

Opioid Dosing For Acute Pain In Patients With High Opioid Tolerance

Significance

- **Higher than normal opioid doses are often necessary** in patients with OUD, especially those who chronically use HPSOs, like fentanyl.^(1,2,3)
- **Undertreated pain worsens outcomes.** Pain increases cravings and risks return to use, patient-directed discharge, longer stays, readmission, and development of chronic pain.^(4,5)
- **OUD stigma drives undertreatment.** Biased assumptions about “drug-seeking behavior” drives inadequate acute pain management in this population.^(6,7)

KEY TERMS:

HPSO – High-potency synthetic opioid

OUD – Opioid Use Disorder

MOUD – Medications for OUD

RR – Respiratory Rate

Why Standard Doses Fail

Patients with OUD have unique pain management needs due to two overlapping mechanisms: tolerance and hyperalgesia. Those who use fentanyl also experience withdrawal. Standard acute pain order sets are designed for opioid-naïve patients. In OUD, those doses may not prevent withdrawal, let alone treat pain.

MECHANISM	MEANING	EXAMPLE
Opioid Tolerance	Repeated opioid exposure reduces receptor response. Higher doses are needed for the same effect. A dose that would sedate an opioid-naïve patient may produce little to no effect. People who chronically use fentanyl or other HPSOs develop profound tolerance.	A patient uses fentanyl every few hours to prevent or treat withdrawal. The opioid dose is titrated to effect. Their dose may look alarming but is necessary to reach the analgesic threshold.
Opioid-Induced Hyperalgesia	Chronic opioid exposure paradoxically increases pain sensitivity via NMDA receptor activation. This pain sensitivity is neurobiological. ^(1,2,3,5,6)	A patient with a wound reports pain out of proportion to the injury. This is not because they are exaggerating, but because their pain threshold has shifted.
Rapid onset of withdrawal	Fentanyl's short half-life means withdrawal can begin within hours of last use. Withdrawal must be controlled to effectively manage pain.	A patient who used several hours ago is already in moderate-severe withdrawal, with increasing pain, nausea, and agitation. These symptoms are physiological, not behavioral.

Assessment and Management

These principles are grounded in evidence and consensus guidelines from 15 professional medical societies.⁽⁷⁾

- 1. Assess Tolerance.** The potency of unregulated drugs varies widely, making exact assessment impossible. However, these indicators can help estimate tolerance and guide planning:

INDICATOR	TOLERANCE INFORMATION
Substance use and withdrawal history	Assess use patterns by asking directly and without judgement; for example: "I want to make sure we treat your pain well. Can you tell me what you've been using, how often, and the last time you used?" Listen for: using fentanyl "all day" or "every few hours," waking up sick, frequently experiencing withdrawal, using "a lot" or more than they used to/ more than others. Specific quantities are not clinically meaningful (potency varies), but patients may report using "a few bags a day."
Current MOUD	Dose may indicate baseline tolerance (e.g., a patient taking 120 mg of methadone daily has a higher tolerance than a patient on 60 mg). Higher doses of short acting opioids are required to compete with the high receptor affinity of methadone and buprenorphine and overcome buprenorphine's partial opioid antagonism.
Response to analgesic doses	This is the most reliable indicator. If a typical dose produces no meaningful relief and RR is normal, tolerance is significant. Titrate doses to effect, not arbitrary limits. ^(2,3,5,6)

- 2. Control opioid withdrawal.** Opioid analgesia cannot be achieved during active withdrawal, because a) withdrawal amplifies pain, and b) during withdrawal, there is an opioid deficit. Pain management cannot be achieved unless the opioid deficit is relieved (with opioids) and the receptors are stabilized; only then can additional opioids provide analgesia. ^(5,6)
- 3. Treat OUD and pain simultaneously.** If the patient is already on methadone or buprenorphine, it should be continued. A maintenance dose of MOUD will not provide analgesia; short-acting full agonist opioids are needed in addition to the regular MOUD dose and can be safely used and titrated to relieve pain. ^(2,5,6)
If not already on MOUD, methadone or buprenorphine can be started during the acute pain episode. If buprenorphine is preferred, it should be initiated either using the up-titration method in combination with analgesic opioids, or with the standard method after analgesic opioids are no longer needed.
See [Acute Pain in OUD protocol](#).
- 4. Titrate opioids to effect.** Titrate opioids to effect. Use the lowest effective dose, not a predetermined dose limit. Patients with OUD may require substantially higher doses. Assess pain early and often. ^(2,3,4)
- 5. Monitor for opioid safety.** Monitor respiratory rate and oxygen saturation and interpret in conjunction with level of consciousness, work of breathing, and overall clinical status. Sedation alone should not determine opioid toxicity in opioid tolerant patients. Stimulant withdrawal, for example, can cause sedation and hypersomnia that mimics opioid over-sedation (see [Opioid and Stimulant Co-Use Info Brief](#)). Polysubstance use is common. ⁽⁸⁾
- 6. Use multimodal analgesia.** Consider acetaminophen, NSAIDs, regional anesthesia, low-dose ketamine, gabapentinoids, alpha-2 agonists, muscle relaxants, local anesthetics, and nonpharmacologic approaches. ^(4,5,7)

7. Consult when needed.

- **UW Psychiatry Consultation Line** (SUD consult, 24/7): 877-927-7924.
- **UW Pain & Opioid Provider Hotline** (M–F 8:30 AM–4:30 PM): 844-520-PAIN (7246).

Key takeaways

1. **Control opioid withdrawal.** Opioids won't provide analgesia until the opioid deficit (withdrawal) is relieved.
2. **Expect higher opioid doses.** Tolerance and hyperalgesia are physiological, not behavioral.
3. **Add opioids to MOUD.** MOUD treats OUD; short-acting opioids treat acute pain.
4. **Undertreated pain worsens outcomes.** Treating acute pain does not worsen OUD.
5. **Titrate to effect.** Arbitrary dose limits are harmful. Use clinical assessment as a safety guide.
6. **Compassion is critical.** Nonjudgmental care builds trust, improves outcomes, and supports recovery.

RESOURCES:

- Clinical protocol: **Acute pain management for patients with OUD**

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