naïve patients and patients taking less than 30 mg oral morphine sulfate equivalents)
Key Instructions	▪ Opioid-naïve patients or patients taking less than 30 mg oral morphine sulfate equivalents: Initiate treatment with a 75 mcg buccal film, once daily, or if tolerated, every 12 hours. • Titrate to 150 mcg every 12 hours no earlier than 4 days after initiation. • Individual titration to a dose that provides adequate analgesia and minimizes adverse reactions should proceed in increments of 150 mcg every 12 hours, no more frequently than every 4 days. ▪ When converting from another opioid, first taper the current opioid to no more than 30 mg oral morphine sulfate equivalents per day prior to initiating Belbuca. • If prior daily dose before taper was 30 mg to 89 mg oral morphine sulfate equivalents, initiate with 150 mcg dose every 12 hours. • If prior daily dose before taper was 90 mg to 160 mg oral morphine sulfate equivalents, initiate with 300 mcg dose every 12 hours. • Titration of the dose should proceed in increments of 150 mcg every 12 hours, no more frequently than every 4 days. ▪ Maximum dose: 900 mcg every 12 hours due to the potential for QTc prolongation ▪ Severe Hepatic Impairment: Reduce the starting and incremental dose by half that of patients with normal liver function. ▪ Oral Mucositis: Reduce the starting and incremental dose by half that of patients without mucositis ▪ Do not use if the package seal is broken or the film is cut, damaged, or changed in any way

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Specific Drug Interactions	▪ CYP3A4 inhibitors may increase buprenorphine levels. ▪ CYP3A4 inducers may decrease buprenorphine levels. ▪ Benzodiazepines may increase respiratory depression. ▪ Class IA and III antiarrhythmics, other potentially arrhythmogenic agents, may increase risk for QTc prolongation and torsade de pointes.
Use in Opioid-Tolerant Patients	Belbuca 600 mcg, 750 mcg, and 900 mcg are for use following titration from lower doses of Belbuca.
Product-Specific Safety Concerns	▪ QTc prolongation and torsade de pointes ▪ Hepatotoxicity
Relative Potency To Oral Morphine	Equipotency to oral morphine has not been established.
Butrans	Buprenorphine Transdermal System, 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr
Dosing Interval	One transdermal system every 7 days
Key Instructions	▪ Initial dose in opioid non-tolerant patients when converting from less than 30 mg morphine equivalents, and in mild to moderate hepatic impairment - 5 mcg/hr dose. ▪ When converting from 30 mg to 80 mg morphine equivalents - first taper to 30 mg morphine equivalent, then initiate with 10 mcg/hr dose. ▪ Titrate in 5 mcg/hour or 10 mcg/hour increments by using no more than two patches of the 5 mcg/hour or 10-mcg/hour system(s) with a minimum of 72 hours between dose adjustments. The total dose from all patches should not exceed 20 mcg/hour ▪ Maximum dose: 20 mcg/hr due to risk of QTc prolongation. ▪ Application • Apply only to sites indicated in the Full Prescribing Information. • Apply to intact/non-irritated skin. • Skin may be prepped by clipping hair, washing site with water only • Rotate site of application a minimum of 3 weeks before reapplying to the same site. • Do not cut. ▪ Avoid exposure to heat. ▪ Dispose of used/unused patches by folding the adhesive side together and flushing down the toilet.
Specific Drug Interactions	▪ CYP3A4 Inhibitors may increase buprenorphine levels. ▪ CYP3A4 Inducers may decrease buprenorphine levels. ▪ Benzodiazepines may increase respiratory depression. ▪ Class IA and III antiarrhythmics, other potentially arrhythmogenic agents, may increase risk for QTc prolongation and torsade de pointe.
Use in Opioid-Tolerant Patients	Butrans 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, and 20 mcg/hr transdermal systems are for use in opioid- tolerant patients only.
Drug-Specific Safety Concerns	▪ QTc prolongation and torsade de pointe. ▪ Hepatotoxicity ▪ Application site skin reactions
Relative Potency To Oral Morphine	Equipotency to oral morphine has not been established.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Dolophine	Methadone Hydrochloride Tablets, 5 mg and 10 mg
Dosing Interval	Every 8 to 12 hours
Key Instructions	▪ Initial dose in opioid non-tolerant patients: 2.5 to 10 mg ▪ Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose and death. Use low doses according to the table in the full prescribing information. ▪ Titrate slowly, with dose increases no more frequent than every 3 to 5 days. Because of high variability in methadone metabolism, some patients may require substantially longer periods between dose increases (up to 12 days). ▪ High inter-patient variability in absorption, metabolism, and relative analgesic potency. ▪ Opioid detoxification or maintenance treatment shall only be provided in a federally certified opioid (addiction) treatment program (Code of Federal Regulations, Title 42, Sec 8).

Specific Drug Interactions	▪ Pharmacokinetic drug-drug interactions with methadone are complex.
	  ▪ CYP 450 inducers may decrease methadone levels.
	  ▪ CYP 450 inhibitors may increase methadone levels.
	  ▪ Anti-retroviral agents have mixed effects on methadone levels.
	▪ Potentially arrhythmogenic agents may increase risk for QTc prolongation and torsade de pointe.
	▪ Benzodiazepines may increase respiratory depression

Use in Opioid-Tolerant Patients	Refer to full prescribing information.
Product-Specific Safety Concerns	▪ QTc prolongation and torsade de pointe. ▪ Peak respiratory depression occurs later and persists longer than analgesic effect. ▪ Clearance may increase during pregnancy. ▪ False positive urine drug screens possible.
Relative Potency To Oral Morphine	Varies depending on patient's prior opioid experience.
Duragesic	Fentanyl Transdermal System, 12, 25, 37.5*, 50, 62.5*, 75, 87.5*, and 100 mcg/hr (**These strengths are available only in generic form*)
Dosing Interval	Every 72 hours (3 days)

Key Instructions	▪ Use product specific information for dose conversion from prior opioid
	▪ Use 50% of the dose in mild or moderate hepatic or renal impairment, avoid use in severe hepatic or renal impairment
	▪ Application
	  • Apply to intact/non-irritated/non-irradiated skin on a flat surface.
	  • Skin may be prepped by clipping hair, washing site with water only
	  • Rotate site of application.
	  • Titrate using a minimum of 72 hour intervals between dose adjustments.
	  • Do not cut.
	▪ Avoid exposure to heat.
	▪ Avoid accidental contact when holding or caring for children.
	▪ Dispose of used/unused patches by folding the adhesive side together and flushing down the toilet.
	Specific contraindications:
	▪ Patients who are not opioid-tolerant.
	▪ Management of acute or intermittent pain, or in patients who require opioid analgesia for a short period of time.
	▪ Management of post-operative pain, including use after out-patient or day surgery.
	▪ Management of mild pain.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Specific Drug Interactions	▪ CYP3A4 inhibitors may increase fentanyl exposure. ▪ CYP3A4 inducers may decrease fentanyl exposure. ▪ Discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in fentanyl plasma concentration.
Use in Opioid-Tolerant Patients	All doses of Duragesic are indicated for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	▪ Accidental exposure due to secondary exposure to unwashed/unclothed application site. ▪ Increased drug exposure with increased core body temperature or fever. ▪ Bradycardia ▪ Application site skin reactions
Relative Potency To Oral Morphine	See individual product information for conversion recommendations from prior opioid
Embeda	Morphine Sulfate ER-Naltrexone Capsules, 20 mg/0.8 mg, 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, 100 mg/4 mg
Dosing Interval	Once a day or every 12 hours
Key Instructions	▪ Initial dose as first opioid: 20 mg/0.8 mg. ▪ Titrate using a minimum of 1 to 2 day intervals. ▪ Swallow capsules whole (do not chew, crush, or dissolve) ▪ Crushing or chewing will release morphine, possibly resulting in fatal overdose, and naltrexone, possibly resulting in withdrawal symptoms. ▪ May open capsule and sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately.
Specific Drug Interactions	▪ Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of morphine. ▪ P-gp inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold.
Use in Opioid-Tolerant Patients	Embeda 100 mg/4 mg capsule is for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	None
Exalgo	Hydromorphone Hydrochloride Extended-Release Tablets, 8 mg, 12 mg, 16 mg or 32 mg
Dosing Interval	Once a day
Key Instructions	▪ Use the conversion ratios in the individual product information. ▪ Start patients with moderate hepatic impairment on 25% dose that would be prescribed for a patient with normal hepatic function. ▪ Start patients with moderate renal impairment on 50%, and patients with severe renal impairment on 25% of the dose that would be prescribed for a patient with normal renal function. ▪ Titrate in increments of 4 to 8 mg using a minimum of 3 to 4 day intervals ▪ Swallow tablets whole (do not chew, crush, or dissolve). ▪ Do not use in patients with sulfite allergy—contains sodium metabisulfite.
Specific Drug Interactions	None
Use in Opioid-Tolerant Patients	All doses of Exalgo are indicated for opioid-tolerant patients only.
Drug-Specific Adverse Reactions	Allergic manifestations to sulfite component.
Relative Potency To Oral Morphine	Approximately 5:1 oral morphine to hydromorphone oral dose ratio, use conversion recommendations in the individual product information.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Hysingla ER	Hydrocodone bitartrate Extended-Release Tablets, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg, and 120 mg
Dosing Interval	Every 24 hours (once-daily)
Key Instructions	▪ Opioid-naïve patients: initiate treatment with 20 mg orally once daily. During titration, adjust the dose in increments of 10 mg to 20 mg every 3 to 5 days until adequate analgesia is achieved. ▪ Swallow tablets whole (do not chew, crush, or dissolve). ▪ Consider use of an alternative analgesic in patients who have difficulty swallowing or have underlying gastrointestinal disorders that may predispose them to obstruction. ▪ Take one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth. ▪ Use 1/2 of the initial dose and monitor closely for adverse events, such as respiratory depression and sedation, when administering Hysingla ER to patients with severe hepatic impairment or patients with moderate to severe renal impairment.
Specific Drug Interactions	▪ CYP3A4 inhibitors may increase hydrocodone exposure. ▪ CYP3A4 inducers may decrease hydrocodone exposure ▪ Concomitant use of Hysingla ER with strong laxatives (e.g., Lactulose) that rapidly increase GI motility may decrease hydrocodone absorption and result in decreased hydrocodone plasma levels. ▪ The use of MAO inhibitors or tricyclic antidepressants with Hysingla ER may increase the effect of either the antidepressant or Hysingla ER.
Use in Opioid-Tolerant Patients	A single dose of Hysingla ER greater than or equal to 80 mg is only for use in opioid tolerant patients.
Product-Specific Safety Concerns	▪ Use with caution in patients with difficulty swallowing the tablet or underlying gastrointestinal disorders that may predispose patients to obstruction. ▪ Esophageal obstruction, dysphagia, and choking have been reported with Hysingla ER. ▪ In nursing mothers, discontinue nursing or discontinue drug. ▪ QTc prolongation has been observed with Hysingla ER following daily doses of 160 mg. Avoid use in patients with congenital long QTc syndrome. This observation should be considered in making clinical decisions regarding patient monitoring when prescribing Hysingla ER in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that are known to prolong the QTc interval. In patients who develop QTc prolongation, consider reducing the dose.
Relative Potency To Oral Morphine	See individual product information for conversion recommendations from prior opioid
Kadian	Morphine Sulfate Extended-Release Capsules, 10 mg, 20mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 80 mg, 100 mg, 130 mg, 150 mg, and 200 mg
Dosing Interval	Once a day or every 12 hours
Key Instructions	▪ Product information recommends not using as first opioid. ▪ Titrate using a minimum of 2-day intervals. ▪ Swallow capsules whole (do not chew, crush, or dissolve). ▪ May open capsule and sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Specific Drug Interactions	▪ Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of morphine. ▪ P-gp inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold.
Use in Opioid-Tolerant Patients	Kadian 100 mg, 130 mg, 150 mg, and 200 mg capsules are for use in opioid-tolerant-patients only
Product-Specific Safety Concerns	None
MorphaBond	Morphine Sulfate Extended-release Tablets, 15 mg, 30 mg, 60 mg, 100 mg
Dosing Interval	Every 8 hours or every 12 hours
Key Instructions	▪ Product information recommends not using as first opioid. ▪ Titrate using a minimum of 1 to 2-day intervals. ▪ Swallow tablets whole (do not chew, crush, or dissolve).
Specific Drug Interactions	P-gp inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold.
Use in Opioid-Tolerant Patients	MorphaBond 100 mg tablets are for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	None
MS Contin	Morphine Sulfate Extended-release Tablets, 15 mg, 30 mg, 60 mg, 100 mg, and 200 mg
Dosing Interval	Every 8 hours or every 12 hours
Key Instructions	▪ Product information recommends not using as first opioid. ▪ Titrate using a minimum of 1 to 2-day intervals. ▪ Swallow tablets whole (do not chew, crush, or dissolve).
Specific Drug Interactions	P-gp inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold.
Use in Opioid-Tolerant Patients	MS Contin 100 mg and 200 mg tablet strengths are for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	None
Nucynta ER	Tapentadol Extended-Release Tablets, 50 mg, 100mg, 150 mg, 200 mg, and 250 mg
Dosing Interval	Every 12 hours
Key Instructions	▪ Use 50 mg every 12 hours as initial dose in opioid nontolerant patients ▪ Titrate by 50 mg increments using a minimum of 3-day intervals. ▪ Maximum total daily dose is 500 mg ▪ Swallow tablets whole (do not chew, crush, or dissolve). ▪ Take one tablet at a time and with enough water to ensure complete swallowing immediately after placing in the mouth. ▪ Dose once daily in moderate hepatic impairment with 100 mg per day maximum ▪ Avoid use in severe hepatic and renal impairment.
Specific Drug Interactions	▪ Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of tapentadol. ▪ Contraindicated in patients taking MAOIs.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Use in Opioid-Tolerant Patients	No product-specific considerations.
Product-Specific Safety Concerns	▪ Risk of serotonin syndrome ▪ Angioedema
Relative Potency To Oral Morphine	Equipotency to oral morphine has not been established.
Opana ER	Oxymorphone Hydrochloride ER Tablets, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg
Dosing Interval	Every 12h dosing, some may benefit from asymmetric (different dose given in AM than in PM) dosing.
Key Instructions	▪ Use 5 mg every 12 hours as initial dose in opioid non-tolerant patients and patients with mild hepatic impairment and renal impairment (creatinine clearance < 50 mL/min) and patients over 65 years of age ▪ Swallow tablets whole (do not chew, crush, or dissolve). ▪ Take one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth. ▪ Titrate in increments of 5 to 10 mg using a minimum of 3 to 7-day intervals. ▪ Contraindicated in moderate and severe hepatic impairment.
Specific Drug Interactions	▪ Alcoholic beverages or medications containing alcohol may result in the absorption of a potentially fatal dose of oxymorphone.
Use in Opioid-Tolerant Patients	No product specific considerations.
Product-Specific Safety Concerns	▪ Use with caution in patients who have difficulty in swallowing or have underlying GI disorders that may predispose them to obstruction, such as a small gastrointestinal lumen.
Relative Potency To Oral Morphine	Approximately 3:1 oral morphine to oxymorphone oral dose ratio
OxyContin	Oxycodone Hydrochloride Extended-release Tablets, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg
Dosing Interval	▪ Every 12 hours
Key Instructions	▪ For Adults: • Initial dose in opioid-naïve and opioid non-tolerant patients is 10 mg every 12 hours. • If needed, adult dosage may be adjusted in 1 to 2 day intervals. • When a dose increase is clinically indicated, the total daily oxycodone dose usually can be increased by 25% to 50% of the current dose. ▪ For Pediatric patients (**11 years and older**): Use only in <u>opioid-tolerant</u> patients (see below, *Use in Opioid-Tolerant Patients* for dosing information). ▪ For all patients: • Hepatic impairment: start with one third to one half the usual dosage • Renal impairment (creatinine clearance <60 mL/min): start with one half the usual dosage. • Consider use of other analgesics in patients who have difficulty swallowing or have underlying GI disorders that may predispose them to obstruction. Swallow tablets whole (do not chew, crush, or dissolve). • Take one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth.
Specific Drug Interactions	▪ CYP3A4 inhibitors may increase oxycodone exposure. ▪ CYP3A4 inducers may decrease oxycodone exposure.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Use in Opioid-Tolerant Patients	▪ For Adults: • Single dose greater than 40 mg or total daily dose greater than 80 mg are for use in adult patients in whom tolerance to an opioid of comparable potency has been established. ▪ For Pediatric patients (**11 years and older**): • For use only in opioid-tolerant pediatric patients already receiving and tolerating opioids for at least 5 consecutive days with a minimum of 20 mg per day of oxycodone or its equivalent for at least two days immediately preceding dosing with OxyContin. • If needed, pediatric dosage may be adjusted in 1 to 2 day intervals. • When a dose increase is clinically indicated, the total daily oxycodone dose usually can be increased by 25% of the current total daily dose.
Product-Specific Safety Concerns	▪ Choking, gagging, regurgitation, tablets stuck in the throat, difficulty swallowing the tablet. ▪ Contraindicated in patients with gastrointestinal obstruction.
Relative Potency To Oral Morphine	Approximately 2:1 oral morphine to oxycodone oral dose ratio.
Targiniq ER	Oxycodone Hydrochloride / Naloxone Hydrochloride Extended-release tablets, 10 mg/5 mg, 20 mg/10 mg, and 40 mg/20 mg
Dosing Interval	▪ Every 12 hours
Key Instructions	▪ Opioid-naïve patients: initiate treatment with 10 mg/5 mg every 12 hours. ▪ Titrate using a minimum of 1 to 2 day intervals. ▪ Do not exceed 80 mg/40 mg total daily dose (40 mg/20 mg q12) of Targiniq ER ▪ May be taken with or without food. ▪ Swallow tablets whole. Do not chew, crush, split, or dissolve, as this will release oxycodone, possibly resulting in fatal overdose, and naloxone, possibly resulting in withdrawal symptoms. ▪ Hepatic impairment: contraindicated in moderate and severe hepatic impairment. In patients with mild hepatic impairment, start with one third to one half the usual dosage. ▪ Renal impairment (creatinine clearance < 60 mL/min): start with one half the usual dosage.
Specific Drug Interactions	▪ CYP3A4 inhibitors may increase oxycodone exposure. ▪ CYP3A4 inducers may decrease oxycodone exposure
Use in Opioid-Tolerant Patients	▪ Single dose greater than 40 mg/20 mg or total daily dose of 80 mg/40 mg are for use in opioid-tolerant patients only
Product-Specific Safety Concerns	▪ Contraindicated in patients with moderate to severe hepatic impairment.
Relative Potency To Oral Morphine	▪ See individual product information for conversion recommendations from prior opioid.
Xtampza ER	Oxycodone Extended-Release Capsules, 9 mg 13.5 mg, 18 mg, 27 mg, and 36 mg (strengths equivalent to 10 mg, 15 mg , 20 mg, 30 mg, and 40 mg oxycodone hydrochloride, respectively)
Dosing Interval	▪ Every 12 hours

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Key Instructions	▪ Opioid naïve and opioid non-tolerant patients: Initiate with 9 mg every 12 hours. ▪ Titrate using a minimum of 1 to 2 day intervals. ▪ Take Xtampza ER capsules with the same amount of food in order to ensure consistent plasma levels are achieved. ▪ Maximum daily dose: 288 mg (8 x 36 mg capsules) because the safety of excipients has not been established for higher doses ▪ For patients that have difficulty swallowing, Xtampza ER can also be taken by sprinkling the capsule contents on soft foods or into a cup and then administering directly into the mouth and swallowing immediately. Xtampza ER may also be administered through a gastrostomy or nasogastric feeding tube. ▪ Hepatic impairment: Initiate therapy at 1/3 to 1/2 the usual dosage ▪ Renal impairment: (creatinine clearance <60 mL/min): Follow a conservative approach to dose initiation and adjust according to the clinical situation.
Specific Drug Interactions	▪ CYP3A4 inhibitors may increase oxycodone exposure ▪ CYP3A4 inducers may decrease oxycodone exposure
Use in Opioid-Tolerant Patients	▪ A single dose greater than 36 mg or a total daily dose greater than 72 mg is for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	▪ None
Relative Potency To Oral Morphine	▪ There are no established conversion ratios for conversion from other opioids to Xtampza ER defined by clinical trials.
Zohydro ER	Hydrocodone Bitartrate Extended-Release Capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg
Dosing Interval	▪ Every 12 hours
Key Instructions	▪ Initial dose in opioid non-tolerant patient is 10 mg. ▪ Titrate in increments of 10 mg using a minimum of 3 to 7day intervals.
Specific Drug Interactions	▪ Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of hydrocodone. ▪ CYP3A4 inhibitors may increase hydrocodone exposure. ▪ CYP3A4 inducers may decrease hydrocodone exposure.
Use in Opioid-Tolerant Patients	▪ Single dose greater than 40 mg or total daily dose greater than 80 mg are for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	None
Relative Potency To Oral Morphine	Approximately 1.5:1 oral morphine to hydrocodone oral dose ratio.
For detailed information, refer to prescribing information available online via DailyMed at www.dailymed.nlm.nih.gov or Drugs@FDA at www.fda.gov/drugsatfda.	

Performance Improvement: The Opiate Use Challenge

Iowa Healthcare Collaborative: 13th Annual Conference

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Disclosures

Brian Isetts has no conflicts of interest to report relative to this workshop. I am currently serving as a medication use quality improvement advisor under contract with the IHC. The views, opinions and reflections expressed are solely my own, and do not represent the official position of any institution, agency or organization.

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Session Objectives

- Understand the vital role of communities
- Identify outcome strategies and measures
- Review evidence on the appropriate, effective and safe use of opiates
- Establish meaningful priorities to reduce adverse drug events and prevent addiction in individuals new to opiates while supporting recovery

IHC Iowa Healthcare Collaborative

Session Agenda

- Big picture overview of opiate use
- Systems perspective of community solutions
- Overview of evidence and best practices
- Setting patient-specific goals of therapy, step-down therapy and care plan responsibilities
- Solutions workshop with actionable improvement priorities

This is Reality in Homes across America

Key Question to Run On

How can your community come together to prevent addiction in individuals new to opiates; ensure the appropriate, effective and safe use of opiates; and support recovery?

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A Medication Use System we can Have and Deserve

Aims of a Rational Medication Use System from the Patient's Perspective

- Patients routinely achieve their drug therapy treatment goals with zero tolerance for preventable medication harms
- Routinely: More than 90% of patients' treatment goals are being achieved
- Preventable: Between 44-60% of medication harms are preventable

Comprehensive Team-based Medication Management

All team members help set patient-specific drug therapy goals for each medical condition:

- Assessment of intended use, effectiveness, safety, and adherence across the care continuum
- When patient is not achieving goals of therapy there is more efficient and effective use of team members
- Coordination of care as we all work together to help patients achieve goals of therapy
- Patients/care-givers help the team understand medication needs in patient-centered health homes

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A Big Picture Perspective of Opioid Use in America

- Where do we start?
- 14,000 Rx overdose deaths/year
- I.H.I. Systems Perspective
- Is Pain really the "fifth vital sign"
- The pain treatment pendulum
- Euphoria - CNS neurotransmitter milieu
- Predisposition and risks for addiction
- Medical & criminal treatment approaches

A Systems Perspective for the Rational use of Opioids

Engaging & aligning all sectors/stakeholders

- Everyone in the community has a role
- Resource rich/coordination poor teams
- Address multiple system components
- Frank discussions about opioid risks
- Re-train the medical community
- Treat addiction as a chronic disease

ADEs Gain Federal Interest

- Data sparked interest of Federal stakeholders
  - Interest from Congress
  - Interest from Secretary of HHS
- ODPHP charged with developing National Action Plan for ADE Prevention
  - Modeled after the National Action Plan to Prevent Healthcare-Associated Infections

The Targets (Phase 1)

- Inpatient and outpatient harms resulting from:
  1. Anticoagulants (orals, injectables)
  2. Diabetes agents (orals, injectables)
  3. Opioids (oral, injectables)
     - Acute pain
     - Non-malignant, chronic pain

High Level Action Items

- Reduce the supply of opioids
- Patient-specific goals of therapy for pain
- Use of non-opioid therapies for pain
- Educational priorities on uses and risks
- Reframe treatment programs & stigmas
- Access to Medication-Assisted Treatment
- Naloxone in every home, cabin & car
- Community measures for "hot spotting"

Best Practices in Pain Management
(or don't send them home with #100 Vicodin)

- Opioid naïve or opioid tolerant person
- Goals of therapy – 0-10 pain scale
- H-CAHPS Item #14 perverse incentive
- Care plan – step down therapy
- Naloxone co-Rx with high dose opioids
- Pain Contracts for long term use
- Prescription drug monitoring programs
- Community-wide "Take Back" Programs

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Checklist for Prescribing Opioids

- Set realistic goals for pain and function
- Assess baseline pain and function
- Optimize non-opioid and non-drug therapies
- Engage persons & families in benefits/risks
- Evaluate risk of harm or misuse
- Establish care plan criteria for dose reduction
- Schedule follow-up and reassessment
- Naloxone: >20-50mg morphine equivalent/day

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Opioid Measurement Strategies

- Concurrence with Opioid Rx Guidelines
- % of patients with opioid goals of therapy
- % of patients with step-down care plans
- Rate of in-hospital naloxone use
- Rate of on-admission naloxone use
- No. of persons refocused through drug courts
- % of naloxone co-Rx with long-acting opioids
- % of patients with pain contracts w/long-acting

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Strategies to Achieve Results in Iowa

- Celebrate success: In-hospital Naloxone rate
- Empower C-3 & accountable communities
- Team-based focus on opioid Rx and use
- Engage patients/families in our strategies
- Harm-minimization treatment perspective
- Meaningful Community-wide measures
- Patient-specific pain goals of therapy

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Opioid Resources

- Closing the Gap Between Science and Medicine

http://www.centeronaddiction.org/addiction-research/reports/addiction-medicine

- Guidelines for Cancer Pain Management

http://jco.ascopubs.org/content/early/2016/07/19/JCO.2016.68.5206.ful

- CDC Guidelines for Prescribing Opioids

http://www.cdc.gov/drugoverdose/data/overdose.html

- CDC Checklist for Chronic Pain Prescribing

http://stacks.cdc.gov/view/cdc/38025

- I.H.I. 100 Million Healthier Lives Toolkit

http://www.100mlives.org/approach-priorities/#opioid

Breakout Session Open Forum Questions to Run On

- What pain management approaches have you found to work best?
- Turn to the person sitting next to you and share your reflections to this query.
- 2 minutes per person
- We will then go around the room so you can share the great ideas and observations from the person sitting next to you!

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A Partnership for Quality, Patient Safety & Value

Thank You

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Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain

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Background: Deaths due to prescription opioid overdoses have increased dramatically. High-quality guidelines could help clinicians mitigate risks associated with opioid therapy.

Purpose: To evaluate the quality and content of guidelines on the use of opioids for chronic pain.

Data Sources: MEDLINE, National Guideline Clearinghouse, specialty society Web sites, and international guideline clearinghouses (searched in July 2013).

Study Selection: Guidelines published between January 2007 and July 2013 addressing the use of opioids for chronic pain in adults were selected. Guidelines on specific settings, populations, and conditions were excluded.

Data Extraction: Guidelines and associated systematic reviews were evaluated using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument and A Measurement Tool to Assess Systematic Reviews (AMSTAR), respectively, and recommendations for mitigating opioid-related risks were compared.

Data Synthesis: Thirteen guidelines met selection criteria. Overall AGREE II scores were 3.00 to 6.20 (on a scale of 1 to 7). The AMSTAR ratings were poor to fair for 10 guidelines. Two received high AGREE II and AMSTAR scores. Most guidelines recommend that clinicians avoid doses greater than 90 to 200 mg of morphine equivalents per day, have additional knowledge to prescribe methadone, recognize risks of fentanyl patches, titrate cautiously, and reduce doses by at least 25% to 50% when switching opioids. Guidelines also agree that opioid risk assessment tools, written treatment agreements, and urine drug testing can mitigate risks. Most recommendations are supported by observational data or expert consensus.

Limitation: Exclusion of non–English-language guidelines and reliance on published information.

Conclusion: Despite limited evidence and variable development methods, recent guidelines on chronic pain agree on several opioid risk mitigation strategies, including upper dosing thresholds; cautions with certain medications; attention to drug–drug and drug–disease interactions; and use of risk assessment tools, treatment agreements, and urine drug testing. Future research should directly examine the effectiveness of opioid risk mitigation strategies.

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For author affiliations, see end of text.
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Across the United States, opioid-related overdoses have been implicated in increasing numbers of emergency department visits, hospitalizations, and deaths. Annual fatalities associated with prescription opioids increased from 4000 in 1999 to nearly 14 000 by 2006 (1). Several factors may explain these trends. First, over the past several decades, the number of patients receiving opioids and the number of doses prescribed have increased dramatically (2–4). Treating chronic pain with opioids went from being largely discouraged to being included in standards of care (2, 5, 6), and titrating doses until patients self-report adequate control has become common practice (5, 7). Today, 8% to 30% of patients with chronic noncancer pain receive opioids, with average doses typically ranging from 13 to 128 mg of morphine equivalents daily; some receive much higher doses (8). Second, the public seems to consider prescription opioids safer to abuse than illicit drugs, influencing patterns of overdose deaths (9, 10). Third, common drug–drug and drug–disease interactions contribute to overdoses. Half of fatal opioid overdoses involve the concomitant use of sedative-hypnotics, particularly benzodiazepines (1).

See also:

Web-Only
Supplement
CME quiz

Given current rates of opioid overdose, policymakers are seeking solutions and standards of care are again evolving. The White House has issued action items, and an Institute of Medicine (IOM) report provides recommendations for policy audiences (11, 12). High-quality clinical practice guidelines would assist clinicians in making informed prescribing decisions and would mitigate the risks associated with using opioids. The objective of the current study was to systematically search for and evaluate the quality of guidelines addressing the use of opioids for chronic pain. A secondary objective was to compare guidelines' recommendations related to mitigating the risk for accidental overdose and misuse, including considering the quality of the evidence that guidelines provide in support of their recommendations.

METHODS

Study steps included searching for guidelines, applying selection criteria, assessing guideline quality, and extracting relevant content.

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Data Sources and Searches

We searched for guidelines addressing the use of opioids in the treatment of chronic pain, which is generally defined as pain that persists beyond normal tissue healing time, assumed to be 3 months (13, 14). The long-term use of opioids has been variably defined as use for 3 to 6 months or longer (14, 15).

Information sources included MEDLINE via PubMed, the National Guideline Clearinghouse, 12 Web sites of relevant specialty societies listed on the American Medical Association Web site (16), Web sites of selected state workers' compensation agencies (17–19), and 12 international search engines (20–31) (**Appendix Figure**, available at www.annals.org). The search was last updated in July 2013.

Search terms included "opioid," "opiate," "narcotic," "chronic pain," and "pain management." For the National Guideline Clearinghouse, names of specific opioids were also used. For PubMed, "narcotic" was omitted (all results addressed substance abuse); this search was limited to documents published after 31 December 2006 because selection criteria included recent updating.

Guideline Selection

We selected English-language documents meeting the following definition: "Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options" (32). Guidelines had to have been published after 2006 because half of guidelines can be outdated after 5 to 6 years (33).

Because we sought to evaluate guidelines that address the use of opioids for chronic pain in adults in general, we excluded guidelines focusing on specific conditions (for example, low back pain or cancer), populations (for example, pediatric patients or homeless persons), types of pain (for example, neuropathic pain or postoperative pain), or settings (for example, long-term care). We excluded guidelines derived entirely from another guideline and those for which we could not identify detailed information on development. Two reviewers applied criteria independently and reached agreement; a third reviewer was available to resolve disputes.

Guideline Quality Assessment

We evaluated guideline quality by using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument (34–36) and the systematic review supporting each guideline by using A Measurement Tool to Assess Systematic Reviews (AMSTAR) (37).

AGREE II

With AGREE II, appraisers rate 23 items across 6 domains (from 1 [strongly disagree] to 7 [strongly agree]), rate the overall quality of each guideline (1 to 7) and recommend for or against use. Scaled domain scores (0% to 100%) are based on the sum of ratings across all appraisers and the difference between the maximum and minimum possible scores (38).

The guidelines were rated by 4 to 6 appraisers, including 5 clinician investigators (2 of whom had limited availability) and 1 trained graduate student. One author who was also the author of a guideline (13) provided general input on content and methods but played no role in appraisals.

AMSTAR

In the original version of AMSTAR, appraisers answer 6 domain questions (yes, no, can't answer, or not applicable). Each domain question typically addresses multiple concepts. For example, 1 question states that "At least two electronic sources should be searched [concept 1] . . . Key words and/or MeSH terms must be stated [concept 2] . . . " (37).

Because including multiple concepts could lead to inconsistent scoring of "yes" or "no" responses, we modified AMSTAR by dividing the original domain questions into separate subquestions addressing single concepts (**Supplement**, available at www.annals.org). Appraisers scored each subquestion (yes, no, can't answer, or not applicable), each of the 6 domains overall (poor, fair, good, excellent, or outstanding), and the overall quality of the review (same categories as for the domains). Four to 5 appraisers rated each review individually and then met to discuss ratings and reach agreement.

Guideline Synthesis and Analysis

Three appraisers abstracted recommendations from each guideline on dosing limits, medications and formulations, titration of dose, switching from one opioid to another, drug–drug interactions, drug–disease interactions, and risk mitigation strategies (opioid risk assessment tools, written treatment agreements, and urine drug testing).

Role of the Funding Source

The Commission on Health and Safety and Workers' Compensation provided funding for this study. The funding source commissioned a synthesis of recent information on the risks and benefits of opioids for chronic pain but had no role in the design or execution of this evaluation.

RESULTS

Search and Selection of Guidelines

Of 1270 documents identified, 1132 unique records were eligible for screening, 19 full-text guidelines were considered for evaluation, and 13 were eligible (**Appendix Figure**). An online report includes a previous version of the search (39). Of 6 guidelines considered but found ineligible, 1 was derived from another guideline (18) and 5 lacked details on development methods (17, 40–43).

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Table. **Selected Guideline Recommendations Related to Mitigating the Risks of Opioid Therapy During Long-Term Use for Chronic Noncancer Pain**

Recommendation	Guideline Development Group (Reference)*			
	ACOEM (55)	AGS (51, 52)	APS-AAPM (13, 57, 58)	ASIPP (49, 59)
Dose that warrants scrutiny, *mg of morphine equivalents per day*				
Most patients successfully treated with lower doses; higher doses associated with adverse effects and overdose	–	–	200†‡ (adverse effects)	90‡§ (risk for overdose)
Medications and formulations				
Methadone: risks for QTc prolongation and bioaccumulation; only experienced providers should prescribe methadone	√	√‡	√‡	√‡
Fentanyl patch: limit to opioid-tolerant patients; variable absorption, exercise, and heat increase risk for overdose	√	–	–	√‡
Immediate-release fentanyl: limit to opioid-tolerant patients; safety unknown for CNCP; risk for overdose and misuse	√	–	–	–
Meperidine: do not use for CNCP because of bioaccumulation and central nervous system toxicity	√	–	–	√‡
Codeine: ability to convert to morphine varies greatly	–	–	–	√‡
Initiation and titration of dose				
Strategies to minimize risk for overdose	Start low-dose, short-acting opioid as needed; visit in 2–3 d	Start low-dose opioid; titrate carefully; reassess often	Trial; individualize dosing§	Start low-dose, short-acting opioid; use caution
Switching between opioids				
Dose reduction: equianalgesic dosing tables omit variability	Decrease dose by 25%–50%	–	Decrease dose moderately‡	–
Switching to methadone: conversion ratios vary with dose	–	√	√‡	–
Drug–drug interactions				
Sedative-hypnotics: risk for sedation, cognitive impairment, motor vehicle accidents, and overdose	Discusses risks‡	High risk from BZDs; rarely justified	Discusses risks	If patient is receiving BZDs, opioids are contraindicated‡
Pharmacokinetic interactions: other medications affect the metabolism of specific opioids	Limited list	–	–	Many occur‖
Drug–disease interactions				
Preexisting substance abuse disorders: increased risk for overdose and misuse	√	√‡	√‡	√‖
Mood, personality, and cognitive disorders: increased risk for overdose and misuse	√	–	√‡	√‡
Sleep and obstructive pulmonary disorders: opioids exacerbate	–	–	√‡	√‡
Chronic kidney disease	–	–	Slowly increase methadone	–
Active metabolites of morphine accumulate	–	–	–	√
Screening tools for assessing risk for misuse (used in addition to patient history)				
Recommends use	√§	√‡	√‡	Consider‡‖
Provides examples	√	–	√	√
Written treatment agreements (used in addition to informed consent)				
Recommends use	√§	If concerned§	Consider‡	√‡
Provides example	√	–	√	√
Urine drug testing				
Recommends use	Baseline and at least quarterly thereafter‡	–	If risk is high; consider otherwise‡	Must use; baseline and at random thereafter‡

AAPM = American Academy of Pain Medicine; ACOEM = American College of Occupational and Environmental Medicine; AGS = American Geriatrics Society; APS = American Pain Society; ASIPP = American Society of Interventional Pain Physicians; BZD = benzodiazepine; CNCP = chronic noncancer pain; DoD = Department of Defense; DWC = Division of Workers' Compensation; ICSI = Institute for Clinical Systems Improvement; NOUGG = National Opioid Use Guideline Group; UDOH = Utah Department of Health; UMHS = University of Michigan Health System; VA = Veterans Affairs.

* Guidelines by the American Society of Anesthesiologists (53), Fine and colleagues (54), and the Work Loss Data Institute (56) are omitted. The American Society of Anesthesiologists guideline did not address topics in the table. The guideline by Fine and colleagues addressed switching from one opioid to another but not the other topics. The Work Loss Data Institute guideline content is proprietary.

† Evidence from randomized, controlled trial.

‡ Evidence from observational study.

§ Evidence from expert consensus.

‖ Evidence from another guideline.

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Table—Continued

Guideline Development Group (Reference)*					
NOUGG (46, 60–62)	Colorado DWC (19)	ICSI (47)	UMHS (44)	UDOH (48, 50)	VA/DoD (45)
200†§ (adverse effects)	120‡ (adverse effects)	200‖ (adverse effects)	100	120–200‖	200§ (trials used ≤300†)
√‡	√‖	√‡	√	√	√‡
√‡	√	√‡	√	√	√
√	Never use for CNCP	Risk for fatal overdose‡	–	–	√
√‡	√	√	–	√	√
√‡	√	√	–	–	√
Start low-dose opioid; increase gradually; monitor§	Trial; visits every 2–4 wk; multidisciplinary pain management	Titrate to maximize benefits and minimize risks‖	Visits weekly to monthly§	Trial; visits every 2–4 wk‖	Titrate up no more than every 5 half-lives‡
Decrease dose by 25%–50%	–	Decrease dose by 30%‖	–	Decrease dose by 25%–50%	Decrease dose by 30%–50%
–	–	–	√‡	√	√
Try to taper BZDs‡	Avoid sedatives or use very low doses	Sedatives sometimes indicated; decrease doses	Avoid prescribing BZDs with opioids	Discusses risks	Watch for increased adverse effects‡
–	List for tramadol	Lists for several opioids	–	Look for interactions	Lists for several opioids
√‡	Comanage with addiction specialist	Comanage with addiction specialist‖	√	√	√
√‡	√‡	√	√	√	√‡
√‡	√	–	√	√	√‡
–	Consider screening	Use hydromorphone	–	–	Decrease oxymorphone
√‡	√	Morphine, codeine	–	Decrease dose	√
Consider‡	–	√‡	Consider‡	√‖	√‡
√	–	√	√	√	√
May be helpful, particularly if risk is high§	√‖	√§	Strongly consider, particularly if risk is high§	Agree on plan; signature is optional	Request that patient sign‡
√	–	√	√	√	√
If using, consider pros and cons§	Mandatory	√	Baseline and at least yearly thereafter§	Consider‖	Baseline and at random thereafter‡

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Selected Guidelines

Appendix Table 1 (available at www.annals.org) lists the 13 eligible guidelines; all were published in 2009 or later. Systematic reviews were conducted in 2008 or later (among guidelines that reported this).

Seven guidelines apply broadly to adults with chronic pain (13, 44–50). Six have slightly narrower scopes: The American Geriatrics Society guideline addresses adults older than 65 years (51, 52); the American Society of Anesthesiologists guideline emphasizes procedures (53); a guideline by Fine and colleagues addresses opioid rotation (54); and guidelines from the American College of Occupational and Environmental Medicine, the Work Loss Data Institute, and the Colorado Division of Workers' Compensation consider individuals with pain due to work-related conditions (19, 55, 56).

Guideline Quality Assessment

AGREE II

Overall guideline assessment scores were 3.00 to 6.20 (**Appendix Table 2**, available at www.annals.org). Rigor-of-development scores were 20% to 84%, clarity-of-presentation scores ranged from 37% to 93%, applicability scores were 13% to 56%, and editorial independence scores ranged from 0% to 88%.

Ratings were highest for a guideline by the American Pain Society and the American Academy of Pain Medicine (APS-AAPM) (13) and one by the Canadian National Opioid Use Guideline Group (46), the only guidelines that more than 50% of appraisers voted to use without modification. Most appraisers recommended against using 4 other guidelines because of limited confidence in development methods, lack of evidence summaries, or concerns about readability (19, 44, 53, 54).

Among the low- to intermediate-quality guidelines (19, 44, 45, 47–56), shortcomings included limited or no descriptions of input from guideline end users or patients; criteria for selecting evidence, strengths and limitations of evidence, and methods for formulating recommendations; external reviews before publication; plans for updating; barriers to implementation, resource implications, and how to implement guideline recommendations; monitoring and auditing criteria; and measures taken to ensure editorial independence.

AMSTAR

Systematic reviews within 10 guidelines were of poor or fair quality (19, 44, 47–56). The APS-AAPM review was of excellent to outstanding quality, the review by the Canadian National Opioid Use Guideline Group was of good to excellent quality, and the review by the Department of Veterans Affairs and Department of Defense (VA/DoD) was of good quality (**Appendix Table 3**, available at www.annals.org) (13, 45, 46).

Reasons for lower scores included limited information about whether inclusion criteria were selected beforehand, whether at least 2 reviewers participated in study selection and data extraction, whether more than 1 database was searched, search terms used, inclusion criteria, lists of included studies, whether the scientific quality of the studies was assessed, how information from different studies was combined, and whether publication bias was considered.

Guideline Synthesis and Analysis

The **Table** compares recommendations from 10 guidelines about mitigating risks when prescribing opioids (3 guidelines had little relevant content). The APS-AAPM, Canadian National Opioid Use Guideline Group, American Society of Interventional Pain Physicians, and VA/DoD guidelines make explicit links between each recommendation and original research evidence more frequently than the other guidelines do (13, 45, 46). Among recommendations in the **Table**, only upper dosing thresholds are reported to be supported by evidence from randomized, controlled trials; others are supported by lower-quality evidence or expert opinion. Even the higher-quality guidelines typically relied on modest numbers of lower-quality observational studies for many recommendations (13, 45, 47, 57, 60). Nonetheless, many recommendations are concordant across the guidelines.

Eight guidelines concur that higher doses require caution (19, 44, 45, 47, 50, 57, 59, 60). Four consider higher doses to be 200 mg of morphine equivalents per day, on the basis of randomized, controlled trials showing that most patients achieve pain control with lower doses and observational data showing that the prevalence of adverse effects increases at higher doses (45, 47, 57, 60). Because recent observational studies detected more overdoses with doses greater than 100 mg, the American Society of Interventional Pain Physicians guideline (2012) recommends staying below 90 mg unless pain is intractable (49, 59). The University of Michigan Health System guideline (2012) advises that patients receiving more than 100 mg be treated by pain specialists (44).

Ten guidelines—6 of which cite observational data—agree that methadone poses risks for dose-related QTc prolongation and respiratory suppression due to a long half-life and unique pharmacokinetics (13, 19, 44–47, 49, 50, 52, 55, 57, 60). These guidelines generally recommend that only knowledgeable providers prescribe methadone. Eight guidelines recommend caution with the fentanyl patch, including limiting use to opioid-tolerant patients and being aware that unpredictable absorption can occur with fever, exercise, or exposure to heat (19, 44, 45, 47, 49, 50, 55, 60, 61). Cited evidence includes an observational study investigating fentanyl overdoses in Ontario, Canada, as well as case reports submitted to the U.S. Food and Drug Administration (47, 49, 60, 63).

Ten guidelines make variable consensus-based statements about initiating and titrating opioids, such as using a trial period, individualizing therapy, engaging multidisciplinary pain management teams, increasing doses slowly,

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and scheduling regular follow-up visits (13, 19, 44–48, 50, 52, 55, 59).

Regarding switching from one opioid to another, 7 guidelines agree that reducing doses by at least 25% to 50% is necessary to avoid inadvertent overdose; the guideline by Fine and colleagues provides nuanced recommendations (13, 45, 47, 48, 50, 54, 55, 60). Two guidelines cite a systematic review of observational studies, which found that patients respond variably to different drugs (13, 54). Five guidelines mention that many persons of Caucasian or Chinese ancestry cannot metabolize codeine to morphine and are therefore less responsive to its analgesic effects and cannot develop tolerance (19, 45, 47, 59–61). Conversely, 5 guidelines note that some patients metabolize codeine to morphine ultra-rapidly, potentially resulting in overdose (19, 47, 49, 59, 60); certain ethnicities are at greater risk, particularly persons from North Africa and the Middle East (45).

Ten guidelines concur, on the basis of observational data, that benzodiazepines and opioids are a high-risk combination, particularly in elderly adults (13, 19, 44, 45, 47, 48, 50, 52, 55, 59–61). Five recommend against prescribing both together unless clearly indicated (19, 44, 49, 52, 60, 61). Six guidelines describe pharmacokinetic interactions between other medications and opioids, particularly methadone, fentanyl, oxycodone, and tramadol (19, 45, 47–49, 55). Six guidelines mention the accumulation of active, toxic metabolites of morphine among patients with kidney disease (19, 45, 47, 49, 50, 60). Ten guidelines consider the leading risk factors for overdose or misuse as having a personal or family history of substance abuse and having psychiatric issues (13, 44, 45, 47–49, 52, 55, 59–61); 3 cite observational studies (13, 52, 60, 61). Seven guidelines identify obstructive respiratory disorders as risk factors for overdose, also on the basis of observational data (13, 19, 44, 45, 48, 50, 59–61).

In terms of mitigating risks, the evidence for opioid risk assessment tools, treatment agreements ("contracts"), and urine drug testing is weak, but recommendations vary in strength from "may consider" to "must." Nine guidelines recommend considering or using opioid risk assessment tools and treatment agreements on the basis of observational studies and expert consensus (13, 44, 45, 47, 48, 50, 52, 55, 59–61). Eight guidelines mention or provide specific risk assessment instruments for use when initiating therapy with long-term opioids, such as the Screener and Opioid Assessment for Patients with Pain (SOAPP), version 1 (64); the revised SOAPP (65); and the Opioid Risk Tool, or monitoring tools for use during follow-up, including the Pain Assessment and Documentation Tool (66, 67) and the Current Opioid Misuse Measure (44, 45, 47–50, 55, 57, 60, 68). For detecting aberrant drug-related behaviors, the self-administered SOAPP, version 1, and the Current Opioid Misuse Measure performed well in higher-quality observational studies (57). Treatment agreements may improve adherence and providers' willingness to prescribe opioids, on the basis of a few small, observational studies (49, 57, 60).

Nine guidelines find urine drug testing to be helpful, but recommendations vary (13, 19, 44, 45, 47, 48, 55, 59, 60). Two recommend mandatory testing for all patients (19, 49), another advises testing for patients at higher risk for substance abuse disorders (13), and 2 comment that screening low-risk populations increases false-positive results and is less cost-effective (13, 60, 61). False-negative results can occur because a common test, the enzyme-linked immunoassay, does not consistently detect hydrocodone, fentanyl, hydromorphone, oxycodone, methadone, or certain benzodiazepines; gas chromatography or mass spectrometry will identify specific substances when requested (44, 46, 50, 60–62). Nonadherence, diversion, tampering, and lactic acidosis can also cause unexpected negative results. The differential for unexpected positive results includes abuse, consulting multiple physicians, self-treatment of uncontrolled pain, interference by other medications, eating poppy seeds, and laboratory error (13, 44, 46, 49, 59–62).

Discussion

Increasing overdoses on prescription opioids have prompted efforts to redefine standards of care, particularly for patients with chronic pain, who may be prescribed opioids for long-term use. We evaluated the quality of 13 guidelines on using opioids to treat chronic pain and compared recommendations related to mitigating risks for overdose and misuse. Two guidelines received high ratings: one by APS-AAPM (13) and another by the Canadian National Opioid Use Guideline Group (46). Both apply to a broad range of adults, were developed using comprehensive systematic reviews and rigorous methods for formulating recommendations, and frequently link recommendations to evidence. Our appraisers found 7 other guidelines to be of intermediate quality and recommended against using the remaining 4. Systematic reviews supporting 10 guidelines were judged, on the basis of publicly available information, to be of poor to fair quality.

Although the guidelines involve varied development methods and clinical emphases, a consensus has emerged across them on several issues. They generally agree about the need for caution in prescribing doses greater than 90 to 200 mg of morphine equivalents per day, having knowledgeable clinicians manage methadone, recognizing risks associated with fentanyl patches, titrating with caution, and reducing doses by at least 25% to 50% when switching from one opioid to another. They also agree that opioid risk assessment tools, written treatment agreements, and urine drug testing can be helpful when opioids are prescribed for long-term use. Recommendations from earlier guidelines are generally similar to those published recently. Most of these recommendations are based on epidemiologic and observational studies showing associations be-

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tween certain exposures, such as drugs or doses, and greater risks for overdose or misuse. Few studies seem to have directly addressed questions of whether changing practice decreases risk. Given the pressing need to address opioid-related adverse outcomes, which some have described as an epidemic (69), developers seem to agree on forging recommendations based on relatively weak or indirect evidence now rather than waiting for more rigorous studies.

It may be unusual for multiple guidelines to make such similar recommendations, but the variability in guideline quality that we observed is not. For example, among 19 breast cancer guidelines, AGREE II rigor-of-development scores were 16.7% to 89.6%, clarity-of-presentation scores ranged from 52.8% to 94.4%, applicability scores were 6.3% to 83.6%, and editorial independence scores ranged from 12.5% to 79.2% (70). Among 3 migraine guidelines, AGREE II rigor-of-development scores were 35% to 93%, clarity-of-presentation scores ranged from 6% to 92%, applicability scores were 20% to 88%, and editorial independence scores ranged from 29% to 86%; overall scores were 2 to 6, and appraisers recommended against using 1 guideline (71). Among 11 mammography guidelines evaluated using the original AGREE instrument and AMSTAR, appraisers recommended against implementing 5 guidelines, and 5 systematic reviews performed poorly (72).

Compared with these previous guidelines, the current opioid guidelines received lower scores on "applicability": None scored higher than 56%. Applicability includes consideration of potential barriers to and facilitators of implementation, strategies to improve uptake by providers, and resource implications of applying the guideline. Barriers to implementation are a major reason that physicians are often slow to incorporate clinical guidelines into their decision making (73). To identify such barriers, guideline developers and implementers are starting to use the GuideLine Implementability Appraisal (GLIA) tool (74–76), which assesses "executability" (know what to do), "decidability" (can tell when to do it), validity, flexibility, effect on process of care, measurability, novelty or innovation, and "computability" (can be operationalized in an electronic health record system) (77). Although GLIA is labor-intensive (76), it probably requires fewer resources than pilot testing and is preferable to issuing a guideline that is not used. Developers of opioid guidelines could incorporate GLIA into the next updating process, thereby improving applicability.

Although we selected guidelines that had been updated within the past 6 years, some evidence has already started to change, particularly regarding the risk for overdose. Five guidelines published before 2012 consider doses greater than 200 mg of morphine equivalents per day to confer higher risk. Three observational studies from 2010 and 2011 show that, compared with patients receiving no more than 20 mg, the risk for serious or fatal overdose increases 1.9- to 3.1-fold with doses of 50 to 100 mg and increases dramatically with doses greater than 100 to 200 mg (78–80). Guidelines published in 2012 use thresholds of 90 to 100 mg. In 2007, the state of Washington implemented workers' compensation guidelines recommending evaluation by a pain management expert for patients receiving more than 120 mg/d as well as other risk mitigation strategies that are similar to or, in some areas, more restrictive than those of the guidelines reviewed here. Although pain control has not been described, the number of patients receiving opioids and the doses prescribed started decreasing in 2007 and fatal overdoses decreased in 2010 (4).

Given that overdoses occur even at lower doses, some may wonder about the overall risks and benefits of using opioids for chronic pain. According to previous systematic reviews of randomized, controlled trials, oral opioids are substantially more effective than placebo or nonsteroidal agents, with 30% to 50% decreases in pain severity and significant improvements in functional status (14, 81–83). However, study quality has not been high, and the duration of follow-up has often been limited (14, 84). At least one third of patients stop opioid use because of adverse effects (46, 81, 82, 85). Abuse occurs in 0.43% to 3.27% of patients and addiction affects 0.042%, but 11.5% engage in aberrant drug-related behaviors or illicit use (14, 85, 86). This evidence has generally been incorporated into the guidelines and is reflected in the supportive but cautious approach that they take toward long-term opioid therapy.

Our evaluation has several limitations. First, we relied on publicly available information, so we were unable to evaluate several guidelines (17, 40–43, 87) or the clarity of the proprietary Work Loss Data Institute guideline. Although AGREE scores can improve when developers provide supplemental information (88), the IOM recently outlined guideline development standards stating, "The processes by which a [clinical practice guideline] is developed and funded should be detailed explicitly and publicly accessible" (32). Second, neither the IOM nor AGREE stipulate how guidelines should select topics. To be useful, guidelines should address the challenges that clinicians face in practice, but developers may exclude clinically important topics when available evidence does not meet minimum standards.

In conclusion, rigorous clinical practice guidelines could help providers to attenuate the increasing rates of opioid misuse and overdose among patients with chronic pain. Recent guidelines make similar recommendations about strategies for reducing these risks despite variability in development methods, suggesting a clinical consensus for practices that could be adopted until more evidence becomes available. They agree on using upper dosing thresholds; cautions with certain medications; attention to drug–drug and drug–disease interactions; and risk assessment tools, treatment agreements, and urine drug testing. Although such recommendations can guide practice now,

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future research should directly examine the effectiveness of opioid risk mitigation strategies, including effects on pain control and overdose rates.

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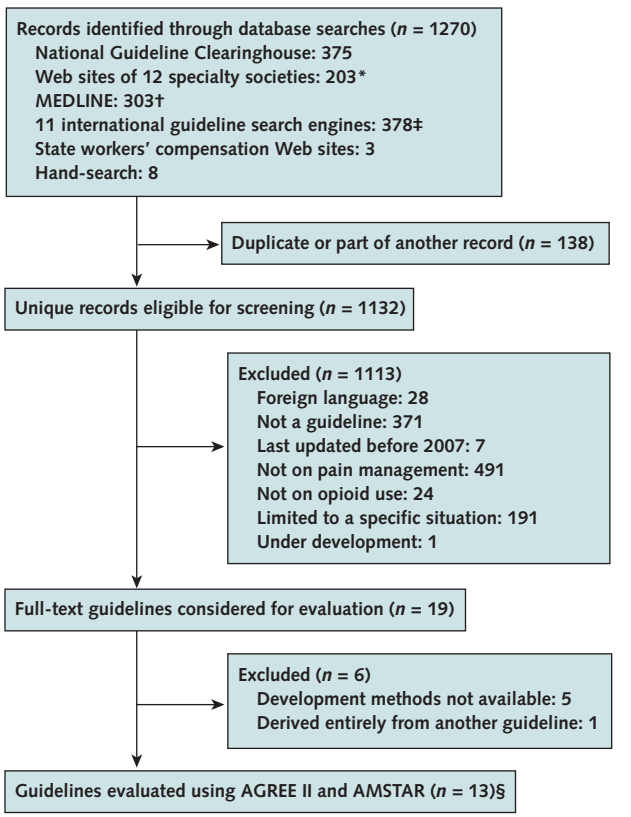
Appendix Figure. **Summary of evidence search and selection.**



AGREE II = Appraisal of Guidelines for Research and Evaluation II; AMSTAR = A Measurement Tool to Assess Systematic Reviews.

* Includes the American Academy of Family Physicians, American Academy of Pain Medicine, American Academy of Physical Medicine and Rehabilitation, American College of Occupational and Environmental Medicine, American College of Physicians, American Geriatrics Society, American Society of Addiction Medicine, American Society of Anesthesiologists, American Society of Interventional Pain Physicians, Association of Military Surgeons of the United States, National Medical Association, and Society of Medical Consultants to the Armed Forces.

† The exact PubMed search terms were "analgesics, opioid"[MeSH], "opioid"[tiab], "opioids"[tiab], "opioid analgesic"[tiab], "opioid analgesics"[tiab], "opiate"[tiab], "opiates"[tiab], "chronic pain"[MeSH], "chronic pain"[tiab], "pain management"[MeSH], and "pain management"[tiab] combined with "guideline"[Publication Type], "guideline*"[tiab], "position statement*"[tiab], "practice parameter*"[tiab], "position paper*"[tiab], and "consensus statement*"[tiab].

‡ Includes the Guidelines International Network; National Institute for Health and Care Excellence; Canadian Medical Association Infobase: Clinical Practice Guidelines; Clinical Practice Guidelines Portal of the Australian Government; Scottish Intercollegiate Guidelines Network; New Zealand Guidelines Group; Biblioteca de Guías de Práctica Clínica del Sistema Nacional de Salud (Library of Clinical Practice Guidelines from the Spanish National Health System); German Agency for Quality in Medicine; German National Disease Management Guidelines Programme: German Disease Management Guidelines; British Columbia Ministry of Health; and Australian Government National Health and Medical Research Council: Guidelines and Publications.

§ The American Geriatrics Society updated its guideline in 2009 and stated that the 2002 guideline, which covers slightly different material, was still up to date. When counting guidelines, we considered these to be components of 1 document.

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Appendix Table 1. **Guidelines Meeting All Selection Criteria and Included in Quality Appraisal**

Guideline	Development Group	Guideline Last Reviewed	Systematic Review Updated	Reference
ACOEM Guidelines for Chronic Use of Opioids	ACOEM	2011	References to primary literature dated 2007 or earlier*	55
Pharmacological Management of Persistent Pain in Older Persons	AGS Panel on Pharmacological Management of Persistent Pain in Older Persons	2009	References to primary literature dated 2008 or earlier	52
The Management of Persistent Pain in Older Persons	AGS Panel on Persistent Pain in Older Persons	2009	–	51
Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain	APS-AAPM	2009	October 2008	13, 57, 58
Practice Guidelines for Chronic Pain Management: An Updated Report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine	ASA	2010	2009	53
American Society of Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain	ASIPP	2012	References to primary literature dated 2012 or earlier	49, 59
Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain	NOUGG	2010	July 2009	46, 60–62
Chronic Pain Disorder Medical Treatment Guidelines	Colorado DWC	2011	November 2011	19
Establishing "Best Practices" for Opioid Rotation: Conclusions of an Expert Panel	Department of Pain Medicine and Palliative Care, Beth Israel Medical Center and Department of Anesthesiology, Pain Research Center, University of Utah School of Medicine	2009	References to primary literature dated 2007 or earlier	54
Assessment and Management of Chronic Pain	ICSI	2011	August 2011	47
Managing Chronic Non-Terminal Pain in Adults, Including Prescribing Controlled Substances	UMHS	2012	January 2010	44
Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain	UDOH	2009	References to primary literature dated 2007 or earlier	48, 50
Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain	VA/DoD	2010	March 2009	45
Pain (Chronic)†	WLDI	2011	Not reported (no references)	56

AAPM = American Academy of Pain Medicine; ACOEM = American College of Occupational and Environmental Medicine; AGS = American Geriatrics Society; APS = American Pain Society; ASA = American Society of Anesthesiologists; ASIPP = American Society of Interventional Pain Physicians; DoD = Department of Defense; DWC = Division of Workers' Compensation; ICSI = Institute for Clinical Systems Improvement; NOUGG = National Opioid Use Guideline Group; UDOH = Utah Department of Health; UMHS = University of Michigan Health System; VA = Veterans Affairs; WLDI = Work Loss Data Institute.

* Excludes such sources as references to other guidelines, narrative and systematic reviews, government reports, and book chapters because these are often identified through means other than systematic reviews of the literature.

† From *The Official Disability Guidelines* product line (including *ODG Treatment in Workers Comp*), which is updated annually.

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Appendix Table 2. **Results of AGREE II Evaluation**

Variable	Guideline Development Group (Reference)													Mean (Range), %
	ACOEM (55)	AGS (51, 52)	APS-AAPM (13, 57, 58)	ASA (53)	ASIPP (49, 59)	NOUGG (46, 60–62)	Colorado DWC (19)	Fine et al (54)	ICSI (47)	UMHS (44)	UDOH (48, 50)	VA/DoD (45)	WLDI (56)	
AGREE II domain score, %														
Scope and purpose (the overall aim of the guideline, the specific health questions, and the target population)	78	68	89	72	85	76	53	39	86	51	49	88	69	69 (39–89)
Stakeholder involvement (the extent to which the guideline was developed by the appropriate stakeholders and represents the views of its intended users)	55	39	73	43	53	77	41	23	69	39	50	58	59	52 (23–77)
Rigor of development (the process used to gather and synthesize the evidence and the methods used to formulate and update the recommendations)	60	44	84	33	56	74	27	24	56	20	43	55	49	48 (20–84)
Clarity of presentation (the language, structure, and format of the guideline)	67	68	84	54	79	93	37	71	80	64	74	78	–*	71 (37–93)
Applicability (the likely barriers to and facilitators of implementation, strategies to improve uptake, and resource implications of applying the guideline)	55	30	41	21	40	56	13	28	41	46	42	42	31	37 (13–56)
Editorial independence (the influence of the funding body on development and disclosure of conflicts of interest)	75	63	88	2	69	56	0	23	52	37	48	8	50	44 (0–88)
Mean domain score	63	49	76	38	61	73	29	33	62	39	49	57	51	52 (28–76)
Overall outcome of guideline development														
Mean overall quality score	4.75	4.00	6.20	3.00	4.67	6.00	3.00	3.40	4.50	3.60	3.60	4.75	3.50	4.23 (3.00–6.20)
Votes to recommend use														
Yes, *n (%)*	2 (50)	1 (20)	5 (100)	0	1 (17)	3 (75)	0	1 (20)	2 (40)	0	0	1 (25)	–*	–
Yes, with modifications, *n (%)*	0	4 (80)	0	0	4 (67)	1 (25)	2 (40)	1 (20)	2 (40)	1 (20)	3 (60)	3 (75)	–*	–
No, *n (%)*	2 (50)	0	0	4 (100)	1 (17)	0	3 (60)	3 (60)	1 (20)	4 (80)	2 (40)	0	–*	–
Total votes, *n*	4	5	5	4	6	4	5	5	5	5	5	4	–*	–

AAPM = American Academy of Pain Medicine; ACOEM = American College of Occupational and Environmental Medicine; AGREE II = Appraisal of Guidelines for Research and Evaluation II; AGS = American Geriatrics Society; APS = American Pain Society; ASA = American Society of Anesthesiologists; ASIPP = American Society of Interventional Pain Physicians; DoD = Department of Defense; DWC = Division of Workers' Compensation; ICSI = Institute for Clinical Systems Improvement; NOUGG = National Opioid Use Guideline Group; UDOH = Utah Department of Health; UMHS = University of Michigan Health System; VA = Veterans Affairs; WLDI = Work Loss Data Institute.

* The guideline is proprietary and text was unavailable, so raters could not assess clarity of presentation or decide whether to recommend use. Domain ratings were based on information the developer has made public about development methods and information related to the other domains.

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Appendix Table 3. **Results of AMSTAR Evaluation**

Question	Guideline Development Group (Reference)												
	ACOEM (55)	AGS (51, 52)	APS-AAPM (13, 57, 58)	ASA (53)	ASIPP (49, 59)	NOUGG (46, 60–62)	Colorado DWC (19)	Fine et al (54)	ICSI (47)	UMHS (44)	UDOH (48, 50)	VA/DoD (45)	WLDI (56)
Was an "a priori" design provided?	F	F	O	F	F	E	P	F	F	G	F	G	G
Was there duplicate study selection and data extraction?	F	P	O	P	P	G	P	P	P	P	P	P	P
Was a comprehensive literature search performed?	G	P	E	P	F	O	F	P	F	F	G	G	G
Was the status of publication (e.g., gray literature) used as an inclusion criterion?	G	F	G	F	F	G	P	P	F	G	F	G	G
Was a list of studies (included and excluded) provided?	P	P	E	F	F	G	F	P	P	P	F	F	P
Were the characteristics of the included studies provided?	P	P	O	P	P	G	F	P	P	P	P	P	P
Was the scientific quality of the included studies assessed and documented?	F	F	E	P	P	G	G	P	F	P	F	G	G
Was the scientific quality of the included studies used appropriately in formulating conclusions?	G	G	O	F	G	G	F	P	F	P	P	E	F
Were the methods used to combine the findings of studies appropriate?	F	F	E	F	F	E	P	P	P	P	P	G	F
Was the likelihood of publication bias assessed?	P	P	P	F	P	G	P	P	P	P	P	P	P
Was the conflict of interest stated?	F	F	O	P	F	F	F	F	P	F	F	F	P
Overall rating	F	P–F	E–O	P–F	F	G–E	P–F	P	P–F	P–F	F	G	F–G

AAPM = American Academy of Pain Medicine; ACOEM = American College of Occupational and Environmental Medicine; AGS = American Geriatrics Society; AMSTAR = A Measurement Tool to Assess Systematic Reviews; APS = American Pain Society; ASA = American Society of Anesthesiologists; ASIPP = American Society of Interventional Pain Physicians; DoD = Department of Defense; DWC = Division of Workers' Compensation; E = excellent; F = fair; G = good; ICSI = Institute for Clinical Systems Improvement; NOUGG = National Opioid Use Guideline Group; O = outstanding; P = poor; UDOH = Utah Department of Health; UMHS = University of Michigan Health System; VA = Veterans Affairs; WLDI = Work Loss Data Institute.

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