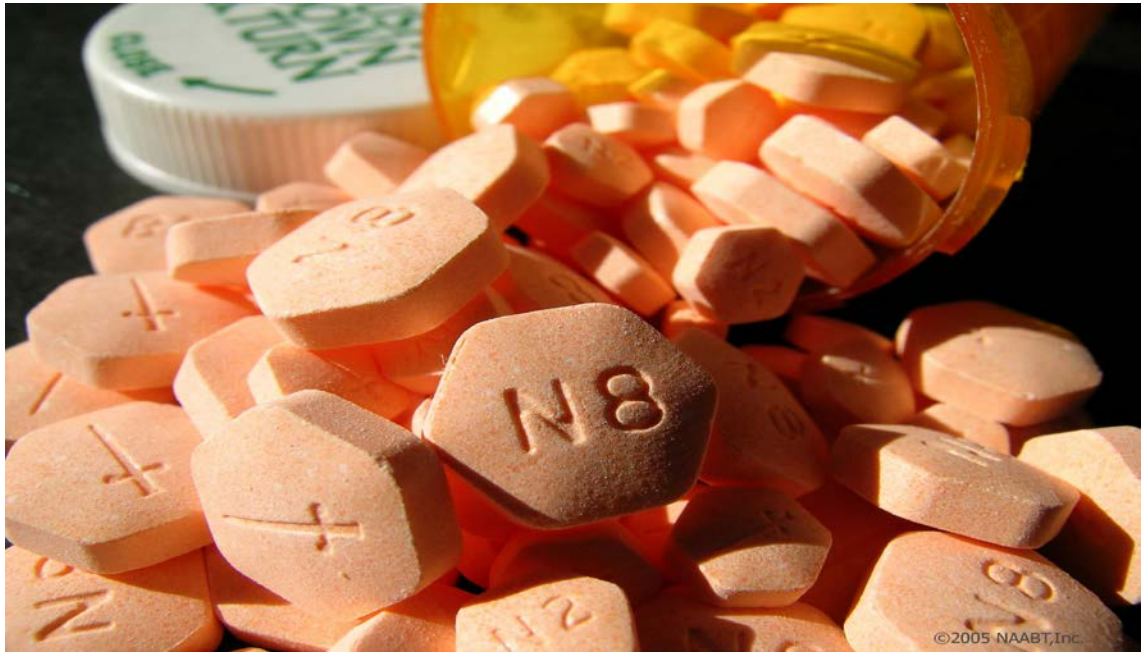
OUD, Initiating Buprenorphine, and Surgical Management of MAT Patients



http://www.naabt.org/tl/pillsinbottle.jpg

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Disclosures

I have no financial interests to disclose.

Graphic courtesy of Joshua Sonkiss MD slideset “The Science of OUD and its Treatment, 3/29/18”

Agenda

1) Define SUD/OUD patients and the overlap with chronic pain management patients

2) Discuss alternate micro-dosing strategies to initiate patients onto buprenorphine that may be especially useful with chronic pain patients

3) Present basic acute pain management strategies for patients on buprenorphine, including recent trends in surgical pain management

https://www.freepik.com/premium-photo/concept-topic-health_4982782.htm#page=2&query=opioid+pills&position=19

Substance Use Disorder

- Biopsychosocial illness

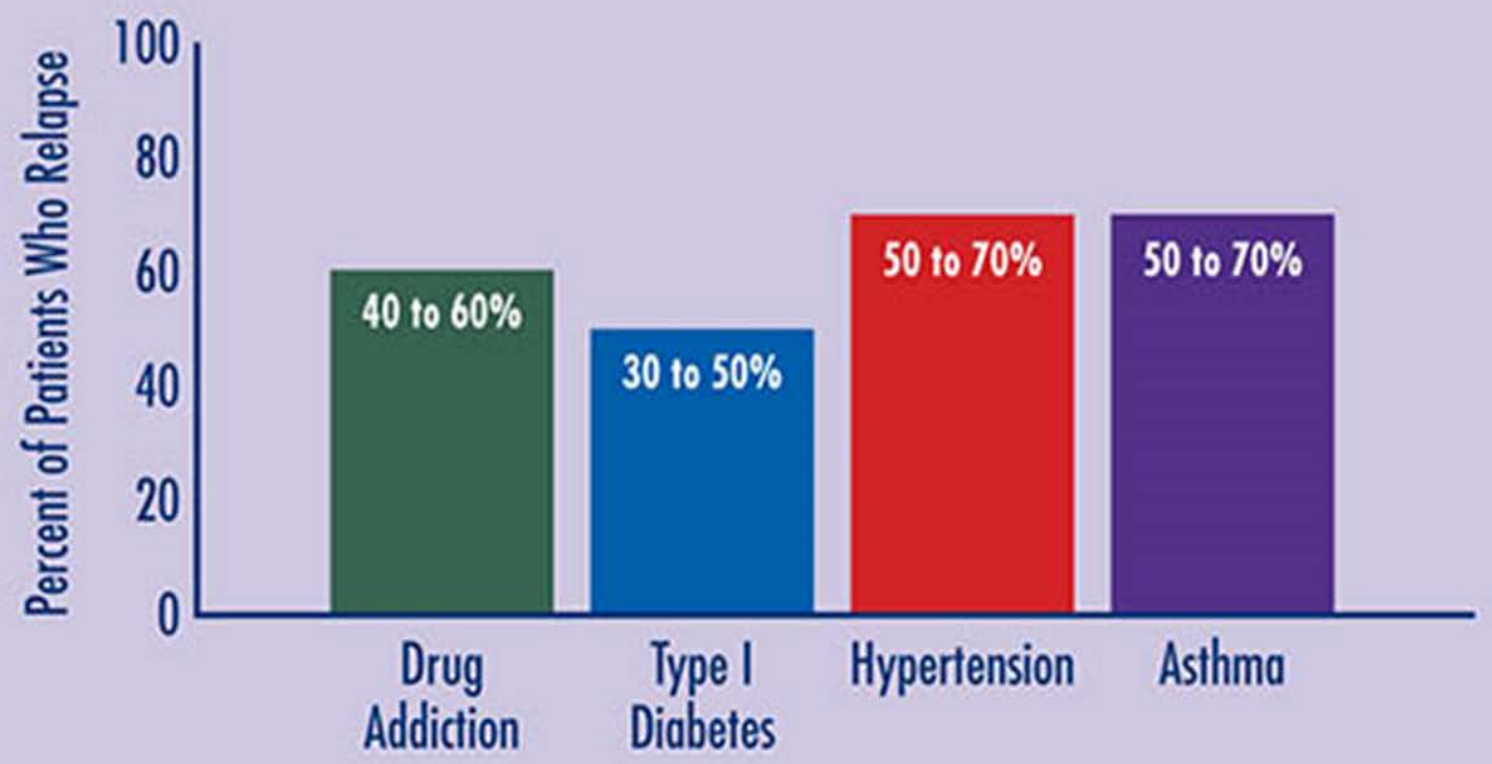
- **Biological**
  - Primary chronic brain disorder
  - Genetic risk

- **Psychological**
  - Characterized by compulsive substance-related behaviors, despite harmful consequences

- **Social**

  Economic, Environmental, Trauma

COMPARISON OF RELAPSE RATES BETWEEN DRUG ADDICTION AND OTHER CHRONIC ILLNESSES



Relapse rates for drug-addicted patients are compared with those suffering from diabetes, hypertension, and asthma. Relapse is common and similar across these illnesses (as is adherence to medication). Thus, drug addiction should be treated like any other chronic illness, with relapse serving as a trigger for renewed intervention.

Source: JAMA 284:1689–1695, 2000.


1 in 7
people
will develop a substance use disorder
at some point in their lives.
#FacingAddiction

Signs and symptoms of SUD/OUD

Biological

- Tolerance
- Withdrawal
- Craving
- Use in physically hazardous situations

Psychological

- Larger amounts or time than intended
- Persistent desire or effort to control
- A great deal of time spent around use
- Continued use despite knowledge of harms

Social

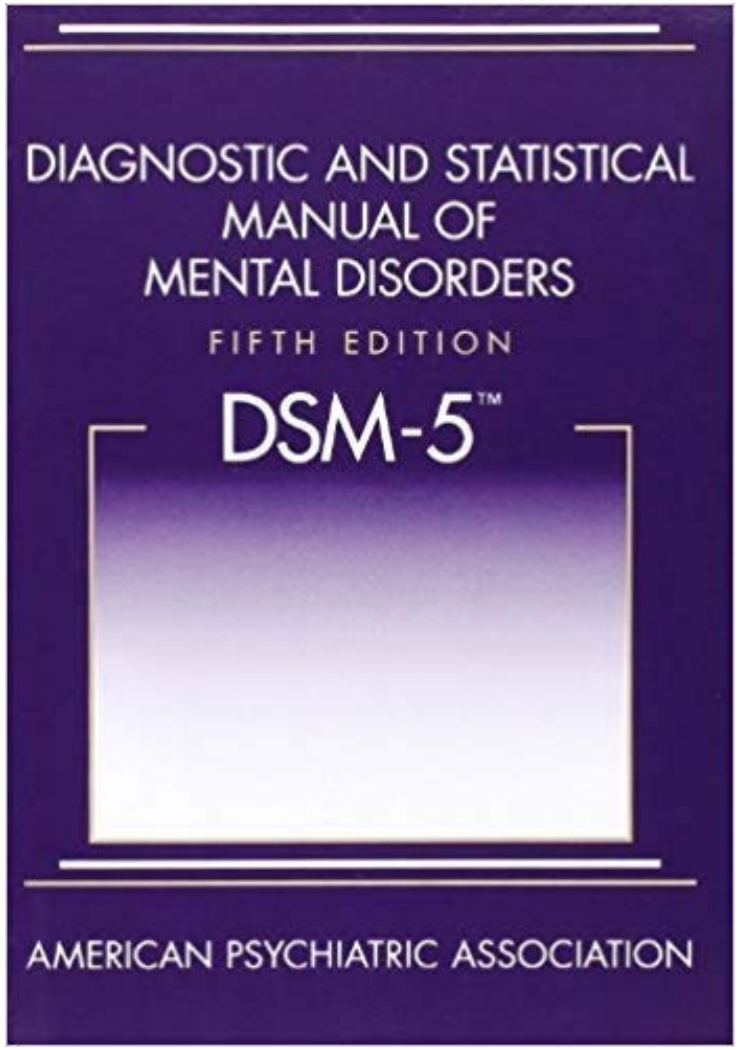
- Failure to fulfill major role obligations
- Use despite social or interpersonal problems
- Social, occupational, or recreational activities are given up

Number of criteria met specifies the severity:

Mild: 2-3

Moderate: 4-5

Severe: 6+



NOT necessarily …

A patient stating that their pain is not being adequately treated and they need to increase their pain medication dose

A patient not showing up for their regularly scheduled pain management appointments but asking for refills

A patient taking their medications more frequently than the way that it is being prescribed

Not wanting or willing to use other pain treatment modalities

But may be …

A patient now taking their medication for different reasons than originally prescribed

Perceived loss of control of use

Psychosocial domains negatively affected, that cannot be explained by the physically limiting chronic pain condition alone

Are there specific distinctions between opioid addiction and chronic opioid pain patients?

- Pain and addiction are not mutually exclusive conditions
  - High rates of comorbidity
  - Chronic opioid use (Rxed or illicit) may result in hyperalgesia
  - Pain that is inadequately treated can lead to behaviors that parallel addictive behaviors
  - Having pain does not protect against the development or expression of addiction

- Pain is influenced by cultural, situational, and individual neuropsychological factors = similar to addiction

- Different types of “pain” that may need to be treated
  - Increasingly recognized as an aspect of chronic pain treatment, and well-established in addiction treatment

- Mental illness comorbidity can be high in chronic pain patients, and is a risk factor for addiction

BOTTOM LINE

- Best evidence now suggests that chronic pain treatment (whether or not an OUD is present) involves:
  - Nonopioid medications
  - Nonpharmacologic treatments
  - Interventional treatments
  - Addressing the psychological component of pain

- Use of opioid therapy considered only if expected benefits for both pain and function outweigh the risks
  - Consider using buprenorphine products such as butrans patches or off-label suboxone
    - ✓ Long-acting, safer, less prone to escalation, less prone to diversion/abuse
  - If not starting with buprenorphine, consider switching as soon as it appears that the patient is developing signs or symptoms of an OUD

Methods for Initiating buprenorphine products other than Standard induction

Micro-induction

With buprenorphine/suboxone

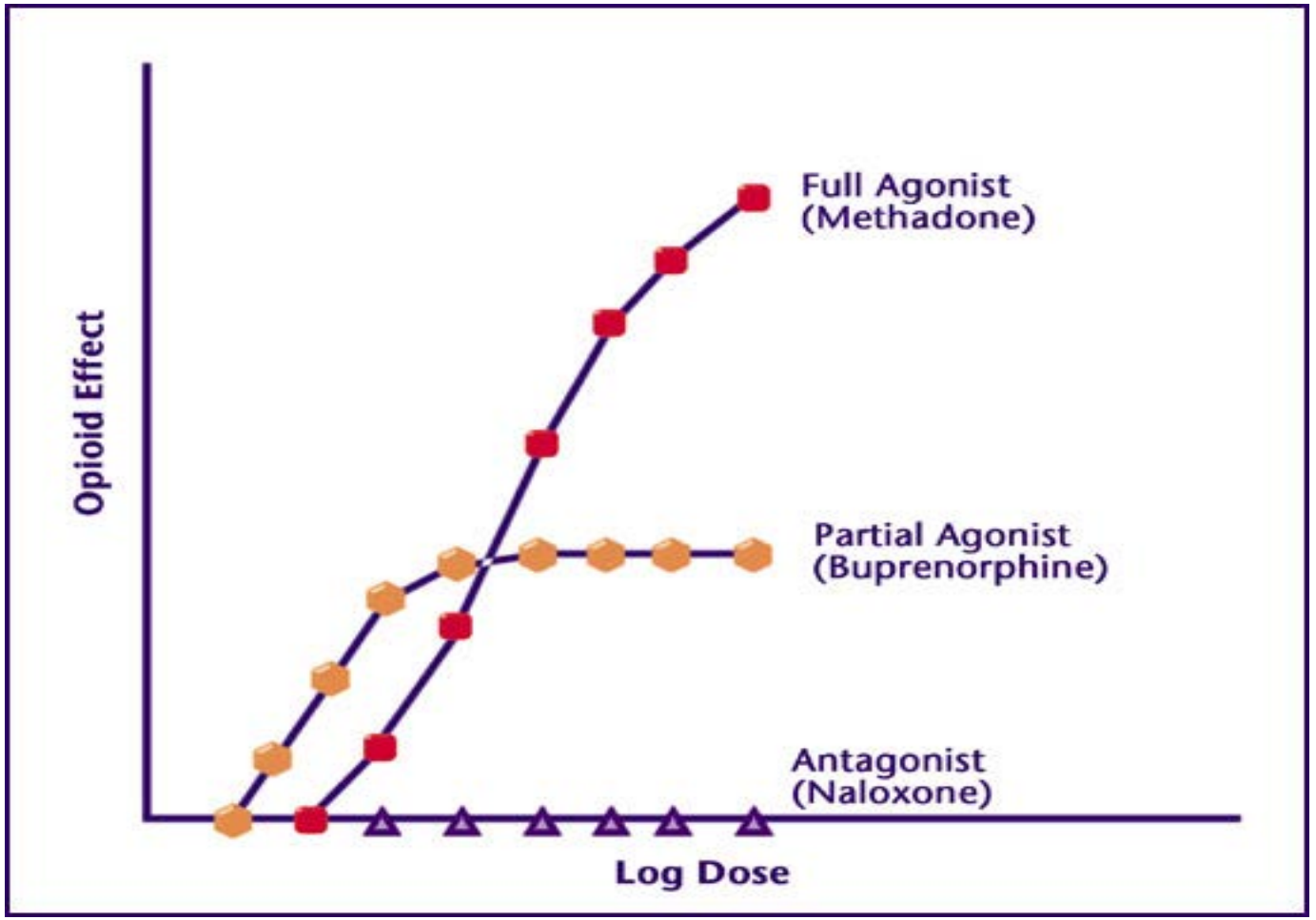
With butrans patch (*for patients with pain)

Relative affinity of buprenorphine

Medication	K_i (nM)
Codeine	734.2
Meperidine	450.1
Oxycodone	25.87
Methadone	3.378
Naloxone	1.518
Fentanyl	1.346
Morphine	1.168
Hydromorphone	0.3654
Buprenorphine	0.2157
Sufentanil	0.1380

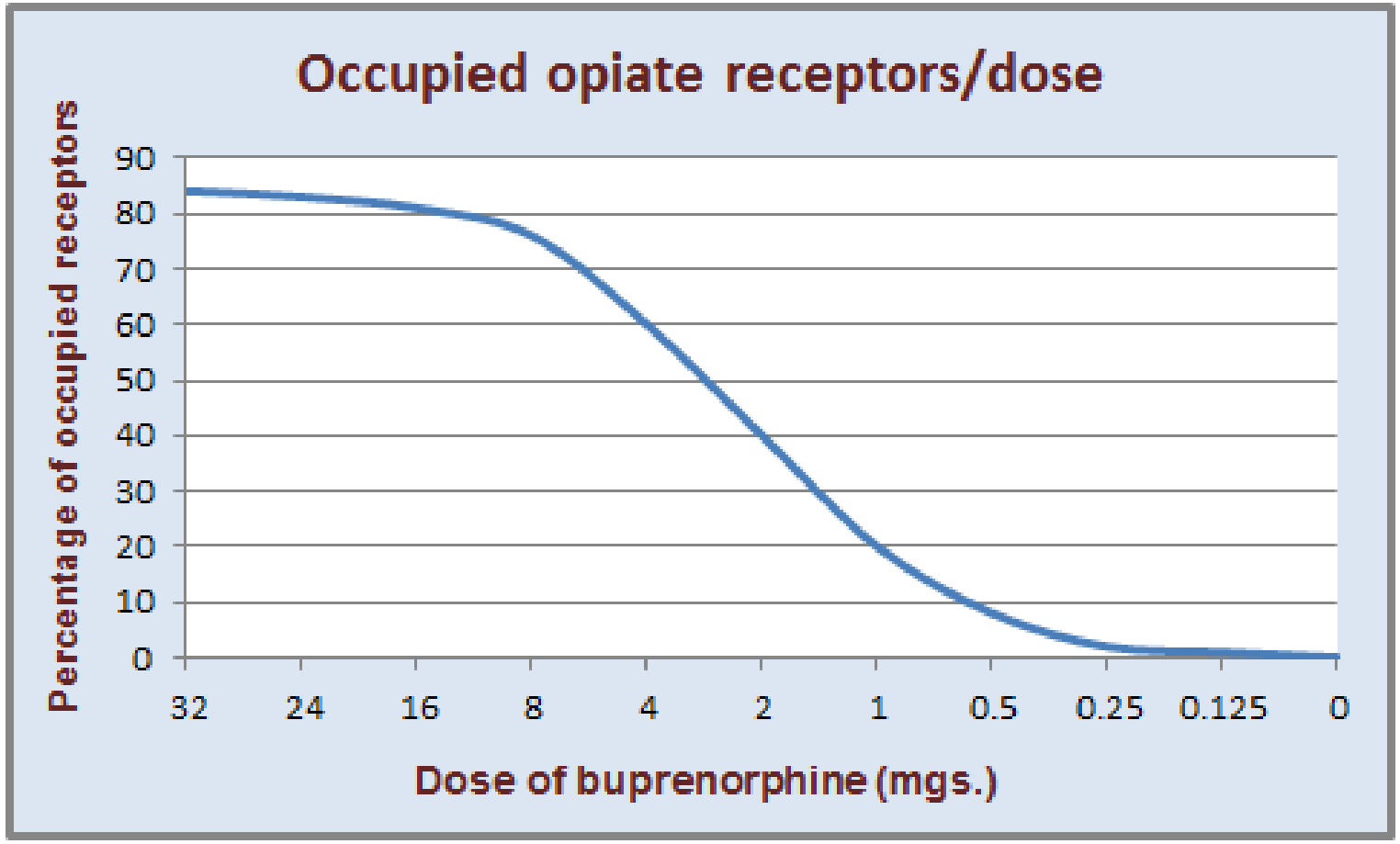
Tung A, Wong C, Fairbairn N. Perioperative Management of Opioid Use Disorder Patients on Buprenorphine/Naloxone. "Ki of commonly used opioids and naloxone to mu-opioid receptors". Anesthesia Tutorial of the Week. Tutorial 370, 9th Jan 2018

Opioid Effect relative to the Log Dose



https://www.naabt.org/education/technical_explanation_buprenorphine.cfm

Opioid receptor occupancy relative to dose



Approximate amount of buprenorphine-occupied mu receptors/dose. Tapering off Buprenorphine. HelpMeGetOffDrugs.com. Buprenorphine Treatment for Opiate Addiction-2018

Sample micro-dosing protocol

Table 1. Buprenorphine Microdosing Protocol Used by Our Team

Day	Buprenorphine dosage	Methadone dose
1	0.5 mg[a] SL once/day	Full dose
2	0.5 mg[a] SL twice/day	Full dose
3	1 mg SL twice/day	Full dose
4	2 mg SL twice/day	Full dose
5	4 mg SL twice/day	Full dose
6	8 mg SL once/day	Full dose
7	8 mg SL in A.M. and 4 mg SL in P.M.	Full dose
8	12 mg SL/day	Stop

SL = sublingually.

[a]For our buprenorphine formulation, one-quarter of a 2-mg sublingual strip was used.

Terasaki D, Smith C, Calcaterra S. Transitioning Hospitalized Patients with OUD from Methadone to Buprenorphine without a Period of Opioid Abstinence Using a Microdosing Protocol. Pharmacotherapy 2019; 39(10): 1023-1029

Utilizing the Butrans patch for micro-dosing

Protocol for patients transitioning from short acting opioids to buprenorphine:

For patients taking 30-80mg morphine equivalents per day:

At initiation	Continue usual opioid regimen.
Day #1	**Add Butrans® 10mcg/hour patch**
Day #2	Start buprenorphine 1mg SL, observe 2 hrs. If pain or withdrawal, administer 1-2mg SL, observe 2 hrs. Repeat above up to buprenorphine 8mg given Day #2. **Discontinue Butrans® patch.**
Day #3	Administer Day #2 Buprenorphine dose. If pain or withdrawal, can titrate to buprenorphine 16mg/day.
Day #4	Administer Day #3 buprenorphine dose. If pain or withdrawal, can titrate to buprenorphine 24mg/day. Consider split dosing of buprenorphine for pain management.
Day #5	Continue established daily buprenorphine dose. **Taper/discontinue other opioids as appropriate.**

Azari S, Zaman T. Transdermal Buprenorphine for Induction of Patients with Co-Morbid Pain. CSAM Webinar. 3/13/19

For patients taking >80mg morphine equivalents per day:

At initiation	Continue usual opioid regimen.
Day #1	**Add Butrans® 20mcg/hour patch**
Day #2	Start buprenorphine 2mg SL, observe 2 hrs. If pain or withdrawal, administer 2mg SL, observe 2 hrs. Repeat above up to buprenorphine 8mg given Day #2. **Discontinue Butrans® patch.**
Day #3	Administer Day #2 Buprenorphine dose. If pain or withdrawal, can titrate to buprenorphine 16mg/day.
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Day #5	Continue established daily buprenorphine dose. **Taper/discontinue other opioids as appropriate.**

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Protocol for patients transitioning from Methadone to Buprenorphine:

At initiation	Administer usual Methadone dose, then discontinue.
At 12hrs	**Add Butrans® 20mcg/hour patch**
At 48hrs	Administer buprenorphine 2mg SL, observe 2 hrs. If pain or withdrawal, administer 2mg SL, observe 2 hrs. If pain or withdrawal, can titrate up to buprenorphine 8mg/day. **Discontinue Butrans® patch.**
At 72hrs	Administer previous day's Buprenorphine dose. If pain or withdrawal, can titrate to buprenorphine 16mg/day.
At 96hrs	Administer previous day's Buprenorphine dose. If pain or withdrawal, can titrate to buprenorphine 32mg/day.

Azari S, Zaman T. Transdermal Buprenorphine for Induction of Patients with Co-Morbid Pain. CSAM Webinar. 3/13/19

Kornfeld H, Reetz H. Transdermal buprenorphine, opioid rotation to sublingual buprenorphine, and the avoidance of precipitated withdrawal: a review of the literature and demonstration in three chronic pain patients treated with Butrans. Am J Ther. 2015 May-June;22(3):199-205.

Hess M, Boesch L, Leisinger R, Stohler R. Transdermal buprenorphine to switch patients from higher dose methadone to buprenorphine without severe withdrawal symptoms. Am J Addictions. 2011;20:480-481.

Treatment of Acute Pain for Buprenorphine MAT patients

1) Non-opioid analgesics, local/regional anesthetics, ice packs, adjunctive therapies, etc.

2) Spread the total daily dose out to TID or QID dosing

3) See above, add prn buprenorphine on top in divided doses

4) Add a short-acting opioid analgesic (i.e. oxycodone) on top at typical dosing intervals

    - May need to use higher than normal dosages (thought to have additive or synergistic effects in regard to pain control)

5) IV Hydromorphone, fentanyl, or high dose morphine may be options in the ER or OR setting

Options for Surgery

1) **Maintain the daily suboxone dose**
    - Evidence from case series, observational studies, RCT, and retrospective cohort studies
    - Intra-operatively, higher anesthetic doses may be required
    - Post-op pain can ***likely*** be adequately controlled with oral or IV full opioid agonists *while maintained on suboxone*

2) **Reduce the daily dose**
    - One case report of an individual who developed severe refractory pain after a surgical procedure, but was able to achieve adequate comfort after dose reduction to 8mg
    - Is currently the protocol in at least one major hospital system

3) **Discontinue suboxone prior to surgery and switch to full agonist treatment**

Newer findings

- Preclinical data suggests that buprenorphine at high doses does exert overriding antagonism of full agonist opioids ***but*** at lower doses yields additive analgesia in combination with full agonists

- Buprenorphine's efficacy at low doses may be similar to higher potency full agonists, possibly through other mechanisms

- Doses of buprenorphine to optimize analgesia may be in the 3-4mg or slightly higher range, however data on craving or risk of relapse are lacking

- Within 24-28 hours of buprenorphine cessation of doses as high as 16mg, 50% of the opioid receptors become available

Massachusetts General Hospital protocol

(in place since March 2018)

1. For procedures with minimal pain levels, continue buprenorphine dose

2. For procedures where moderate to high pain is expected (i.e., historically require perioperative full mu agonist opioids):

   A. Continue buprenorphine through the day before surgery; if usual doses are > 16mg buprenorphine a day, taper to 16 mg the day prior to surgery (ideally 8 mg BID).

   B. Use 4mg bid throughout the perioperative period.

   C. Use full mu agonist opioids as required.

Acampora GA. Special Issues for Patients With SUDs Undergoing Surgery. Psychiatric Times Vol 37, Issue 5, May 2020.

9/2020 case at ANMC utilizing this protocol

50 y/o female on 20mg suboxone for opioid addiction/chronic pain (12mg/8mg)

Diagnosis: R hip avascular necrosis w/ severe shortening/deformity; R acetabular deficiency
Proposed surgery: R total hip arthroplasty and R acetabular reconstruction

Day -1 (Day prior to surgery): 8mg BID (16mg dose)
Day 0 (Day of surgery): 4mg BID suboxone (8mg) (pre-op oxycodone 10mg ER) (intra-op: fentanyl, hydromorphone, propofol)
Day 1 (Post-op): 4mg BID suboxone (8mg); oxycodone 5mg q4h; hydromorphone 2mg po q4hr po prn/0.5mg IV q 2hr prn
Day 2: 6mg BID suboxone (12mg); oxycodone 5mg q4h; hydromorphone 1mg q4hr po prn; 0.5mg IV q2hr prn
Day 3: 6mg BID suboxone (12mg); oxycodone 5mg q4h; no change hydromor po/IV prn
Day 4: 8mg BID suboxone (16mg); oxycodone 5mg q4hr; no change hydromor po/IV prn
Day 5: D/C 8mg BID suboxone (16mg); oxycodone 5mg 1-2 q4hr prn (NTE 12/d)

UDS on follow up 12 days post d/c: pos bup, pos oxy only
Resumed 20mg baseline dose of suboxone, no further adjunctive opioids
“It was good – it worked well and my pain was controlled.”

Take-aways

- OUD is a chronic biopsychosocial illness; chronic pain may precede, coincide, or postcede its development, and the two diagnoses often overlap
- Consider using suboxone if pain treatment requires the use of a chronic opioid
- For patients already on buprenorphine, acute pain needs to be treated with additional methods, and untreated acute pain may lead to relapse. Multiple strategies are available for treating acute pain for MAT patients
- Consider micro-dosing techniques when switching patients from full opioid agonists to buprenorphine products
- Surgical management of suboxone MAT patients is now trending towards keeping the patient on their same or reduced dose of suboxone

https://www.naabt.org/images/SuboxoneFilm8mgs_22mm_X_13mm.jpg