Welcome to Induction Basics

- ***As you join you will be promoted to presenter.***
- ***You will be muted.***
- ***Please unmute yourself by clicking on the microphone icon for asking questions and participation in discussions.***
- ***You may also put your questions and comments in the Chat box.***
- ***We encourage active participation!***

Induction Basics: Tips from the Trenches

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Monthly Webinars

- ***Virtual CO MAT Learning Forum***

  1st Thursday 12:30pm-1:30pm

  REGISTER

- ***Induction Basics: Tips from the Trenches****

  2nd Tuesday 7:30am-8:30am

  REGISTER

  **same topic each month*

- ***Denver Health Learning Collaborative***

  3rd Wednesday 12:15pm-1:15pm

  REGISTER

Denver Health Addiction Journal Club

Scheduled dates for 2020

- *Every fourth Tuesday January-October*
- *November 10th*
- *December 8th*

Time; noon to 1 pm

To join; email ITMATTTRs2@UCDENVER.EDU

- See our website for previous presentations & resources as well as upcoming topics
  - https://www.practiceinnovationco.org/itmatttrs2/mat-forum/

Buprenorphine Induction

Lesley Brooks, MD
Chief Medical Officer, Sunrise Community Health Center
Medical Director – Quality, North Colorado Health Alliance
January 14, 2020

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Objectives

- Review barriers to bupe
- Do a little “myth busting” – academia vs reality
- Review models of buprenorphine induction
- Review specifics of dosing and timing
- Let’s talk specifics at your clinical setting!

Barriers – Provider

- Many trained prescribers never actually prescribe

- Prescriber inexperience w/ concern related to
  - Precipitated withdrawal, other complications
  - Dosing/timing
  - Logistics
  - Billing

Barriers – Patient

- Need to be in withdrawal, stop opioid ingestion
- Access to services
  - Rural location – long distances
  - Transportation
- Fear of recovery – life w/o drugs?

Buprenorphine Care: Comparison

Previous Approaches

- Do not exceed 12 mg on first day or 16mg on 2nd day
- Benzodiazepine and buprenorphine; coprescription is toxic
- Relapse indicates that the patient is unfit for buprenorphine-based treatment
- Counseling or participation in a 12-step program is mandatory
- Drug testing is a tool to discharge patients from buprenorphine treatment or compel more intensive
- Use of other substances is a sign of treatment failure and grounds for dismissal from buprenorphine treatment
- Buprenorphine is a short-term treatment, prescribed with tapering or for weeks to months

New Findings and Recommendations

- Retention in treatment, elimination of WD symptoms often demands higher doses in first few days
- Buprenorphine should not be withheld from patients taking benzodiazepines - caution
- Relapse indicates the need for additional support and resources rather than cessation of buprenorphine treatment
- Behavioral treatments and support are recommended and provided as desired by the patient
- Drug testing is a tool to better support recovery and address relapse
- Buprenorphine treatment does not directly affect other substance use, and such use should be addressed in this context
- Buprenorphine is prescribed as long as it continues to benefit the patient

Sabate´ E, ed. Adherence to Long-Term Therapies: Evidence for Action. World Health Organization. 2003. Accessed at www.who.int /chp/knowledge/publications/adherence_report/en on 21 September 2018. National Institute on Drug Abuse. Principles of effective treatment. Principles of drug addiction treatment: a research-basedguide. 3rd ed. 2012. Accessed at www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/principles-effective-treatment on 16 May 2017. Massachusetts Department of Public Health Bureau of Substance Abuse Services. Practice guidance: responding to relapse 2013. Accessed at www.mass.gov/eohhs/docs/dph/substance-abuse/care-principles/care-principles-guidance-responding-to-relapses.pdf on 16 May 2017.American Society of Addiction Medicine. National practice guideline for the use of medications in the treatment of addiction involving opioid use. 2015. Accessed at www.asam.org /quality-practice/guidelines- and-consensus-documents/npg/complete-guideline on 25 February 2018 44. Knopf A. No proof that buprenorphine treatment requires counseling. Alcoholism & Drug Abuse Weekly. 2017;29:3-5. American Society of Addiction Medicine. The ASAM appropriate use of drug testing in clinical addiction medicine. 2017. drug-testing on 15 May 2017. Substance Abuse and Mental Health Services Administration. TIP 63: Medications for Opioid Use Disorder. Rockville: Substanceuse and Mental Health Services Administration; 2018. https://annals.org/aim/article-abstract/2708164/next-stage-buprenorphine-care-opioid-use-disorder

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Induction Models

- Many considerations
  - Access to pharmacy, urine drug testing

- Office → How do meds get to patient?
- Home
- Inpatient

↗ Meds stored on site (req careful documentation), dispensed to pt

↘ Pt given rx, brings meds to visit.
Hybrid w/ use of on site pharmacy.

Induction

Office Visit
- Dx w/ OUD
- (+/-) w/d

Pharmacy
- p/u short supply

Home
- cont dosing @ home
- community support

Office Visit/Follow Up
- groups/indiv
- provider f/u
- continued support

1st dose in office
- Meds stored on site
- Meds brought by pt to visit

Office Induction

1st dose at home
- Meds picked up at pharmacy

Home Induction

Goals of Induction

- Reduce withdrawal
- Reduce craving
- Avoid side effects
- Eliminate illicit/other opioid use
- Establish rapport. Non-judgmental.
  - *Positive regard for our patients.*
  - *Non-defensive response to hostility, negativity, poor decision-making.*

Checklists – Based on BTOD/REMS

https://www.btodrems.com/Portal/Content%20Library/Appropriate%20Use%20Checklist.pdf

Buprepnorphine Checklists

- **Induction Checklist**

- ☐ 1. Appropriate Diagnostic Criteria Verified
- ☐ 2. Review Patient's Medications (opioids, CNS depressants)
- ☐ 3. Urine Drug Screen, Other Labs – confirm patient's stated use, confirm lack of w/d sx in persons not currently chemically dependent; presence of opioids not CI for induction
- ☐ 4. Check Prescription Drug Monitoring Program
- ☐ 5. Discussed the risks and side effects, i.e. fatal additive effects with benzodiazepines and other CNS depressants, including alcohol
- ☐ 6. Safe Storage - out of the sight and reach of all others, especially children
- ☐ 7. Induction Performed Under Appropriate Supervision (home vs office)
- ☐ 8. Limited Amount of Medicine Prescribed – enough until next appt
- ☐ 9. Professional Counseling Offered - provided onsite or referred
- ☐ 10. **Schedule next visit** at interval commensurate with patient stability
    - Continuum: Weekly in early recovery, monthly once stable

Diagnostic Criteria for OUD

Patient's Name:	Date of Birth:	MRN:

Worksheet for DSM-5 criteria for diagnosis of opiate use disorder

Diagnostic Criteria* (Opioid Use Disorder requires at least 2 within 12 month period)	Meets criteria Yes	No	Notes/supporting information
1. Opioids are often taken in larger amounts or over a longer period of time than intended.			
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.			
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.			
4. Craving,or a strong desire to use opioids.			
5. Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home.			
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.			
7. Important social, occupational or recreational activities are given up or reduced because of opioid use.			
8. Recurrent opioid use in situations in which it is physically hazardous			
9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.			
10. *Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of an opioid			
11. *Withdrawal, as manifested by either of the following: (a) the characteristic opioid withdrawal syndrome (b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms			

- This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision.

Severity: **Mild**: 2-3 symptoms, **Moderate**: 4-5 symptoms. **Severe**: 6 or more symptoms.

Signed_____Date_____

Criteria from American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition,. Washington, DC, American Psychiatric Association page 541.

Induction – Lab Evaluation

- Lab evaluation is important, should not defer induction if not done
- Key labs
  - Pregnancy test
  - Urine Drug Screen
  - STI Testing: GC, CT, RPR, HIV and viral hepatitis serologies
- Other Recommended Labs *(Case-by-case, provider preference)*
  - CBC, Liver function tests
    - ✓ If patients present with elevated liver function 3 to 5 times above normal, monitoring is important.
    - ✓ If patients present with elevated liver function >10 times above normal, medication should be stopped, and further investigation undertaken.

Safe Medication Storage & Disposal

- AMA guidance (2017) for providers:
  - Talk to pts about opioid misuse, 70% come from family med cabinet
  - Safe storage of Bupe is important - Individuals not tolerant of opioids can overdose on a relatively low dose
  - Emphasize risk to children! "Even very brief exposure…can result in sedation, respiratory depression, cerebral anoxia, and death."

Criteria for Induction is Withdrawal – 2 Factors

Time since last opioid

+

Signs/Sx of withdrawal

- Optimal induction occurs when the majority of opioid receptors are free of other opioids as measured by time since last opioid use and presence of mild-mod withdrawal.

Induction – Timing + Withdrawal

- Short acting opioids – 12-16 hrs abstinent.
  - ***NOTE:*** *Regular, daily heroin users probably look more like intermed or long acting opioid users and deserve 24hrs abstinence.*
- Intermediate acting opioids – 17-24 hrs abstinent
- Long acting opioids (methadone) 24-36hrs abstinent

- Establish withdrawal - Utilize COWS SCALE
  - Patients often know the timing from experiences with running out of the drug they take.

- Gunderson E. Models of Buprenorphine Induction PCSSMAT Train. 2014 http://pcssnow.org/wp-content/uploads/2015/02/Buprenorphine-Induction-Online-Module.pdf. Accessed March 3, 2016.

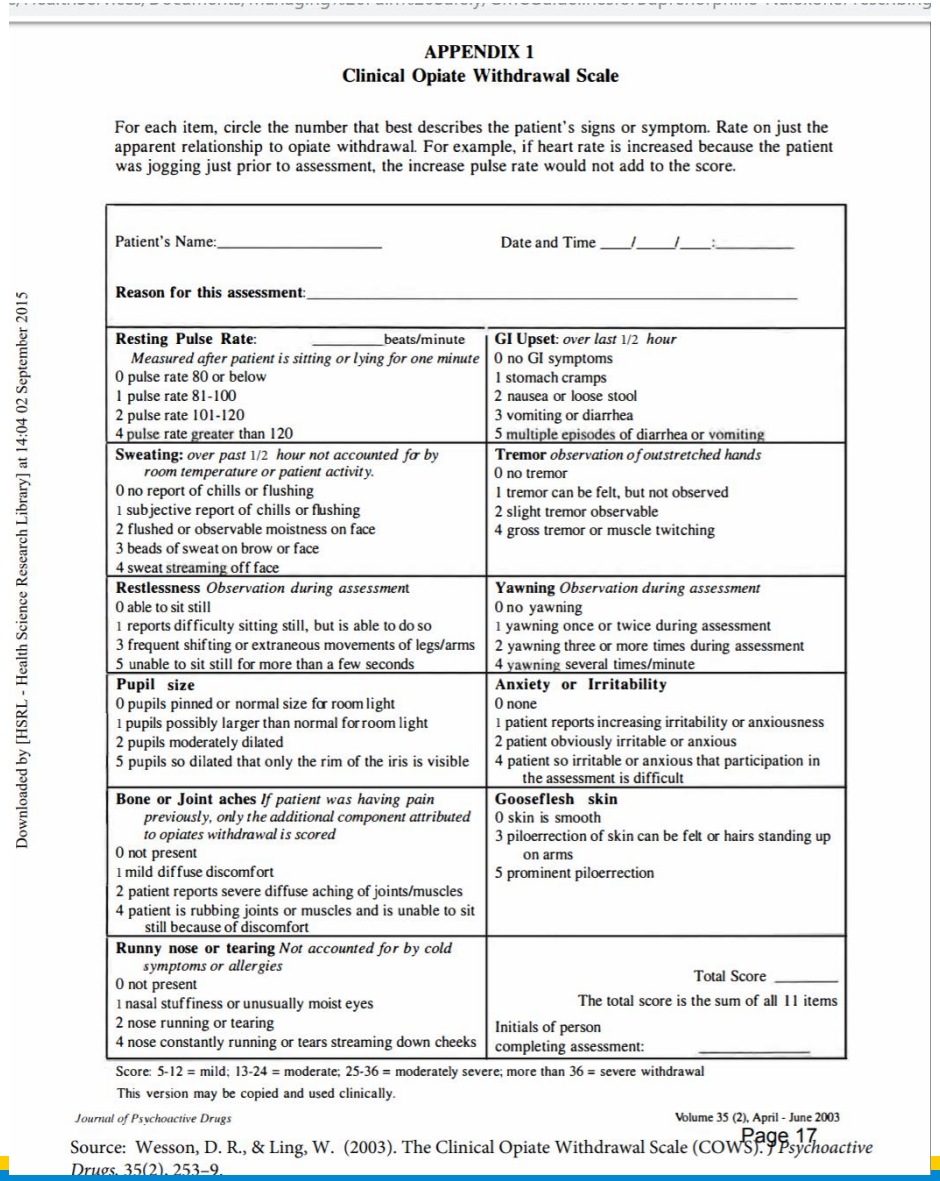
Maintanence – Dose

- Average dose for many patients is 12-16 mg bupe/day
- Range can be 4-24 mg/day
- Very individualized

Clinical Opioid Withdrawal Scale (COWS)

- **COWS > 8 Some use 12-16**
- **COWS 13-15 for Fentanyl**

- Other w/d scales exist - Objective Opiate Withdrawal Scale (OOWS), may also be used.



APPENDIX 1
Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name:_____ Date and Time ____/____/____:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.

Journal of Psychoactive Drugs Volume 35 (2), April - June 2003

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*, 35(2), 253–9.

Downloaded by [HSRL - Health Science Research Library] at 14:04 02 September 2015

Key Points – Day of Induction

https://www.youtube.com/watch?v=yl1mmnclAHs

- Encourage transparency: *"If you have used more recently, please let me know. Doesn't mean we can't induce you today and it can avoid you getting really sick."*
- Suggest rinsing mouth, eating a mint prior to taking bupe to help with taste.
- May need comfort meds for residual w/d symptoms before and/or after induction
- Taking doses as directed; no unsanctioned dose escalation
- Each buprenorphine tablet/film will take some time to dissolve under the tongue (6-15 min)
- While medication is dissolving,
  - No talking, drinking, swallowing
  - Salivation may be excessive; may need to tilt head forward
- No more than 2 tablets or films at one time.

Induction – Office – PCSS Guidelines

Office Visit
- Dx w/ OUD
- (+) w/d based on COWS
- If not in w/d, convert to home indxn

Pharmacy
- p/u short supply

Home
- cont dosing @ home
- community support

Office Visit/Follow Up
- groups/indiv f/u 7 days
- provider f/u 5-7 days
- continued support

1st dose in office
- Start with 2-4mg
- Meds stored on site
- Meds brought by pt to visit

Office Induction

- 1-2hrs after dose→Repeat COWS→D/C to home if COWS <5 or 6 and improved from starting.
- If w/d persists: Repeat 2-4mg→1-2hrs→Repeat COWS→D/C to home if COWS <5 or 6 and improved.
- Total time in office depends on comfort level, efficiency of workflows.

Induction – Office – Updated PCSS Guidance

http://pcssnow.org/wp-content/uploads/2015/02/Buprenorphine-Induction-Online-Module.pdf

- Consider w/d meds before or after.
- Relief occurs w/in 30-45 min.
- Can continue at home. Instructions/phone #'s. Max 16mg on day 1.
- If not in w/d or not certain, convert to home induction
- Can remain in contact via telephone on day 1-2 even w/ successful induction.
- Give sufficient medication only until the next visit, within 3-7 days

Induction - Sunrise "Hybrid"

Office Visit
- Dx w/ OUD
- (+) w/d based on COWS
- If not in w/d, convert to home indxn

Pharmacy
- p/u short supply

Home
- cont dosing @ home
- community support

Office Visit/Follow Up
- groups/indiv
- provider f/u
- continued support

1st dose in office
- 4 or 8mg
- Rx written, MA goes to on-site pharmacy to retrieve first dose, gives to pt

Office Induction

- 30-45 min after dose→Repeat COWS→D/C to home if COWS <5 or 6 and improved from starting.
- If w/d persists: Repeat.

Total time in office @ 1.5-2hrs. Longer if 2nd dose nec.

Induction – Office – Sunrise “Hybrid”

- Pt can take next dose at home, 8-12hrs later (later that day, in AM).
- Often BID dosing.

Induction Guidance: Buprenorphine Nuts & bolts:

Slide borrowed with permission from D. Stader, MD

Older protocols suggested starting at lower doses, and observing for an hour…**many ED protocols deviated from this.**

Effective dosing is related to the volume/dose of the patient's habit or tolerance.

THE APPROACH OF 2 OF EMERGENCY MEDICINE'S BEST MAT EXPERTS

Dr Eric Ketcham's

<50mg / day Oxycodone <0.5g / day Heroin	**Bupe 2 – 4mg SL**
50mg – 150mg / Day Oxycodone 0.5g – 2g / day Heroin	**Bupe 8mg SL**
150mg – 200mg / day Oxycodone 2g / day + of Heroin	**Bupe 16mg SL**

Dr. Andrew Herring

(ED BRIDGE program dosing for non-waivered ED Docs)

- Higher single dose Buprenorphine
- Start everyone on 8mg SL
- Re-dose or load…if appropriate (up to 24 to 32mg total if can't get next day appointment)

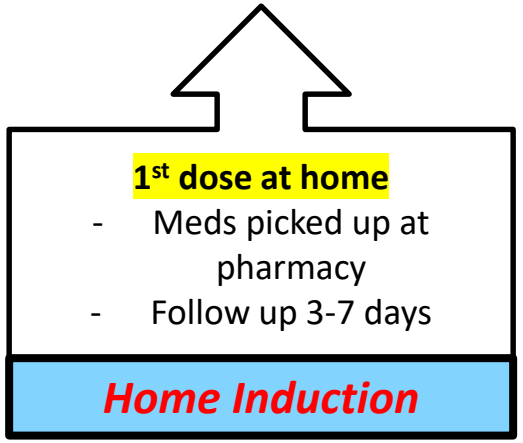
Induction – Home

Office Visit
- Dx w/ OUD

Pharmacy
- p/u short supply

Home
- cont dosing @ home

Office Visit/Follow Up
- groups/indiv
- provider
- continued support



Induction – Home

- Many clinicians using this approach.
- Safe and convenient.
- As effective as office-based induction.
  - Alford D, Labelle C, Richardson J, et al. Treating Homeless Opioid Dependent Patients with Buprenorphine in an Office-Based Setting Soc Gen Intern Med. 2007;22:171-176. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1824722/. Accessed October 9, 2013. Lee J, Grossman E, DiRocco D, et al. Home buprenorphine/naloxone induction in primary care J Gen Intern Med. 2009;24(2):226-232.
- ASAM recommends home induction be offered experienced providers
  - American Society of Addiction Medicine (ASAM). The ASAM National Practice Guideline For the Use of Medications in the Treatment of Addiction Involving Opioid Use June 2015. https:// www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asamnational-practice-guideline-supplement.pdf. Accessed October 6, 2015.
- Follow-up visit is recommended; between 3 and 7 days

Induction – Home

- Provide explicit instructions on how and when to start buprenorphine, how/when to seek guidance

- Ideal candidates:
  - Previously treated patients, patients who demonstrate ability to follow instructions

- Sub-optimal Candidates:
  - Significant fear of withdrawal, anxiety; may start too early causing precipitated withdrawal.

Induction – Home – PCSS Guidance

- Day 1
  - 1-2mg to start, then 1 film every 2hrs, max 8mg (16mg ok'd via phone)

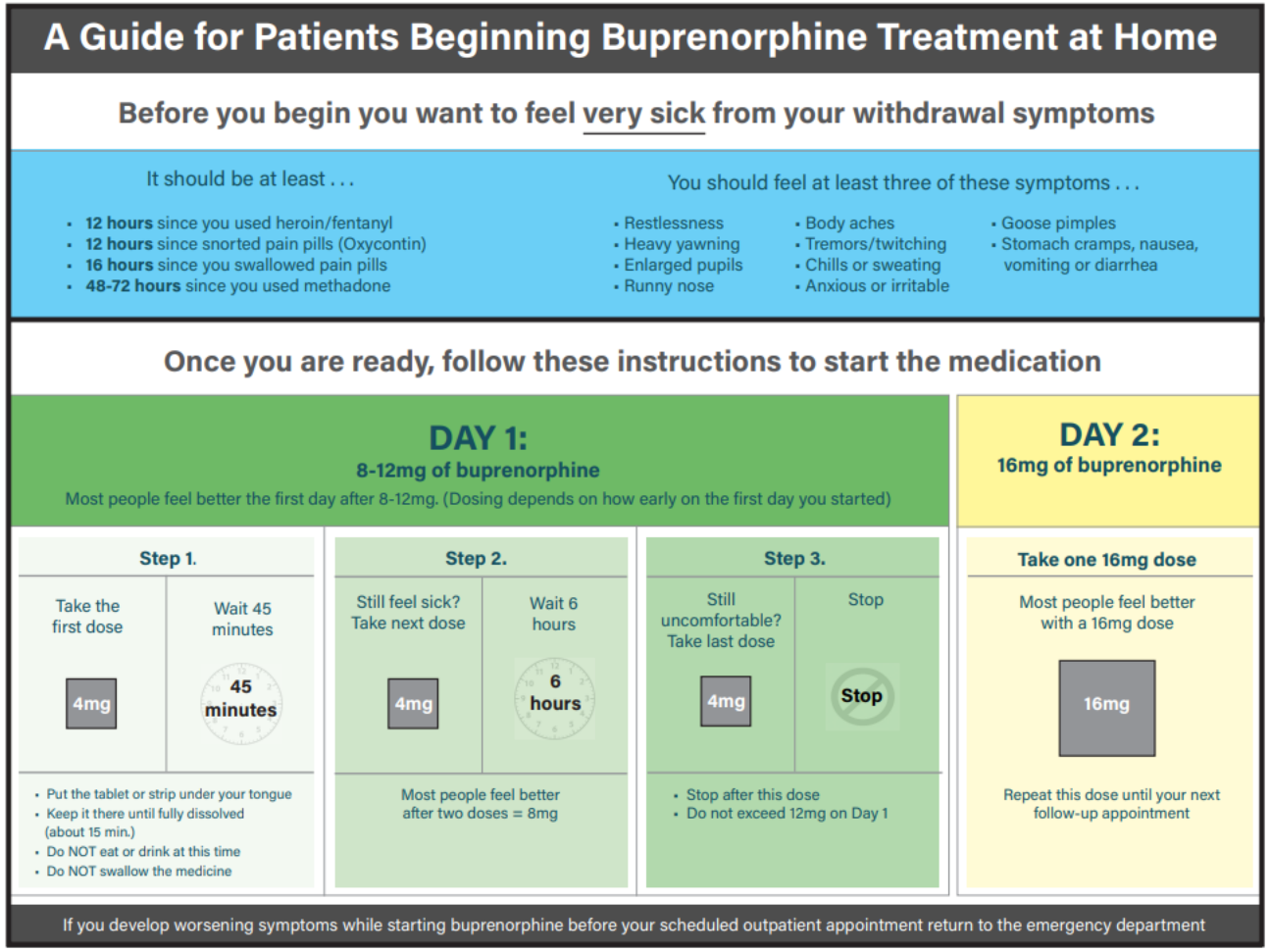
- Day 2
  - Start with Day 1 final dose, div BID. OR
  - 2mg every 2hrs prn, max 16mg (24mg max – ok'd via phone)

Induction – Home – Other Examples

- 8mg films – ½ film (4mg) every 2 hrs until out of WD, fall asleep, or 12 mg on first day (max 16 on 2nd day)
- 8mg films – ½ tid for day 1, then 1 film bid day 2 and after
- 8mg films - ¼ film every 90 minutes until out of WD, fall asleep, or 12 mg on first day (max 16 on 2nd day)
- 8mg films – 1 film in am, ½ film in afternoon, ½ - 1 film at night (caution with 16mg/1st day)
- 4 Protocol Examples; https://www.ncbi.nlm.nih.gov/books/NBK64246/

Education Handout Example

https://d14rmgtrwzf5a.cloudfront.net/sites/default/files/home_buprenorphine_initiation.pdf



A Guide for Patients Beginning Buprenorphine Treatment at Home

Before you begin you want to feel very sick from your withdrawal symptoms

It should be at least . . .

- **12 hours** since you used heroin/fentanyl
- **12 hours** since snorted pain pills (Oxycontin)
- **16 hours** since you swallowed pain pills
- **48-72 hours** since you used methadone

You should feel at least three of these symptoms . . .

- Restlessness
- Heavy yawning
- Enlarged pupils
- Runny nose
- Body aches
- Tremors/twitching
- Chills or sweating
- Anxious or irritable
- Goose pimples
- Stomach cramps, nausea, vomiting or diarrhea

Once you are ready, follow these instructions to start the medication

DAY 1:
8-12mg of buprenorphine
Most people feel better the first day after 8-12mg. (Dosing depends on how early on the first day you started)

Step 1.
Take the first dose — 4mg
Wait 45 minutes — 45 minutes

- Put the tablet or strip under your tongue
- Keep it there until fully dissolved (about 15 min.)
- Do NOT eat or drink at this time
- Do NOT swallow the medicine

Step 2.
Still feel sick? Take next dose — 4mg
Wait 6 hours — 6 hours

Most people feel better after two doses = 8mg

Step 3.
Still uncomfortable? Take last dose — 4mg
Stop — Stop

- Stop after this dose
- Do not exceed 12mg on Day 1

DAY 2:
16mg of buprenorphine

Take one 16mg dose
Most people feel better with a 16mg dose — 16mg

Repeat this dose until your next follow-up appointment

If you develop worsening symptoms while starting buprenorphine before your scheduled outpatient appointment return to the emergency department

Subjective Opioid Withdrawal Scale (SOWS)

Instructions: Wait until you are in mod w/d (>17 per PCSS) and start dose as instructed.

Often useful to indicate what time to start meds.

Name: _____

DOB: _____

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Subjective Opiate Withdrawal Scale (SOWS)

Instructions: We want to know how you're feeling. In the column below today's date and time, use the scale to write in a number from 0-4 about how you feel about each symptom right now.

Scale: 0 = not at all 1 = a little 2 = moderately 3 = quite a bit 4 = extremely

DATE						
TIME						
	SYMPTOM	SCORE	SCORE	SCORE	SCORE	SCORE
1	I feel anxious					
2	I feel like yawning					
3	I am perspiring					
4	My eyes are tearing					
5	My nose is running					
6	I have goosebumps					
7	I am shaking					
8	I have hot flushes					
9	I have cold flushes					
10	My bones and muscles ache					
11	I feel restless					
12	I feel nauseous					
13	I feel like vomiting					
14	My muscles twitch					
15	I have stomach cramps					
16	I feel like using now					
TOTAL						

Mild Withdrawal = score of 1 – 10
Moderate withdrawal = 11 – 20
Severe withdrawal = 21 – 30

Source: Reprinted from Handelsman et al. 198

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Education Handout Example

https://www.oregonpainguidance.org/wp-content/uploads/2018/02/At_Home_Buprenorphine_Induction_Patient_Pamphlet.pdf?x91687

NYU School of Medicine Division of General Internal Medicine & Bellevue Hospital Center/ contact: danae.dirocco@nyumc.org

Buprenorphine - Beginning Treatment

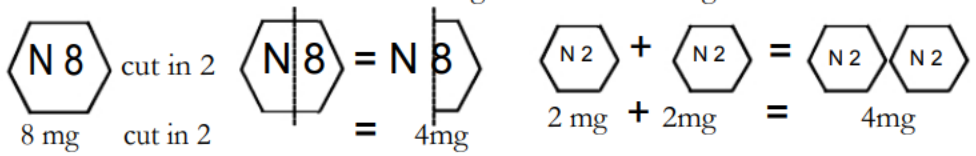
Day One: Before taking a buprenorphine tablet you want to feel lousy from your withdrawal symptoms. Very lousy. It should be at least 12 hours since you used heroin or pain pills (oxycontin, vicodin, etc.) and at least 24 hours since you used methadone.

Wait it out as long as you can. The worse you feel when you begin the medication, the better it will make you feel and the more satisfied you will be with the whole experience.

You should have a least 3 of the following feelings:
- joint and bone aches
- bad chills or sweating
- anxious or irritable
- goose pimples
- twitching, tremors or shaking

- very restless, can't sit still
- heavy yawning
- enlarged pupils
- runny nose, tears in eyes
- stomach cramps, nausea, vomiting, or diarrhea

First Dose: 4 mg of Buprenorphine (Bup) under the tongue.
This is one half of an 8 mg tablet or two 2 mg tablets:



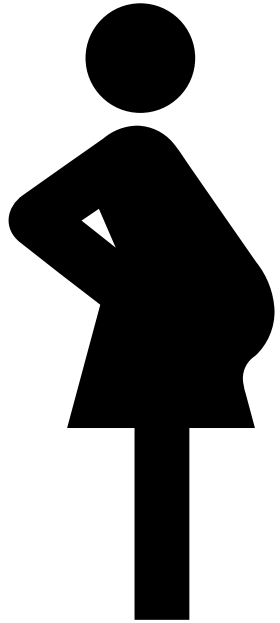
Put the tablet (one half tablet of 8mg tabs, or two tablets if 2mg tabs) under your tongue. Keep it there. If you swallow Bup tablets they will not work, the medicine is best absorbed through the thin skin on the bottom of your tongue.

It takes 20-45 minutes for the medication to be absorbed and have an effect. Feel better? Good, the medicine is working. Still feel lousy after 45 minutes? Don't worry, you just need more medication.

At 1-3 hours (60-180 minutes) after your first dose, see how you feel. If you feel fine after the first 4 mg, don't take any more, this may be all you need. If you have withdrawal feelings, take another 4 mg dose

Induction in Pregnancy

- Consider office induction after 24 weeks; home induction prior
- Evidence suggests Mom-baby dyad manage cardiovascular changes of mild-mod w/d reasonably well
- Dosing guidelines same
- Incidence of NAS/NOWS does not change based on type of MAT; management, severity milder with buprenorphine



Management of precipitated withdrawal

- Apologize. Keep moving. Additional bupe dose.
- Supportive treatment: support continuation of the Buprenorphine
  - Repeated 2 mg doses of buprenorphine every 1-2 hours
  - Clonidine 0.1 mg – 0.2 mg every 6- 8 hours (caution regarding hypotension)
  - Antiemetics for nausea
  - Non-steroidals for arthralgias and myalgias
  - More intensive Psychosocial support - Some patients may resist supportive treatment and return to full agonist opioid use as a method to self-medicate their precipitated withdrawal

Microdosing

Induction Challenges

- Conventional Bupe Induction
  - Despite precautions, can lead to precipitated w/d
  - Can be a difficult experience for the person with OUD
  - Can lead to risk of relapse to illicit opioid use

- Hammig et al (University of Basel Psychiatric Hospital, Switzerland)
  - Published “Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method”, Substance Use and Rehabilitation, 2016
  - Will review this method today

Hammig et al: Microdosing Hypotheses

- Based on slow bupe kinetics, observation that small doses of IV bupe did not produce w/d in MTD patients…
  - Repetitive admin of small bupe doses w/ short (12hr) intervals should not → w/d
  - Bupe will accumulate at the receptor
  - Over time, increasing amounts of full agonist will be replaced by bupe at receptor

- Proposed: overlapping induction of bupe in persons with ongoing use of street heroin or high-dose full agonist (MTD) <u>w/o severe w/d sx</u>

Hammig: Case 1

- F, middle-class, Swiss family
  - Hx of…sexual abuse, PTSD, poly-SUD (cocaine, psilocybin, MDMA, cannabis, heroin), MDD w/ suicide attempt, bulimia…all b/w 12-18yrs
  - Mult attempts at bupe maintenance; bupe mono as bup/ntx not avail in SZ
  - 30yrs of age at time of presentation to Univ Basel, 3g/day street heroin
- Conventional induction → severe w/d, trauma-related flashbacks, anxiety
  - Returned to heroin use after 2 weeks
  - Again returned to program for re-induction but nervous about tolerability of process

Hammig: Case 1

- Implemented Bernese Method/Microdose Induction
  - Started with low dose bupe – 0.2mg
  - overlapping with heroin use
  - small daily dose increases
  - abrupt cessation of heroin/full agonist when target dose reached

- Case 1 stabilized at 12mg/d bupe
  - Has relapsed several times w/ heroin, re-initiated bupe with Bernese method
  - Experienced another episode of MDD, tx'd with escitalopram & therapy
  - Stable off heroin x 2.5yrs

Microdosing Protocol (Heroin)

- Hammig group asked pharmacy to cut tablets into quarters
- Pharmacy board does not allow pharmacists to cut
  - Ask for guidance

Table 1 Buprenorphine dosing and use of street heroin in case 1

Day	Buprenorphine (sl)	Street heroin (sniffed)
1	0.2 mg	2.5 g
2	0.2 mg	2 g
3	0.8+2 mg	0.5 g
4	2+2.5 mg	1.5 g
5	2.5+2.5 mg	0.5 g
6	2.5+4 mg	0
7	4+4 mg	0
8	4+4 mg	0
9	8+4 mg	0

Abbreviation: sl, sublingual.

Microdosing Protocol (Methadone)

- Hammig group asked pharmacy to cut tablets into quarters
- Pharmacy board does not allow pharmacists to cut
  - Ask for guidance

Day #	Bupe Dose	Bupe Dose-2mg (#tabs)	Methadone Dose
1	0.5mg X 1	1/4 tab	30mg
2	0.5mg BID	1/4 tab X 2	25mg
3	1mg BID	1/ 2 tab X 2	20mg
4	2mg BID	1 tab X 2	15mg
5	4mg BID	1 tabs X 4	10mg
6	8mg Daily	4 tabs	5mg (last day)

Hammig: Naltrexone Microdosing Protocol

- Case 1 desired complete abstinence; wanted NTX for craving
  - Hammig et al. assumed NTX could be started similar to overlapping bupe induction
- Case 1 tapered off bupe to 2mg/d then
  - Used small amounts of NTX ("scratched off from 50mg tablet") with daily increases
  - Did not develop w/d sx or cravings
  - Stopped bupe, increased NTX to 25mg/d
  - After several months, stopped NTX → 3yrs 3mos abstinent at publication

Naltrexone Microdosing (Methadone)

- Oral NTX comes in 50mg tabs
- Microdosing of 0.125, 0.250, 1mg, etc
- Requires compounding pharamcy
- Local solution for microdosing…??

Day #	NTX Dose	Methadone Dose
1	0.125/0.250mg	30mg
2	0.125/0.250mg	25mg
3	0.125/0.250mg	20mg
4	0.125/0.250mg	15mg
5	0.125/0.250mg	10mg
6	0.125/0.250mg	5mg (last day)

2008, Mannelli et al

Conclusions

- Find a Mentor
- Easier than it sounds
- We give much more dangerous medicines for less severe issues
- MAT has been a game changer in treating Opioid Use Disorder
- Close Follow up is key to retention and leads to a gentler induction and stabilization

Thank you!

Questions?

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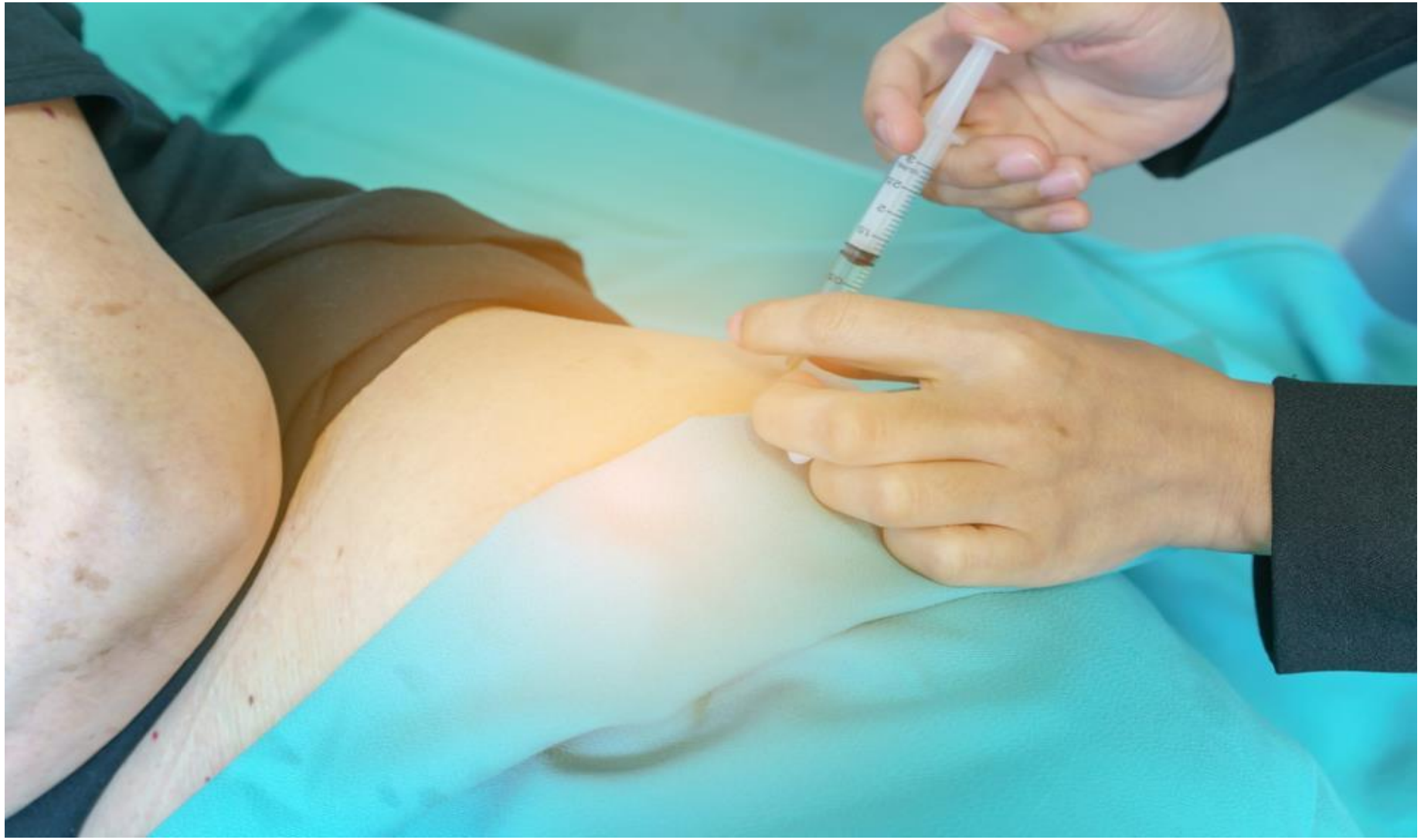
#: 970-350-4636

Extended-Release Injectable Naltrexone



Extended-Release Naltrexone

- Marketed as Vivitrol®. **Does NOT require special license for prescribing.**
- **Dosing:** 380mg injection @ deep gluteal muscle q 4 weeks; alternate sides.
- Blocks opioid receptors for **one entire month.**
- **Adverse effects:** injection site reactions, nausea/vomiting, precipitated opioid withdrawal, depression, elevated LFTs
- ***Note:*** *Large doses of opioids may be required to override the blockade in a medically monitored setting*.

Research on Extended-Release (XR) NTX for AUD

Persons tx'd with XR NTX had greater **reduction in the number of heavy drinking days** than those receiving placebo.

Effects on heavy drinking were greatest in those who had **at least four days of abstinence from alcohol** prior to treatment initiation.

In the subset abstinent for at least 4 days prior to treatment initiation, extended-release naltrexone **also improved continuous abstinence rates**.

O'Malley et al., 2007

Good Candidates for Naltrexone Treatment

Not interested or able to be on agonist therapies
Abstinent from opioids but remain at risk for relapse
Failed prior treatment with agonist
Less severe forms of a disorder
Young adults living with involved parents who supervise treatment
Young adults unwilling to commit to long-term agonist therapy
Successful on agonist therapy who wish to discontinue medication

Getting Started…

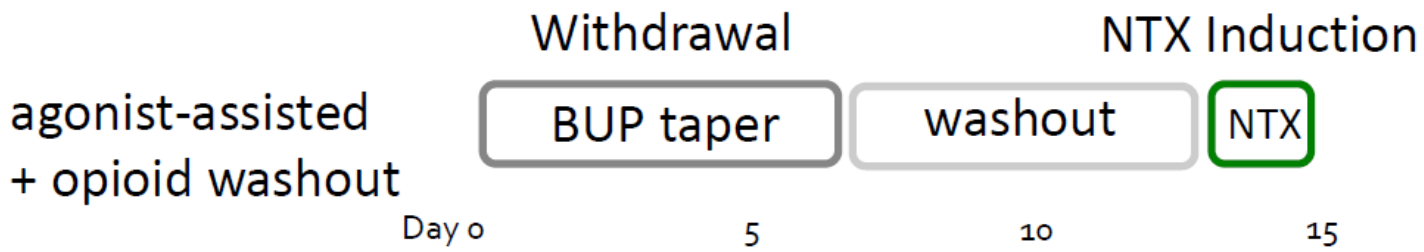
Therapeutic doses of NTX will precipitate severe and prolonged w/d in pts who are physically dependent or have large amount of opioids on board

Always confirm absence of opioids/absence of physical dependence prior to 1st NTX dose

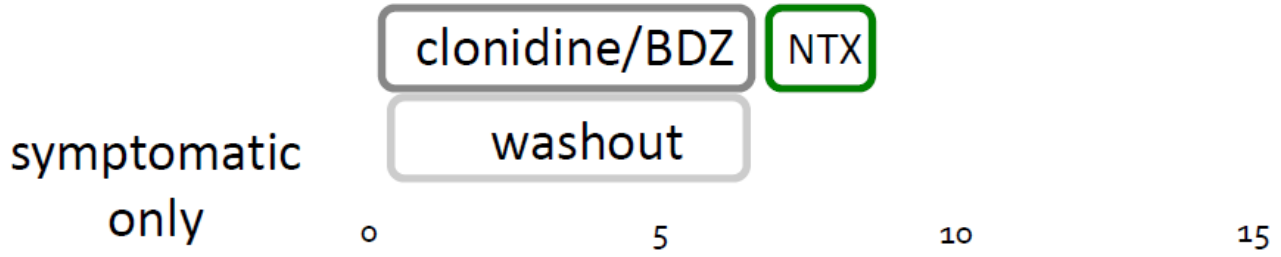
- Labs: UDS (must be neg for opioids), LFTs (NOT required prior to initiation), STDs, Hep C, HIV, HCG
- Perform naloxone challenge if unsure (25mg), esp if on edge of washout period
- Must understand the risks of precipitated withdrawal if underreporting

Initiating Naltrexone

- Two phases of treatment: 1) withdrawal, 2) naltrexone induction
- Current FDA-sanctioned method involves 7-10 days “washout” between the last dose of opioid and first dose of NTX BUP taper NTX



Best managed by bup-waived providers.



Best approach for most of our clinicians.

Pregnancy

Naltrexone = Pregnancy Class C
Not currently recommended, however…
ACOG (#711, 2017): *"…information regarding its use in pregnancy is limited to small case series and case reports, with normal birth outcomes reported. However, significant concerns exist regarding unknown fetal effects, as well as risk of relapse and treatment dropout with subsequent return to opioid use and risk of overdose."*

- Decision to continue person already on ER NTX: increasing data suggest okay to do. Though still open question for research.

Recent (2017) SAMHSA report to Congress called for research to answer this question.
More to come…

Testing the Blockade

Up to 1/3rd will “test blockade”, often w/in 1-2 days of XR-NTX
Most commonly, pts will test 1-2 times with small amounts, after which they are “reassured” blockade works and do not resume use
Some pts will use large amounts, for few weeks, but rarely persist if they receive full blocking doses of the medication
Very few patients try intentionally to “override the blockade”
Continuous blockade prevents pts from relapsing to physical dependence and many patients prefer to remain on the medication

Resources

General information about buprenorphine treatment and the treatment of addiction are available through numerous sources, including but not limited to:

- SAMHSA website (*https://www.samhsa.gov/medication-assisted-treatment*)
- American Society of Addiction Medicine website (*www.asam.org*)
- American Academy of Addiction Psychiatry website (*www.aaap.org*)
- Colorado Consortium for Prescription Drug Abuse Prevention (http://www.corxconsortium.org/)

Resources

Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD)

- **Materials for Prescribers:**
  - Dear Prescriber Letter
  - *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers*
  - Appropriate Use Checklist

- **Materials for Pharmacists:**
  - Dear Pharmacist Letter
  - *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Pharmacists*

- **Materials for Patients:**
  - Medication Guides

Acute and perioperative pain in patients on MAT

For Patients w/ Acute Pain on Methadone…

Continue existing dose of methadone **(verify by calling OTP)**

Opioid Treatment Programs have 24 hr emergency contact phone numbers

Half life is 5-130 hours
Analgesic effect lasts 6-8 hours.
Most patients have single daily dose of methadone
Some have split-doses (pregnant and rapid metabolizers)
Can slit doses while in the hospital

For Patients w/ Acute Pain on Methadone…

Add short acting opioids

opioid debt: no analgesia until debt paid

higher doses and frequencies, PCA's

Avoid butorphanol (Stadol), nalbuphine (Nubain), and pentazocine (Talwin)

agonist/antagonist opioids that precipitate withdrawal

For Patients w/ Acute Pain on Methadone…

Drug-drug interactions: Inhibit or induce CYP450
Inhibitors increase methadone levels and cause sedation (ciprofloxacin, Zithromax, cimetidine, fluconazole, sertraline, amiodarone)
Inducers decrease serum methadone levels and cause opioid withdrawal (rifampin, carbamazepine, phenytoin, antiretrovirals)
Careful adding or discontinuing these meds

For Patients w/ Acute Pain on Buprenorphine…

OK to give other full mu opioids to patients already taking buprenorphine; avoid other partial agonists (tapentadol, stadol)

The naloxone in Suboxone has no bio-availability unless injected and will not cause withdrawal

May increase buprenorphine dose and frequency for acute pain (Q 6-8 hours)

Acute Pain
Buprenorphine Maintenance Treatment
Case Series

- 5 patients underwent 7 major surgeries (colectomy, knee replacement, small bowel resection, bilateral mastectomy)
- All maintained on stable doses of SL buprenorphine (2 mg – 24 mg) for chronic musculoskeletal pain – some with remote history of opioid use disorder
- By chart review, postoperative pain was adequately controlled using oral or IV full agonist opioids

Kornfeld H and Manfredi L. Am J Therapeutics 2010

Acute Pain
Buprenorphine Maintenance Treatment
Accumulating Research

- Observational study of peripartum acute pain management of buprenorphine (n=8) stabilized patients
  - Patients responded to additional opioid medication given for pain control

Jones HE et al. Am J Drug Alc Abuse 2009

- DB RCT comparing IV patient-controlled analgesia (PCA) with buprenorphine and morphine alone and in combination for postoperative pain in adults undergoing abdominal surgery
  - In the combination group, buprenorphine did not appear to inhibit the analgesia provided by morphine

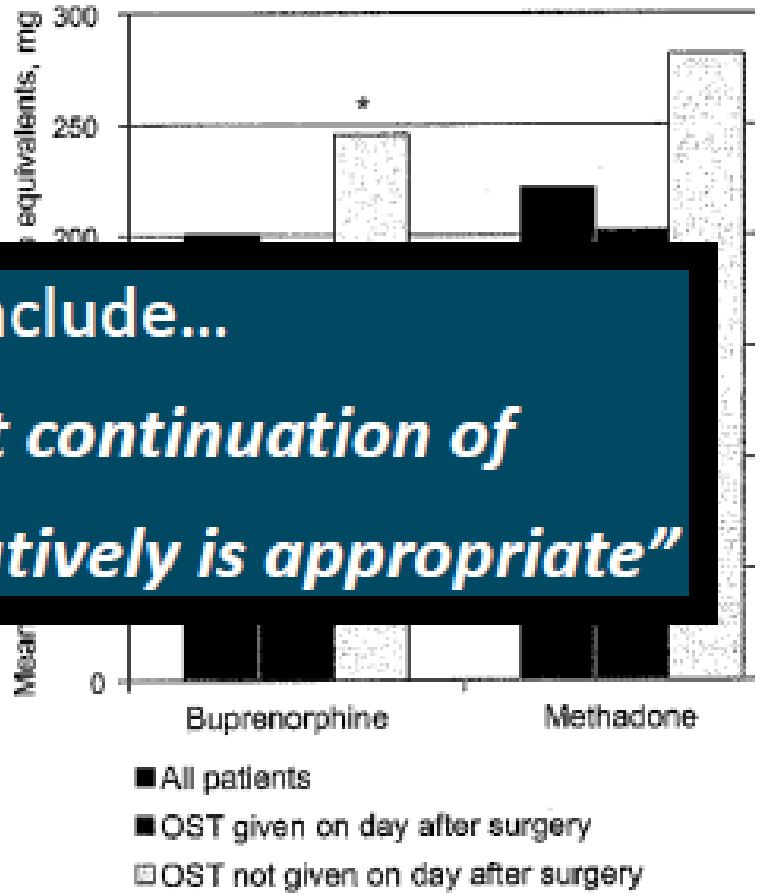
Oifa S et al. Clin Ther. 2009

- Sub-analysis of the MOTHERS Study, no differences in pain management during delivery and the 1st three days postpartum for MM (n=21) and BM (n=19)

Hoflich AS et al. Eur J of Pain. 2011

Acute Pain
Buprenorphine Maintenance Treatment
Accumulating Research

- Retrospective cohort of 1st 24 hours after surgery in 11 BM and 22 MM patients on patient



Authors conclude…

"results confirm that continuation of buprenorphine perioperatively is appropriate"

PCA morphine requirements

Macintyre PE et al. Anaesth Intensive Care 2013

For Patients w/ Acute Pain on Naltrexone…

Blocks opioid analgesia

Half life is 14 hours

With 50 mg tablets, discontinue 24-72 hours prior to procedure

With Q month depot injection (Vivitrol):

- Consider scheduling surgery for 30 days after last injection
- Need 6-20 times usual dose of opioid to overcome blockade (hydromorphone, fentanyl)
- Serious risk of respiratory depression
- Consult anesthesia

Case Examples / Questions

Appropriate Use Checklist; https://www.btodrems.com/Portal/Content%20Library/Appropriate%20Use%20Checklist.pdf

BTOD|REMS

APPROPRIATE USE CHECKLIST:

BUPRENORPHINE-CONTAINING TRANSMUCOSAL PRODUCTS FOR OPIOID DEPENDENCE

This checklist is a useful reminder of the safe use conditions and monitoring requirements for prescribing buprenorphine-containing transmucosal products for opioid dependence.

Requirements to address during each patient's appointment include:

- understanding and reinforcement of safe use conditions
- the importance of psychosocial counseling
- screening and monitoring patients to determine progress towards treatment goals

If a patient continues to abuse various drugs or is unresponsive to treatment, including psychosocial intervention, it is important that you assess the need to refer the patient to a specialist and/or a more intensive behavioral treatment environment.

Additional resource: Providers Clinical Support System for Medication Assisted Treatment: http://pcssmat.org/

The following checklist may be used during the induction period and filed in the patient's medical record to document safe use conditions. After the induction period, use the maintenance checklist on the next page.

INDUCTION CHECKLIST

ASSESSMENT TO ENSURE APPROPRIATE USE		NOTES
Date:		
CHECK	**INDUCTION**	
○ **Appropriate Diagnostic Criteria**	Verified patient meets **appropriate diagnostic criteria** for opioid dependence	
○ **Prescription Drug Monitoring** ○ **Opioids/CNS Depressants**	Checked patient's prescription profile in the **Prescription Drug Monitoring Program** (PDMP), as appropriate • Reviewed **all medications (e.g., benzodiazepines, other opioids, CNS depressants) and illicit substances** to assess for appropriateness of co-prescribing	
○ **Risks and Side Effects**	**Discussed the risks and side effects** described in professional labeling and Medication Guide with patient including • potential for abuse and misuse • potential for fatal additive effects with benzodiazepines and other CNS depressants, including alcohol	
○ **Conditions of Safe Storage**	Explained or reviewed **conditions of safe storage** of medication • Reinforced importance of secure storage and keeping the medication out of the sight and reach of all others, especially children	
○ **Induction Doses**	Provided **induction doses** under appropriate medical supervision	
○ **Limited Amount of Medication**	Prescribed **limited amount of medication** at first visit • enough to last until next visit	
○ **Professional Counseling**	Provided or referred to **professional counseling** and support services	

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○ **Induction Doses**	Provided **induction doses** under appropriate medical supervision	
○ **Limited Amount of Medication**	Prescribed **limited amount of medication** at first visit • enough to last until next visit	
○ **Professional Counseling**	Provided or referred to **professional counseling** and support services	
○ **Scheduled Next Visit**	**Scheduled next visit** at interval commensurate with patient stability • Weekly, or more frequent, visits are recommended for the first month	

The **Induction Checklist** may be used during the induction period and filed in the patient's medical record to document safe use conditions. After the induction period, use the maintenance checklist on the next page.

CHECK	INDUCTION	
○ **Take Medication As Prescribed** ○ **Pill/Film Count/Dose Reconciliation**	Assessed and encouraged patient to **take medication as prescribed** • Consider **pill/film count/dose** reconciliation	

○ **Appropriateness of Dosage**	Assessed **appropriateness of dosage**
	• Buprenorphine combined with naloxone is recommended for maintenance:
	  • Buprenorphine/Naloxone SL tablet and film (generic equivalents of Suboxone®): doses ranging from 12 mg to 16 mg of buprenorphine are recommended for maintenance
	  • Buprenorphine and naloxone sublingual film (Cassipa®): a target dose of 16 mg of buprenorphine is recommended for maintenance
	  • Buprenorphine/Naloxone SL tablet (Zubsolv®): a target dose of 11.4 mg buprenorphine is recommended for maintenance
	  • Buprenorphine/Naloxone Buccal Film (Bunavail®): a target dose of 8.4 mg of buprenorphine is recommended for maintenance
	• Doses higher than this should be an exception
	• The need for higher doses should be carefully evaluated	

○ **Urine Drug Screens**	Conducted **urine drug screens** as appropriate to monitor compliance with prescribed buprenorphine treatment plan or ascertain use of illicit substances	
○ **Prescription Drug Monitoring Program**	Checked patient's prescription profile in the **Prescription Drug Monitoring Program** (PDMP), as appropriate	
○ **Professional Counseling**	Assessed participation in **professional counseling** and support services	
○ **Benefits vs. Risks**	Assessed whether **benefits of treatment with buprenorphine-containing products outweigh risks** associated with buprenorphine-containing products	
○ **Progress Toward Treatment Goals**	Assessed whether patient is making adequate **progress toward treatment goals** • Considered results of urine drug screens as part of the evidence of the patient complying with the treatment program • Considered referral to more intensive forms of treatment for patients not making progress	
○ **Scheduled Next Visit**	**Scheduled next visit** at interval commensurate with patient stability • Weekly, or more frequent, visits are recommended for the first month	

Maintenance Checklist may be used during the maintenance period and filed in the patient's medical record to document safe use conditions.

CO-SLAW