MINNESOTA

Chronic pain opioid prescribing recommendations

While the safest possible course of treatment is to avoid initiating chronic opioid analgesic therapy (COAT) for chronic pain, patients already receiving COAT must be carefully managed to mitigate the potential for opioid-related adverse effects. This includes opioid use disorder (OUD), non-fatal overdose and fatal overdose.

The Opioid Prescribing Work Group recommends that patient safety is a paramount treatment consideration when prescribing opioids for chronic pain. Improving functional status and reducing pain intensity also remain important treatment goals. Careful management of patients receiving COAT requires thorough and systematic risk benefit assessment of continued opioid therapy on an ongoing basis. When the risk benefit assessment reveals continued pain or dysfunction, providers should work with their patients to improve the patient's safety and quality of life.

Clinical recommendations

1. Perform a thorough assessment of mental health conditions prior to initiating COAT and continue assessment for the duration of the opioid therapy. See Biopsychosocial assessment (/dhs/opip/opioid-guidelines/factors-in-treatment/biopsychosocial-assessment.jsp).
2. Establish specific, measurable treatment goals with the patient prior to initiating COAT. Create treatment goals in terms of improvement in function and quality of life. Treatment goals must be realistic and obtainable. Resolution of pain should not be a treatment goal for chronic opioid therapy, as evidence indicates that this is not an achievable goal.
3. Assess potential barriers to active participation in the treatment plan with the patient. Assess the patient's physical limitations and document physical recommendations in clear and simple language. Help the patient identify modifications that will allow him or her to maintain daily routines, when needed.
4. Identify in the treatment plan the person who will coordinate care across the providers and services identified. Offer the patient access to a care coordinator via the telephone in case an issue arises. If possible, identify the pharmacy that the patient will use to fill all medications included in the treatment plan.
5. Initiate a patient provider agreement (PPA) or understanding prior to beginning COAT for every patient, or continuing opioid therapy in a new patient.
6. Use caution when prescribing opioids at any dosage and make every effort to keep daily dosage under 50 MME/day. Re-evaluate the patient's individual risks and benefit of continued treatment when increasing dosage. Avoid increasing daily dosage to ≥ 90 MME/day. Clinicians who decide to increase the daily dosage to ≥ 90 MME/day must carefully document that the risks and benefits were weighted and benefits warrant the risk.

7. **Limit the duration** of the prescription to one month and prescribe so that the prescription does not end during a weekend or on a holiday. Face to face visits with the prescribing providers should occur at least every three months, based on the patient's risk profile. Patients at higher risk for adverse events should be seen more frequently.
8. Offer to taper to a reduced dose or to discontinuation at every face to face visit. See Opioid taper or discontinuation (/dhs/opip/opioid-guidelines/tapering-opioids/index.jsp).
9. Avoid initiating COAT for pain in patients with untreated substance use disorder or a history of substance use disorder.

Formulation recommendations

10. Prescribe immediate release/short acting opioids when initiating COAT. Long-acting/extended-release opioids should be reserved for patients with established opioid tolerance and in whom the prescriber is confident of the patient's medication adherence.
11. Avoid routine rotation or substitution of opioids. If substitution or conversion is indicated, use opioid conversion tables only as guidance. Doses of the new opioid should be reduced by 30-50% of the daily MME dose of the previous stable opioid agent to account for incomplete cross-tolerance.
12. Avoid using methadone interchangeably with other extended-release/long-acting opioids for chronic pain. Only clinicians trained or experienced in the appropriate dosing and management of methadone therapy should consider using methadone for chronic pain.
13. Exercise extreme caution when considering fentanyl therapy for pain, given the potential for diversion and harm. Clinicians trained or experienced with the dosing and absorption properties of transdermal fentanyl are best equipped to prescribe, educate and monitor patients appropriately.

Risk mitigation strategies

14. Monitor reproductive health in all women of childbearing age (/dhs/opip/opioid-guidelines/factors-in-treatment/childbearing-age-women.jsp) who receive COAT or MAT. Provide family planning services and counsel women on using effective contraception while on COAT or MAT. Effective contraception is the primary way to prevent unintended pregnancy and risk of delivering a baby with Neonatal Abstinence Syndrome (NAS) or Neonatal Opioid Withdrawal Syndrome (NOWS).
15. Complete a urine drug screen (UDS) prior to initiating or continuing COAT in a new patient and consider a random UDS at least twice a year. Complete a UDS when patients come to the clinic for a pill count. Standardize UDS policies at the clinic or health system level in order to destigmatize their use. Use the UDS results to guide treatment decisions, improve patient-clinician communication and monitor patient safety. Consider ordering a confirmatory test for positive results to confirm substance identification. Clinicians should not dismiss patients from care solely based on UDS results that contradict the patient's self-reported adherence to therapy.
16. Consider pill count callbacks for high risk patients. Callbacks generally require patients to come to the clinic to count remaining opioid pills within 24 hours of being notified. If the pill count results in fewer or greater pills than expected, schedule a visit with the patient to discuss the results.
17. Monitor patients receiving COAT for the presence of opioid use disorder (OUD). Clinicians who are unable to diagnose OUD using the DSM-5 criteria can use a brief, standardized screening tool and make a referral as appropriate.

18. Offer or arrange evidence-based treatment for patients with OUD. Clinicians who are not authorized to provide evidence-based treatment should work with their practice group to build capacity for treatment and/or build a referral network of treatment providers.
19. Consider consulting specialists trained in pain, addiction or mental health conditions when initiating COAT. Early consultation may help identify the potential for increased risk, even in patients at low risk of adverse events, if opioid therapy continues. Refer patients receiving COAT to addiction and mental health specialists when there is a significant risk for opioid-related harm, as appropriate for the patient's needs. The referring clinician should continue to treat the patient until a successful transfer of care has occurred, or until the patient fails to follow through on the referral and continues to be at risk.

Discussion

Assessment: Pain and function

Assessment of pain intensity alone for patients experiencing chronic pain is insufficient. Research demonstrates that pain intensity scores of chronic pain patients are not predicted by etiology of the pain *(Hashmi, 2013)*. Therefore, assessment tools are more likely to be useful when function and quality of life are included in the assessment.

Diagnose or confirm the origin of the pain at the time of assessment. Former injuries and diagnoses should be considered in the differential diagnosis, however it is possible that they are no longer the pain generator. Consider opioid-induced hyperalgesia in the differential diagnosis when the patient has long-term opioid exposure. The correct diagnosis of the etiology of the pain is necessary to guide effective selection of patient-specific treatment modalities. Diagnostic evaluation should be complete, but should avoid exhaustive testing that has no reasonable expectation of providing a nociceptive etiology.

Treatment planning: Barriers to treatment

Not all patients have the resources needed to use health care services, engage in healthy behaviors and participate in treatment plans. Socioeconomic factors clinicians need to consider include, but are not limited to: geographic location; housing; employment; transportation; social support; education. Health care systems or practices with access to a social worker should include the social worker in the health care team. Social workers can help patients address resource/socioeconomic barriers that hinder patient engagement in the treatment plan.

Treatment planning: Goals

Clinicians should carefully discuss goals with patients experiencing chronic pain. Explain to patients that while a reduction in pain intensity is an important treatment goal, the goals should also include engagement in valued life activities through improved social function and social interaction. Elimination of pain is never a realistic goal. Treatment goals should be tailored to the individual. Clinicians should encourage the patient to drive the goal-setting process and provide input on improvement that is objective, attainable and measurable.

Patient Provider Agreement (PPA)

Patient Provider Agreements (PPAs) are typically written treatment plans that identify the clinician and patient's roles and responsibilities related to initiating long-term opioid therapy. Clinicians should approach initiating the PPA as a means to educate the patient about best practices for opioid use. In addition, the PPA may serve as a diagnostic tool to identify concerns as the patient continues his or her opioid therapy. Review the agreement with the patient at regular intervals determined by the patient's risk profile. In general, review the agreement with the patient at least annually.

Components of an effective PPA include:

- Clearly defined roles and responsibilities for both the clinician and the patient
- Requirements related to other pain medications
- One physician/one pharmacy
- Consent to disclose information to or discuss care with other prescribers identified in the Prescription Monitoring Program (PMP)
- Agree to take the medication as prescribed/no early refills
- Patient responsibility for safeguarding the prescription and supply, including planning ahead so that supply does not end on weekend or holiday
- Required reporting of side effects
- Required appointments and screenings
- An exit strategy for when it is determined that harms outweigh the benefit of continued COAT
- 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 *(CDC, 2016a)*.
- Training of family members, friends, or caregivers in naloxone administration
- Referral or evaluation of OUD if patient becomes unable to follow the terms of the agreement, or the provider or patient become concerned about OUD.

It is not demonstrated that PPAs improve clinical outcomes related to opioid therapy, however the PPA can serve as an important educational, communications and diagnostic tool. *(CDC, 2016a; Starrel, 2006).* Clinicians should consider the multiplicity of objectives that a PPA serves and stress the importance of the PPA to set expectations about both the clinician's and patient's responsibilities during opioid therapy. When used appropriately, a PPA can help prevent patient provider disagreement and allow the clinic to insist on consistent and universal practices for opioid-receiving patients *(ICSI, 2017)*.

Clinicians should avoid dismissing patients from care when the patient is unable to comply with the terms provided in the PPA. This may be an indicator that the patient is developing dependence or OUD and the patient should be referred to the appropriate care.

Prescribing: Dose and duration

Clinicians should consider opioid-induced pain, a newly onset OUD and/or the potential for drug diversion prior to increasing the daily dose. Tolerance at high doses is not a sufficient reason to increase dosage to ≥ 90 MME/day. Dosages greater than 90 MME/day should be considered temporary (e.g., acute on chronic pain for verifiable new condition) and every effort should be made to reduce the dosage as soon as possible.

Several studies have examined the relationship between the total daily dose of oral opioids—expressed as total MME per day—and opioid related harm. Evidence supports a dose-response relationship, with risk of overdose-related death increasing significantly at 100 MME/day. Studies examining other opioid-related harms demonstrate increasing risk of harm between 50 and 100 MME/day *(Han, 2015; Gomes, 2011; Dunn, 2010)*. It is the belief of the work group that as the dose-response relationship is further studied, the evidence may support even lower daily doses of opioids to avoid opioid-related harm. Clinicians are encouraged to keep daily doses under 50 MME/day and continually offer to reduce doses for those patients whose daily dose exceeds the 50 MME/day limit.

Opioids incur greater risk of overdose in certain populations, including patients with substance use disorder *(CDC, 2016a; Han, 2015; Turner, 2015)*. Given the inherent risk of prescribing opioids to a patient with untreated substance use disorder, clinicians should use non-opioid and non-pharmacologic therapies when treating the patient's pain.

Formulation

Extended release/long acting (ER/LA) opioids include extended-release versions of oxycodone, oxymorphone, hydrocodone and morphine. There is limited evidence on the increased efficacy or safety of ER/LA opioids versus intermittent use of immediate-release opioids *(CDC, 2016a)*. One clinical study found a higher risk for overdose among patients initiated on treatment with ER/LA than among those initiated on treatment with immediate release opioids *(Miller, 2015)*.

The FDA notes that "because of the greater risks of overdose and death with extended-release opioid formulations, reserve ER/LA opioids 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." *(FDA, 2014)*. 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, 8 mg oral hydromorphone/day, 25 mg oral oxymorphone/day, or an equianalgesic dose of another opioid) *(FDA, 2014)*.

Contraindications to ER/LA opioids listed in the FDA safety information include, but are not limited to:

- Respiratory depression that is significant
- Asthma that is severe or acute, in an unmonitored setting or without equipment for resuscitation
- Paralytic ileus
- Hypersensitivity to the opioid

Rotation and substitution

Routine rotation or substitution of opioids should be avoided, however there may be circumstances in which it is appropriate to change to a different opioid. These circumstance include, but are not limited to:

- Patients with renal failure
- Change of health insurance and/or drug formulary
- Hospice/terminal cancer care

Opioid conversion tables do not account for incomplete cross-tolerance in opioid-tolerant patients *(AMDG, 2015, Webster, 2012)*. Therefore, doses of the new opioid should be reduced by 30-50% of the previous daily MME dose to avoid any harm related to incomplete cross-tolerance.

Methadone and fentanyl

Methadone has unique pharmacokinetic and pharmacodynamics properties, including a long and variable half-life that is not consistent among patients. It is highly lipophilic and the respiratory depressant effect lasts longer than the analgesic effect (Chou, 2009). Clinicians trained in prescribing methadone are better prepared to educate patients on methadone's unique risk profile, dose appropriately and provide the ongoing monitoring and assessment necessary to manage risk appropriately.

Methadone treatment for chronic pain may be indicated for a small, sub-set of patients, including patients with incurable, chronic neuropathic pain that has not responded to other opioid formulations.

Transdermal fentanyl is a long-acting, renal-safe synthetic opioid. Clinicians who prescribe fentanyl for chronic pain should consider the following:

- Patients initiated on transdermal fentanyl must be opioid tolerant (greater than 60 MME/day) and possess the cognitive ability to apply, remove and dispose of the patches safely (FDA, 2013).
- Patients require ongoing education about appropriate use and disposal of fentanyl patches. Patches should be removed after 72 hours, folded upon themselves sticky side inward and promptly flushed down the toilet. Note: This disposal recommendation is unique to fentanyl patches given the high risk that even used patches pose to children and other family members.
- Transdermal fentanyl should not be given in addition to any other long-acting agents.
- Do not prescribe fentanyl to patients with a history of substance use disorder.

Sublingual fentanyl should be reserved for only those in need of palliative care for extreme pain and unable to take any alternatives.

Monitoring and risk mitigation

All patients receiving COAT should be monitored for opioid-related harms and misuse, however there is not a specific monitoring protocol indicated in the scientific literature. Clinicians should monitor use using the following risk management strategies, depending on the patient's risk:

Prescription Monitoring Program

Query the PMP each time opioids are prescribed to patients on COAT.

Urine drug screening

Urine drug screens can play an important role in monitoring patients on COAT. Although there is limited evidence that routine use of UDS improves patient outcomes, current opioid prescribing guidelines recommend routine use of UDS in chronic pain patients *(CDC, 2016a; ICSI, 2017)*. Urine drug screens can identify other substances used by the patient and/or when the patient is not adherent to his or her treatment regimen. Clinicians should use the results of a UDS to guide treatment decisions and referral to the appropriate level of care. The results of UDS cannot be used to diagnose substance use disorder or confirm diversion.

Interpreting urine drug screens is highly complex. In order for UDS to be an effective component of clinical management of chronic pain patients, clinicians must develop knowledge regarding proper specimen collection and validation, interpretation of positive and negative results and the role and need for confirmatory testing. Clinicians and health systems are encouraged to take an active role in the design and development of their UDS processes. An “on-call” toxicologist or addictionologist is a useful resource for assistance with inconsistent drug screens.

Pill count callbacks

Although the medical literature has shown no well-established benefit of callbacks, it is the opinion of the Opioid Prescribing Work Group that pill count callbacks are useful for certain patient populations. These patient populations include those with demonstrated difficulty taking their medicine as prescribed and those for whom there is suspicion of diversion *(ICSI, 2017)*.

Pill count callbacks are often a burden to patients. Include pill count callbacks in the patient-provider agreement and risk monitoring discussions, if appropriate. Patients should be aware that pill counts are possible as part of their COAT and contact information should be kept updated. If the pill count results in fewer or greater pills than expected, schedule a visit with the patient to discuss the results. Possible reasons for a discrepancy in the number of pills include diversion and misuse, but may also be a result of misunderstood directions, overprescribing, opioid-induced hyperalgesia, or an attempt to cope with an emerging mental health condition.

Consultation and referral

Patients who receive COAT should be managed by a multi-disciplinary care team, including, but not limited to, medical providers, mental health providers and other providers such as physical therapists. In addition, health care providers who prescribe opioids should develop a referral network of specialists for patients at higher risk of opioid related harm. The network should include mental health providers, addiction specialists, pain medicine specialists and medication-assisted treatment providers. These services can also be provided in the clinic, especially in situations where an office based medication-assisted treatment program exists.

Clinicians, especially those who practice in rural settings, are encouraged to develop referral networks using existing and developing technology, such as telemedicine and Project ECHO.

Clinicians are encouraged to complete the DATA 2000 Qualifying Buprenorphine training in order to be able to treat OUD in emergency department, primary care, obstetric, or pain medicine settings. Clinicians, especially those who practice in rural settings, are encouraged to develop referral networks or obtain support for their medication-assisted treatment (MAT) practice using existing and developing technology, such as telemedicine and Project ECHO.

The guidance below provides an overview of when referral to a specialist or a substance use disorder evaluation program may be appropriate. The guidance is not intended to be all-inclusive.

a. Addiction specialists and medication-assisted treatment (MAT) providers

- Assessment and/or diagnosis of substance use disorder;
- Patient gains access to MAT for an established or past OUD;
- Patient presents with behaviors suggestive of substance use disorder (any substance), including but not limited to:
    - Failed opioid taper
    - Concerning aberrant behaviors, including overuse or misuse of opioids and dangerously combining opioids with other substances
    - Known harm from opioids with an ongoing indication for opioid analgesia
- Patient presents with evidence of an emerging OUD or other substance use disorder, or an untreated OUD; or
- Patient is unable to taper in an outpatient setting or OUD is unmasked during the taper process.

b. Pain medicine specialists physicians are certified as specialists in the treatment of pain through the American Board of Medical Specialties and the American Board of Pain Medicine.

Pain medicine specialists provide a broad range of services and not all specialists treat pain with the same modalities. Referring clinicians should become familiar with the pain specialists in their geographical area and the types of treatment modalities provided. When a referral is appropriate, refer the patient to a pain medicine specialist with experience in the appropriate treatment modality and who is able to engage in multi-disciplinary patient care.

c. Mental health providers

All patients receiving opioids, regardless of the patient's risk profile, should receive care from a multi-disciplinary team, including mental health screening and monitoring. It is the opinion of this work group that most chronic pain patients with functional limitations will benefit from treatment by a pain psychologist.

Coping with limitations caused by pain is a major reason to refer a patient to a pain psychologist, even if no mental health disorder or no behavioral issues are present.

The indications for referral listed below—with exception—address circumstances in which the patient is at high-risk for opioid-related harm. DSM-5 Axis One disorders confer mortality risk and predict development of OUD in patients who are prescribed opioids for chronic pain. Any patient receiving chronic opioids for pain who has such a mental health disorder should be evaluated and optimally treated for their mental health. This may require a psychology or psychiatric referral. Determine whether referral to a psychologist or a psychiatrist is appropriate based on the patient's risk factors and medical history.

Indications for referral:

- Patient expresses interest in alternative approaches
- Patient demonstrates behavioral issues in the clinic
- Patient does not regain function or social relationships after treatment is initiated
- Patient demonstrates high-risk behaviors suggestive of suicidal ideation or verbalization of suicidal thoughts
- Exacerbation of underlying psychotic disorder
- Patient has an uncontrolled, severe psychiatric disorder or emotional instabilities
- Patient has psychological trauma-related conditions.

A psychiatry referral is appropriate at any time a patient has a major mental illness that cannot be satisfactorily managed by the primary care provider. The patient should be seen by a psychiatrist as a condition of being on opioids. A psychiatry referral is also appropriate when seeking a diagnosis or for suicidal/homicidal/psychotic thoughts or emotional instability.

Screening for opioid use disorder (OUD)

A systematic review of 38 studies by Vowles et al. (2015) found that the rates of opioid misuse averaged between 21 and 29% among adult patients with chronic non-cancer pain. Misuse in this review was defined as opioid use contrary to the directed or prescribed pattern of use, regardless of the presence or absence of harm or adverse effects *(Vowles, 2015)*. Opioid misuse and OUD are adverse events that can occur in all patients and clinicians should monitor all patients and provide universal screening *(Volkow, 2016b; Kirschner, 2014; Dowell, 2013)*.

Patients with OUD receiving opioid analgesia for pain are at high risk for opioid-related harm, including fatal overdose. Clinicians who prescribe COAT are responsible for being able to recognize the symptoms of OUD in their patients and provide referrals to treatment, or offer medication-assisted treatment with behavioral therapies. The State recognizes that while many clinicians are largely untrained to recognize OUD, there are a growing number of resources available to clinicians to enhance their training and knowledge about this disease.

Consider the current OUD diagnostic criteria when monitoring patients for signs of opioid misuse *(APA, 2013)*. Clinicians who are unable to provide a diagnostic assessment for OUD should screen patients using the Tobacco, Alcohol, Prescription medication and other Substance abuse (TAPS) tool. The TAPS tool consists of a 4-item screening for tobacco use, alcohol use, prescription medication misuse and illicit substance use in the past year and can detect clinically relevant problem substance use in a primary care setting *(McNeely, 2016)*. Refer patients who screen positive for substance use disorder for treatment.

Evidence-based treatment for OUD

Clinicians should be knowledgeable about evidence-based OUD treatment options (see below) and consider offering MAT to their patients with OUD. Clinicians who choose not to directly offer MAT should work within their group to provide treatment capacity or develop a strong referral network for MAT and behavioral therapies.

MAT offers stabilization of OUD through buprenorphine-containing products or opioid antagonists integrated with behavioral health interventions and recovery-based supports. MAT has been shown to be safe and effective in suppressing illicit use, improving physical and mental well-being and reducing all cause and overdose mortality *(Mattick, 2014; Department of Veterans Affairs, 2015)*. MAT has also been shown to be successful among patients who experience chronic pain *(Weiss, 2011; Dennis, 2015)*.

Clinicians may refer to the Department of Human Services Health Services Advisory Council Recommendations for Medication-Assisted Recovery.

Evidence-based OUD treatment options

The following evidence-based treatment [modalities] should be delivered in conjunction with behavioral health interventions and recovery-based supports:

- Medication-assisted treatment with buprenorphine containing products. A DATA 2000 waiver is needed to prescribe sublingual buprenorphine products for OUD in an office-based setting.
- Methadone liquid from a federally licensed opioid treatment program (OTP). It is illegal to prescribe methadone tablets for OUD.
- Intramuscular naltrexone delivered under direct supervision by a physician with appropriate training.

Pain management in patients with OUD

Patients receiving COAT can develop an OUD. Patients with OUD may continue to have chronic pain *(Neumann, 2013; Alford, 2006)*. Patients who have developed OUD as a result of COAT tend to be more sensitive to pain and develop painful conditions *(Compton, 2012; Doverty, 2001)*.

In some instances, the pain provider may discover that there is an OUD and in fact, no pain generator, or the pain generator has resolved but the OUD persists. In these cases, OUD may masquerade as pain and the pain treatment can be discontinued.

When OUD is diagnosed, pain management should continue in conjunction with addiction treatment when there is ongoing chronic pain. Address ongoing chronic pain with a selection of non-opioid and non-pharmacologic therapies, concurrent with initiation of an evidence-based addiction treatment modality. Clinicians who are unable to directly provide addiction treatment in an office-based setting should work closely with the addiction treatment provider to address ongoing pain. This requires ongoing consultation including a specific patient release to consult with the addiction treatment provider.

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