Acute Pain and OUD

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General Considerations

- History SUD/active use should not preclude the use of OPI to treat pain
- MTD and BUP have analgesic effect
- Addiction medicine and MOUD are an ever-changing science
- General medicine may still view MOUD the same as COT

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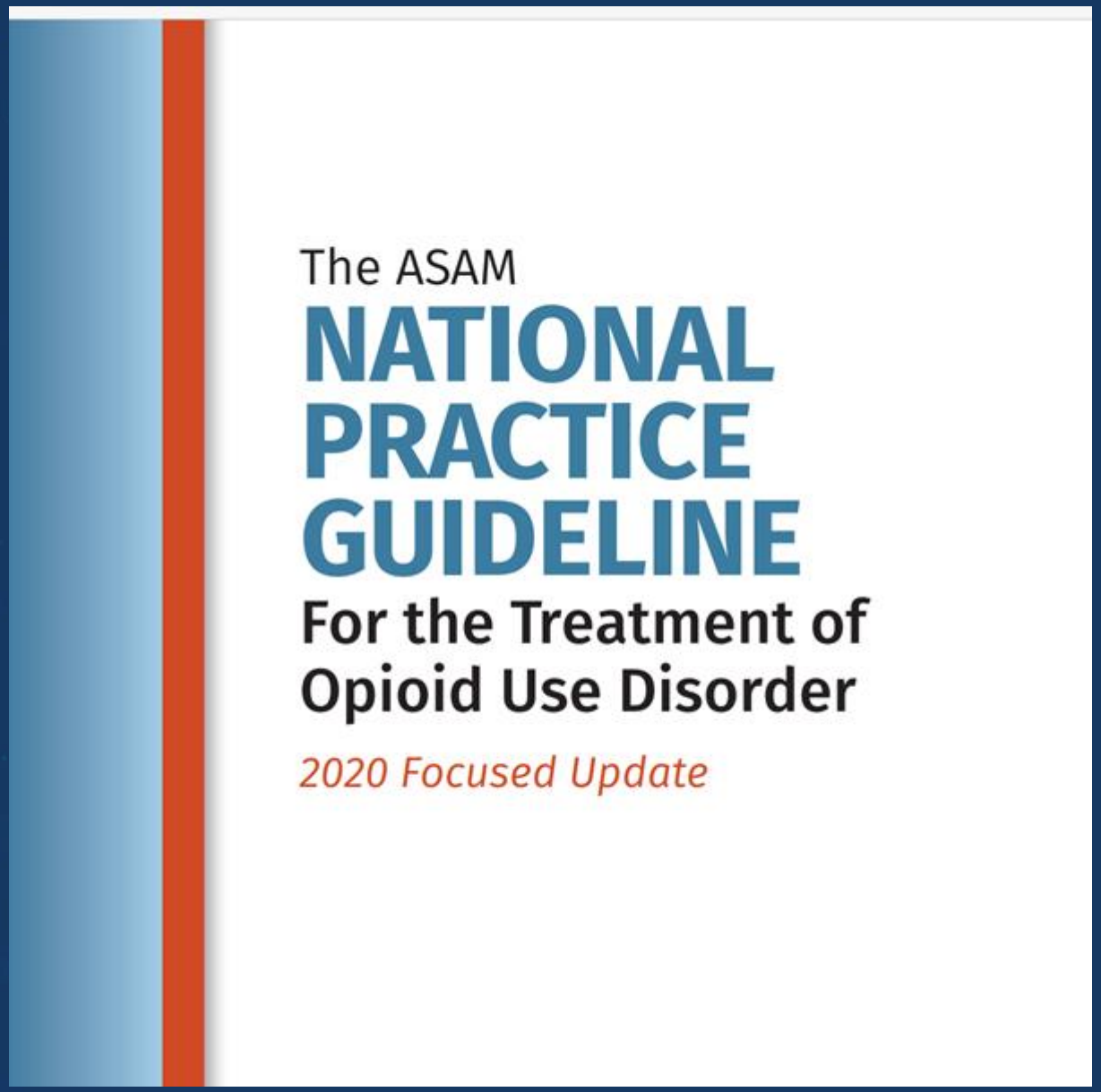

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Overview of Recommendations

- Discontinuation of MTD and BUP before surgery IS NOT REQUIRED
- NTX blockade can be overcome with high potency full agonist OPI
- Pt treated with MOUD may require higher doses of shirt acting opioids to achieve analgesia vs. opioid naïve patients (3X on average)

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Overview of Recommendations

- Pt treated with MTD for OUD can add a short acting full agonist OPI to regular MTD dose for acute pain
- If MTD or BUP is discontinued preoperatively, this should occur the DAY OF SURGERY
- MTD and BUP can be restarted at maintenance dose if withheld less than 2-3 days

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Overall Recommendations

- Correct diagnosis, acknowledge pain reports
- Non-opioid analgesics, non-opioid medications first
- Pt with OUD and NOT in treatment, manage OUD and PAIN together
- Pt treated with MOUD may benefit from increasing dose/frequency as first intervention

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Google Medicine

- Search “how to manage BUP/MTD preoperatively?”
  - 90% of search results say STOP BUP AND MTD
  - Many anesthesiologists/surgeons were trained this way
  - Pharmacists still believe patients can’t be treated with an OPI if they also are treated with BUP/MTD (and decline to fill RX)
  - “So you have had success with this?”
- University of Michigan Protocol
  - Stop BUP/MTD 5 days before surgery “so OPI will work”
  - U of M took back-no evidence

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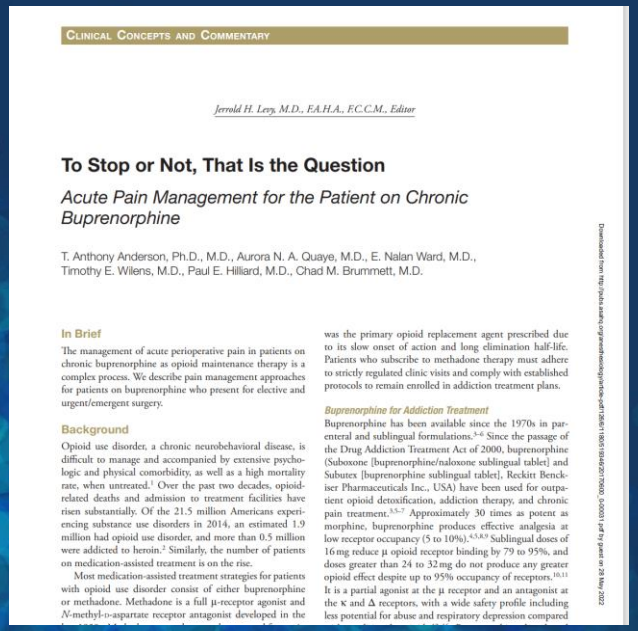
Growing Data Collection



CLINICAL CONCEPTS AND COMMENTARY

Jerrold H. Levy, M.D., FA.H.A., F.C.C.M., Editor

To Stop or Not, That Is the Question

Acute Pain Management for the Patient on Chronic Buprenorphine

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In Brief

The management of acute perioperative pain in patients on chronic buprenorphine as opioid maintenance therapy is a complex process. We describe pain management approaches for patients on buprenorphine who present for elective and urgent/emergent surgery.

Background

Opioid use disorder, a chronic neurobehavioral disease, is difficult to manage and accompanied by extensive psychologic and physical comorbidity, as well as a high mortality rate, when untreated.[1] Over the past two decades, opioid-related deaths and admission to treatment facilities have risen substantially. Of the 21.5 million Americans experiencing substance use disorders in 2014, an estimated 1.9 million had opioid use disorder, and more than 0.5 million were addicted to heroin.[2] Similarly, the number of patients on medication-assisted treatment is on the rise.

Most medication-assisted treatment strategies for patients with opioid use disorder consist of either buprenorphine or methadone. Methadone is a full μ-receptor agonist and *N*-methyl-D-aspartate receptor antagonist developed in the

was the primary opioid replacement agent prescribed due to its slow onset of action and long elimination half-life. Patients who subscribe to methadone therapy must adhere to strictly regulated clinic visits and comply with established protocols to remain enrolled in addiction treatment plans.

Buprenorphine for Addiction Treatment

Buprenorphine has been available since the 1970s in parenteral and sublingual formulations.[3–6] Since the passage of the Drug Addiction Treatment Act of 2000, buprenorphine (Suboxone [buprenorphine/naloxone sublingual tablet] and Subutex [buprenorphine sublingual tablet], Reckitt Benckiser Pharmaceuticals Inc., USA) have been used for outpatient opioid detoxification, addiction therapy, and chronic pain treatment.[3,5–7] Approximately 30 times as potent as morphine, buprenorphine produces effective analgesia at low receptor occupancy (5 to 10%).[4,5,8,9] Sublingual doses of 16 mg reduce μ opioid receptor binding by 79 to 95%, and doses greater than 24 to 32 mg do not produce any greater opioid effect despite up to 95% occupancy of receptors.[10,11] It is a partial agonist at the μ receptor and an antagonist at the κ and Δ receptors, with a wide safety profile including less potential for abuse and respiratory depression compared

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OXFORD

ACUTE & PERIOPERATIVE PAIN SECTION

Perioperative Management of Buprenorphine: Solving the Conundrum

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Abstract

Objective. There is no consensus on the optimal perioperative management of patients on buprenorphine (BUP) for opioid use disorder (OUD). This article will review the available literature on BUP and the analgesic efficacy of BUP combined with full mu-opioid agonists and discuss the conflicting management strategies in the context of acute pain and our institution's protocol for the periprocedural management of BUP. **Methods.** We searched published data on BUP periprocedural management from inception through March 2018 without language restrictions. Study selection included publications reporting outcomes on perioperative pain management in OUD patients maintained on BUP. **Results.** Our search resulted in four case reports supporting periprocedural discontinuation of BUP and two case series, one secondary observational study, one prospective matched cohort study, and four retrospective cohort studies supporting periprocedural continuation of BUP. No clinical trials were identified. **Conclusions.** Maintaining BUP perioperatively does not lead to worsened clinical outcomes. Patients can receive adequate pain control from mu-opioid agonists while maintained on BUP. Based upon available evidence, we recommend continuing BUP at a reduced dose when indicated to avoid withdrawal symptoms and to facilitate the analgesic efficacy of mu-opioid agonists administered in combination for acute postoperative pain.

Key Words: Buprenorphine; Suboxone; Postoperative Pain; Opioid Use Disorder; Surgery; Acute Pain

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“Opioid Debt”

- False assumption that:
  - Maintenance MOUD treats pain
  - BUP will block full agonist OPI during surgery
- Consider risks:
  - Pt with OUD and no MOUD for days prior to surgery?
  - Pt with OUD and need to restart BUP after surgery?

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Addiction Medicine Specialist

- Our job to advocate for evidence best practices
- Advocate for our patients
- “Drug Seeking”
- Avoidance of needed procedures due to fear of stigma, lack of pain control
- Assistance with recovery goals after introduction of OPR

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Buprenorphine Pharmacology

- Potent partial μ agonist
- **Peak analgesic effect 4-6 hours**
- High affinity, slow disassociation (t ½ 24+ hours)
- Ķ receptor antagonist

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Theoretical Reasons to Stop BUP

- "Ceiling Effect"
  - Only respiratory depression was studied, not analgesia (Walsh, 1995)
  - 20 patient series- confirmed ceiling for respiratory depression but not analgesia (Dahan, 2006)
- High affinity μ receptor=blockade of OPR as well
  - BUP increases μ receptor expression
  - BUP doesn't occupy 100% of μ receptor
- "Partial Agonist"= partial analgesia
  - Patient reports conflict this

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Reasons to Continue BUP

- Prevent need for reinduction after surgery
  - Risk of lack of follow up
  - Relapse rate 50%
- Patient preference
- Risks of physical withdrawal SX day of surgery

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Stopping BUP Perioperatively

- Most evidence is gathered by case reports
- Patients with continued MOUD-→poor pain control→ stop MOUD→ better (effective) pain control
- However-
- Case reports also show that pain control is challenging in patients treated with MOUD regardless
- Risk of depressive symptoms returning
- Complex, multifactorial decision making

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Alice, H et al. Clinical Pain 11/2019

- 50 patients treated with BUP/N
- 28 continued BUP, 22 discontinued BUP preoperatively
- No difference in pain scores
- Higher MME in patients with discontinued BUP

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Stanford Policy

- One of many
- PREOP:
  - Continue BUP
  - Alert AM provider
  - Consult pain service
- DAY OF SURGERY/INTRAOPERATIVE
  - Take BUP (keep patch on)
  - Non-OPI analgesic (NSAID, acetaminophen, gabapentinoid)
  - Note dose of OPI required to reduce RR at induction

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- POSTOP
  - Reapply transdermal BUP
  - Continue regular BUP dose
    - Consider changing to TID, QID
    - Consider adding PRN dose BUP
  - Pain Consult
    - PCA with higher dose
    - Ketamine, lidocaine infusion
    - Non-opioid analgesia
- DISCHARGE
  - 1 week supply OPR
  - Follow up plan with AM

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Stopping BUP Postoperatively

- Several case reports
- Poor analgesic response with escalating doses of OPR
- Stopping BUP→ better response
- Always a consideration to have

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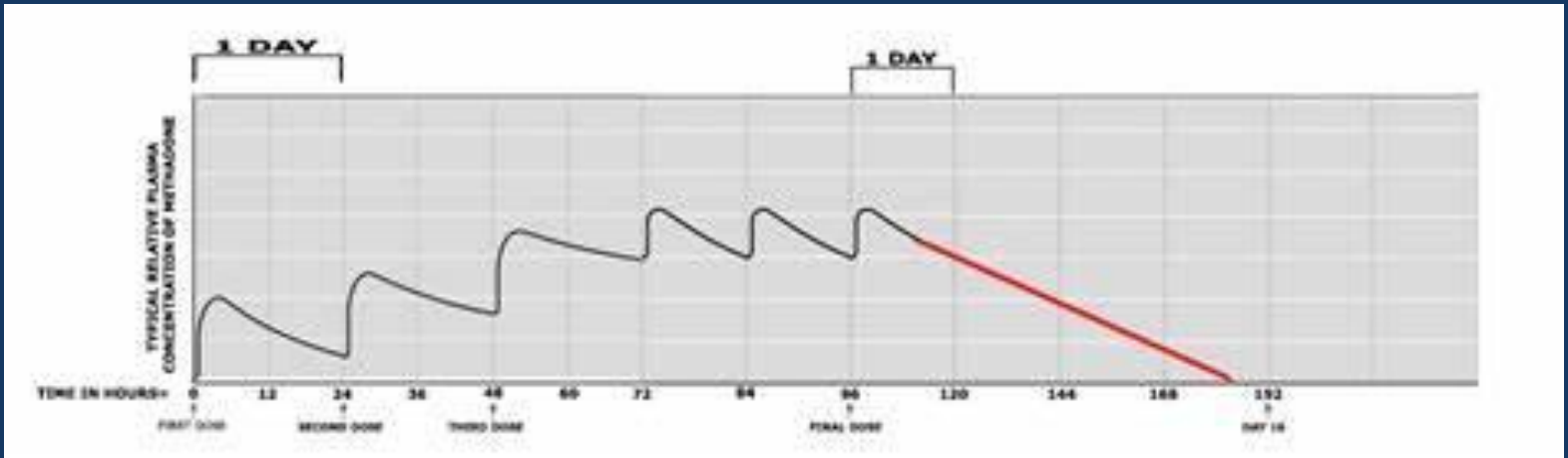
Methadone Pharmacology



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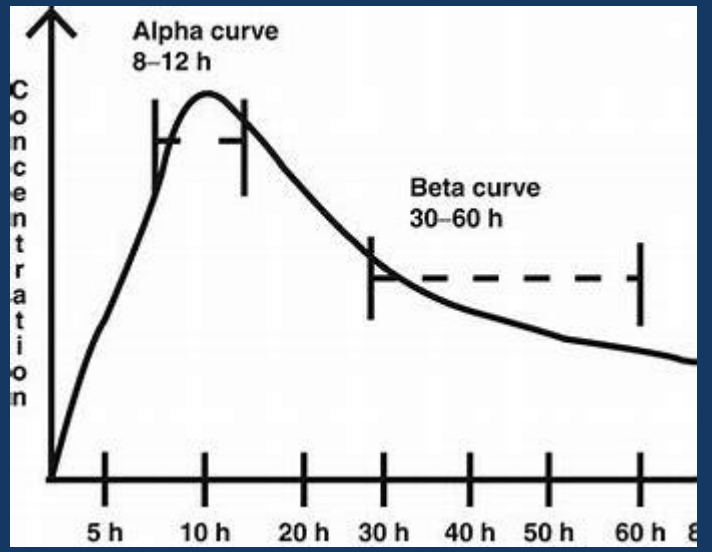
Methadone Pharmacology

- Alpha Curve-analgesia
  - Initially 4-6 hours
  - Repeated dosing 8-12 hours
- Beta Curve-withdrawal prevention, 30-60 hours
- Tmax 2.5-4 hours
- T1/2 **100 fold** variability (4-130 hours)



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Acute Pain with MMT

- Continue maintenance dose
- Consider splitting dose to TID
- If need IV methadone, 50% oral dose
- Short acting OPR on top of MTD
- Non-opioid analgesics/medicine that modulates pain
  - Caution with gabapentin/pregabalin >1 week
- If MTD is stopped, start at maintenance dose if less than 48-72 hours

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Acute Pain with ER NTX

"Yes, it's kind of like going up the creek without a paddle. You'll probably make it- it will be more difficult and you'll have to use just about everything else you can think of besides a paddle… but you'll make it"

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Naltrexone and Acute Pain

- Nonopioid therapies:
  - Acetaminophen
  - NSAIDs
  - NMDA antagonists (ex. Ketamine)
  - Alpha-2 agonists (ex. Clonidine)
  - Antispasmotics (ex. Baclofen)
  - Antineuropathic agents (ex. Gabapentin
- Nonpharmacologic therapies:
  - Peripheral nerve block
  - Centroneuraxial block
  - Local anesthetic infiltration

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So I tried that and it isn't working…

- Can override the μ receptor blockade with escalating doses of short acting opioids agonists
- Risks
  - Upregulation of opioid receptors
  - Exaggerated response to OPR
- Needs to be done with anesthesia support or ICU setting

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Elective Surgery and NTX

- Oral NTX
  - t ½ 14 hours
  - Stop 72 hours prior to surgery-98% clearance
- ER NTX
  - t ½ 5 days
  - Stop 25 days for 98% clearance
  - Risk for return to use→ can switch to oral NTX and stop 72 hours prior to procedure

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Restarting NTX

- Start oral NTX 3-6 days after last dose of OPR
- Start ER NTX 3-4 weeks after last dose OPR
- NTX challenge

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OUD Remission and NO MOUD

- Tolerance to OPI is usually lost in weeks
- Can consider BUP for mild-moderate pain
- Acknowledge risk of return to use
- Discharge planning in treatment

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OUD and no MOUD (Active Addiction)

- Can start BUP (microdose)
- Can also start MTD
  - 20-30 mg; can add 10 mg after 4 hours
  - If plans on continuing MMT-titrate to 80 mg (cravings)
  - If not planning on continuing MMT- titrate to 40 mg and try and titrate down prior to discharge
  - Arrange follow up for BUP

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Ketamine and Acute Pain

- Indications:
  - Analgesic in EM
  - Adjuvant in perioperative medicine
  - Opioid resistant pain in palliative care
  - Mood disorders
- NMDA receptor antagonist (low dose)
- Opioid receptor agoinst
  - Reduction in OPI tolerance
- Anti-inflammatory effects

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Ketamine

- IV most common
  - Reduction in postoperative nausea, emesis
  - Reduction in opioid requirements
- Low oral availability
- Insufflation (esketamine)
- Risk of misuse with OP administration

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Lidocaine vs. Ketamine

- RCT 2019
- 180 patients, OUD, orthopedic surgeries
  - 60-TAU
  - 60-ketamine bolus and infusion intraoperatively
  - 60-lidocaine bolus and infusion intraoperatively
- Lidocaine Group
  - Less postoperative sedation
  - Reduced morphine requirement 24 hours postoperative

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Communication

- Get to know PACU, ED, dentists, PHARMACISTS
- Be a resource for all patients with OUD
- Expect stigma, stereotyping but redirect
- Emphasize MOUD results in recovery
- Have protocols available to share or help develop guidelines for your institutions

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