Office-Based Management of Opioid USE Disorder (OUD):

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Learning Objectives

1. Which MAT for which patient?
2. Induction principles
3. Induction caveats
   -precipitated withdrawals
   -microinductions

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WHICH MAT ?

	METHADONE	BUPRENORPHINE	NALTREXONE
EFFICACY	Most proven, higher retention (70% vs 50%)	Close if not equal to methadone	Less but mostly due to dropouts during induction
SIDE EFFECTS	Prolonged QT Constipation Low testosterone Respiratory depression Sweating Pituitary suppression	Constipation Low testosterone(less) Nausea, LE edema, HA Insomnia Sweating Blistering in mouth	Nausea LFTs Dizziness, drowsiness Injection site tenderness
RISK OF OVERDOSE	+++ if dose is too high or patient mixes with sedatives (6x OD risk)	Very low, possible when mixed with sedatives but low	None
PAIN CONTROL	Yes	Yes	No

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Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicenter open-lable, randomized controlled trial, Lee J.D, et al., The Lancet. 391 2018

- 24 week, open label, RCT
- 570 patients , recruited as inpts, 24 weeks outpt follow up
- 369 patients completed the study (65%)
- Major findings"
  - large induction hurdle (72% in naltrexone, 94% bup)
  - induction rates for naltrexone varied greatly from site to site
  - once successfully on medication
    52% opioid relapse rate in naltrexone
    56% opoid relapse rate in buprenorphine

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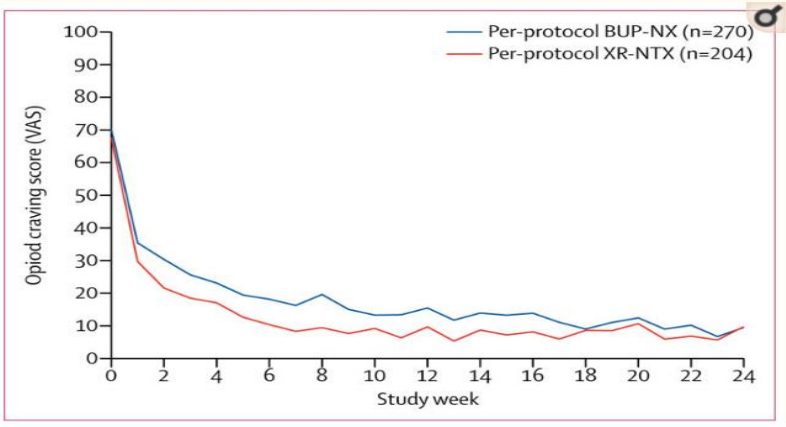
- 

Figure 3
Opioid craving during the trial

Craving was self-reported with an opioid craving VAS, range 0–100. VAS=Visual Analogue Scale. XR-NTX=extended-release naltrexone.

BUP-NX=buprenorphine-naloxone.

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Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicenter open-lable, randomized controlled trial, Lee J.D, et al., The Lancet. 391 2018

Conclusions by authors

1) More difficult to start naltrexone
   28% dropout for naltrexone vs 6% for buprenorphine
2) Nearly all induction failures had relapse
3) For patients who were successfully started the relapse the 2 were equally effective
4) The safety profile was similar in both

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RISK OF OVERDOSE	+++ if dose is too high or patient mixes with sedatives (6x OD risk), elderly, COPD, CHF	Very low, possible when mixed with sedatives	None while on it

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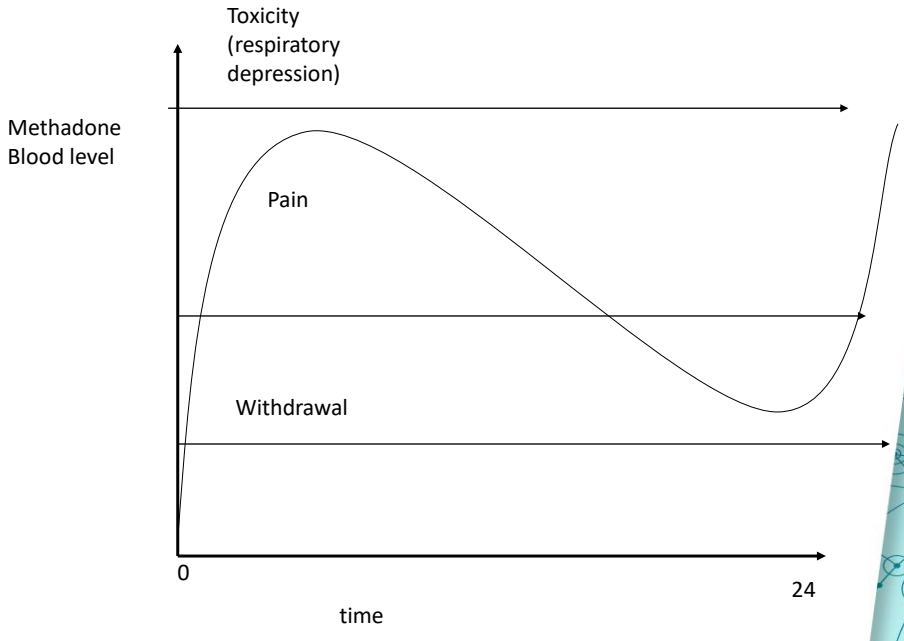

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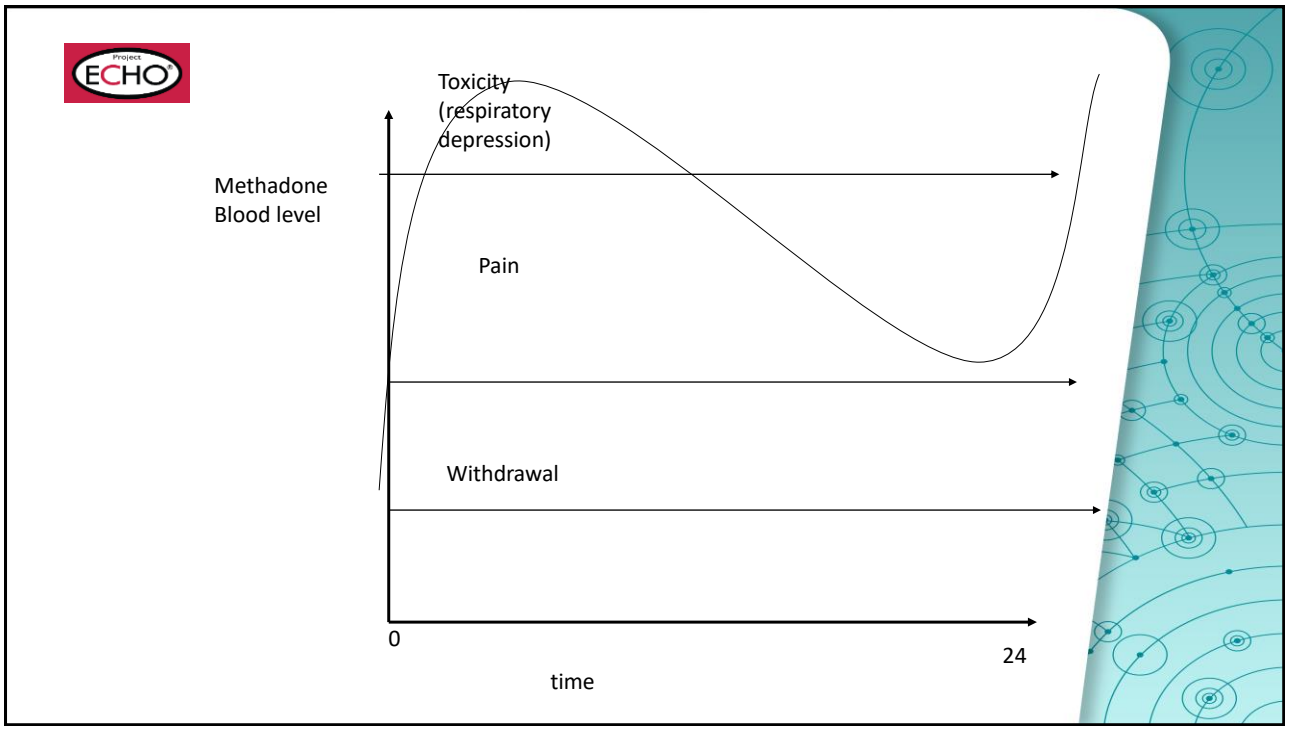
Toxicity
(respiratory
depression)
Methadone
Blood level
Pain
Withdrawal
0
24
time

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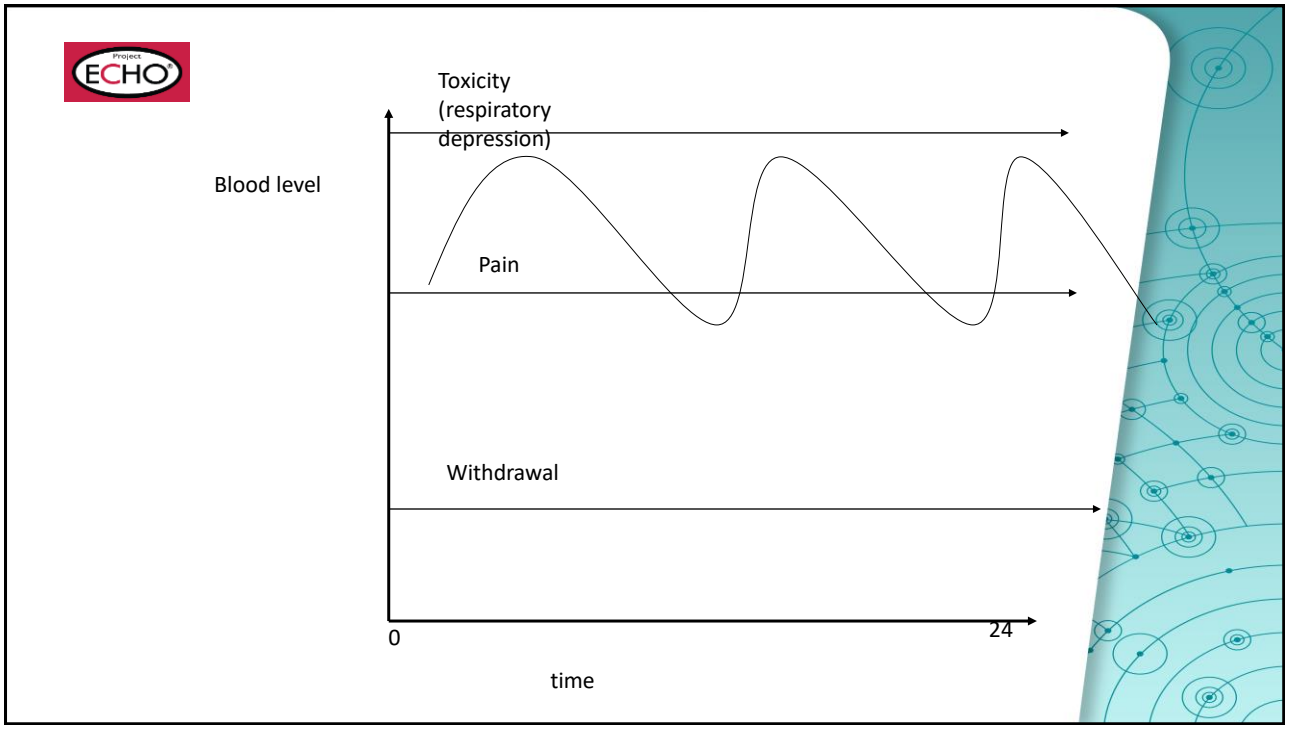
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WHICH MAT ?

	METHADONE	BUPRENORPHINE	NALTREXONE
MEDICATION INTERACTIONS	Yes (anticonvulsants, HIV meds, antidepressants…)	Few (less severe)	Opioids
REGULATION	VERY High	Moderate	Minimal
CONVENIENCE	Daily visits for at least 3 months (Covid changes) Limited number of clinics-19	Monthly visits	Monthly visits
COSTS	Medicaid	Medicaid	Medicaid
WORK / MILITARY STATUS	Prohibited in certain job situations (CDL)	Less restrictive but often prohibited in CLD	None
DIVERSION RISK	Very low for 1st three months but higher after take homes are granted	Initially > methadone but less dangerous when diverted	None

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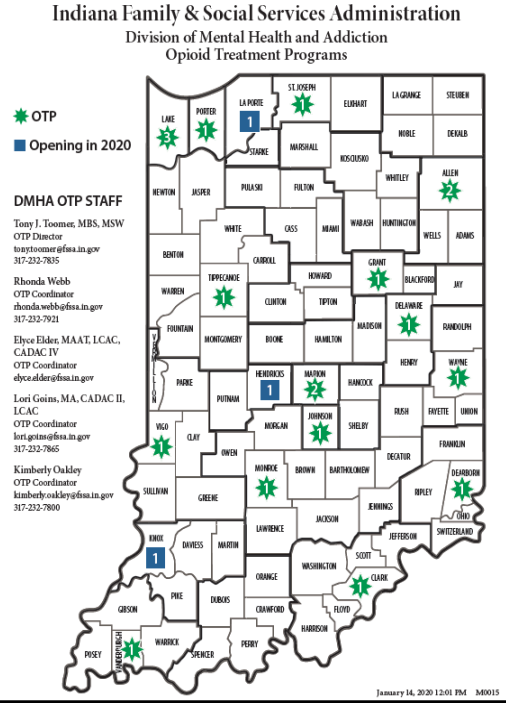

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Buprenorphine vs Methadone vs XR-Naltrexone vs Abstinence

- Prior experience of patient (or friends) with MAT often drives the decision
- Many patients will not tolerate the required withdrawal period for naltrexone
- Prior use of diverted buprenorphine does not preclude OUD treatment with buprenorphine
- Opioid agonist therapy should not be denied to patients solely because they take benzodiazepines or other drugs
- Prior failure should not preclude another attempt

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Who shouldn't be placed on MAT for opioid use disorder?

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Who shouldn't be placed on MAT for opioid use disorder?

- There is no opioid use disorder (? Chronic pain patients)
- They already are getting MAT from someone else
- If they are clearly intoxicated
- They are transitioning to somewhere soon where they will not have access to MAT
- If their employment precludes it and they need to maintain that position
- Known allergy
- Unwilling to engage in other therapy (not always)

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Medical Management Alone

- 4 studies that suggest no additional benefit of behavioral intervention with buprenorphine but…

- Regular medical management that included weekly appointments for early phase
- Regular urine monitoring
- Physician counseling on addiction that stressed importance of abstinence, outside meetings.

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Office Based Induction

- educate the patient on proper way to take the medication
- visual verification of opioid withdrawal (COWS)
- ensure the lack of over sedation
- enhance therapeutic relationship
- advise pt to abstain from tobacco before dosing (vasoconstriction)
- no need to use buprenorphine without naloxone as induction medication
- pt returns next day for dose titration
- can patient drive after induction?

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Office Based Induction

- Educate about precipitated withdrawal; timing varies
  - Advise to abstain for roughly: 6-8 hrs. for short-acting opioids, 24 hrs. for long-acting opioids, and 48-72 hrs. for methadone
- Patient should be in mild to moderate withdrawal
- Initial dose can be 2-4mg with repeat of 4mg first day, max 8-12mg on day 1
- Wait 2 hours before repeating dose
- Goal of induction is to reach stable dose that reduces or eliminated cravings and withdrawal
- Office-based vs home inductions are likely equivalent *

* Sohler NL J Subst Abuse Treat. 2010 Mar

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Home Based Induction

- Experienced clinicians (and patients) probably better suited for unobserved approach
- Patient needs to understand withdrawal and when to take first dose (written instructions- teach back)
- Still requires initial face to face contact for evaluation and diagnosis
- Phone contact next day or two
- Titrations instructions
- Follow up visit within 2-7 days
- How much for the first prescription?
- Do not try with methadone conversions

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Precipitated opioid withdrawal

1- Administration of naloxone or buprenorphine while pure mu agonist are present

2- It is more severe then typical opioid withdrawal (naltrexone > buprenorphine)

3- Unlike withdrawals from stopping these withdrawals can manifest with
- delirium
- autonomic hyperactivity (severe hypertension)
- require supportive management in ER or hospital

4- If not severe can be managed with clonidine, Imodium,

5- Overriding with pure mu agonists not recommended (risk of rebound respiratory depression)

6- If in doubt consider Naloxone (0.1mg SQ/IV) challenge first to avoid precipitated withdrawal

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Precipitated opioid withdrawal

High dose fentanyl increases risk of precipitated withdrawal

Fentanyl is lipid soluble and may results in delayed withdrawal

Increasing reports of using microdosing to successfully transition the patient to buprenorphine without requiring patient to experience withdrawal

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MANAGEMENT OF PRECIPITATED WITHDRAWAL

- Buprenorphine
  - hold further dosing and wait a day
  - continue the buprenorphine in attempt to provide enough agonist effect
- Naltrexone
  - supportive therapy
  - emerging strategy of using buprenorphine (avoid rebound respiratory depression)

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Transferring from Methadone to Buprenorphine

- Reasons patients may want to convert to buprenorphine:

  - believe it is easier to come off buprenorphine
  - side effects of methadone
  - methadone “not holding”
  - want more flexibility in their dosing
  - toxicity: prolonged QT, constipation
  - discharged from a methadone program

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Transferring from Methadone to Buprenorphine

- Strategies for conversion

A- abstinence from methadone long enough to make conversion

B- micro-inductions with buprenorphine (Bernese method)

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Transferring from Methadone to Buprenorphine –abstinence method

- Clarify why patient is transferring
- Methadone is especially long-acting opioid; risk of precipitated withdrawal is higher and dose dependent.
- Confirm patient is in withdrawal prior to induction – the timeline will vary amongst patients (72 or longer hours typically)
- Ideally patient should be stable around 30-35mg for one week, success has been shown for pts up to 100 mg, higher conversions seek expertise and hospitalization
- Use small test dose , i.e. 2 mg, repeat, but if no PW then escalate dose the 1st day for total of 4-8mg
- Patients need lots of support – ok to go back to methadone if buprenorphine fails

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Micro-dosing as method of induction

- Concept: slow displacement of the pure agonist over several days to avoid precipitated withdrawal
- Add very small amounts of buprenorphine while allowing the longer acting opioids (methadone) to slowly clear

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Micro-dosing conversion

- Allows conversion from methadone to buprenorphine without stopping the methadone
- Literature:
  -case report of 2 patients 2016 (Vogel M et al., 2016)
  -case report of 2 patients on heroin (Hamming R et al., 2016)
  -case report of 3 hospitalized patients (Terasaki et al., 2019)
  -case report of 2 hospitalized patients (Sukhpreet et al., 2019)

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BERNESE METHOD

Day	Order	Number of tablet(s) per dose when using buprenorphine-naloxone 2 mg – 0.5 mg tablet	Agonist
1	buprenorphine 0.5 mg – naloxone 0.125 mg sublingual BID	One quarter tablet	Full dose
2	buprenorphine 0.5 mg – naloxone 0.125 mg sublingual TID	One quarter tablet	Full dose
3	buprenorphine 1 mg – naloxone 0.25 mg sublingual BID	One half tablet	Full dose
4	buprenorphine 2 mg – naloxone 0.5 mg sublingual BID	1 tablet	Full dose
5	buprenorphine 2 mg – naloxone 0.5 mg sublingual QID	1 tablet	Full dose
6	buprenorphine 4 mg – naloxone 1 mg sublingual TID	2 tablets	Full dose
7	buprenorphine 12 mg – naloxone 3 mg sublingual daily	Refer to MAR for directions	Stop

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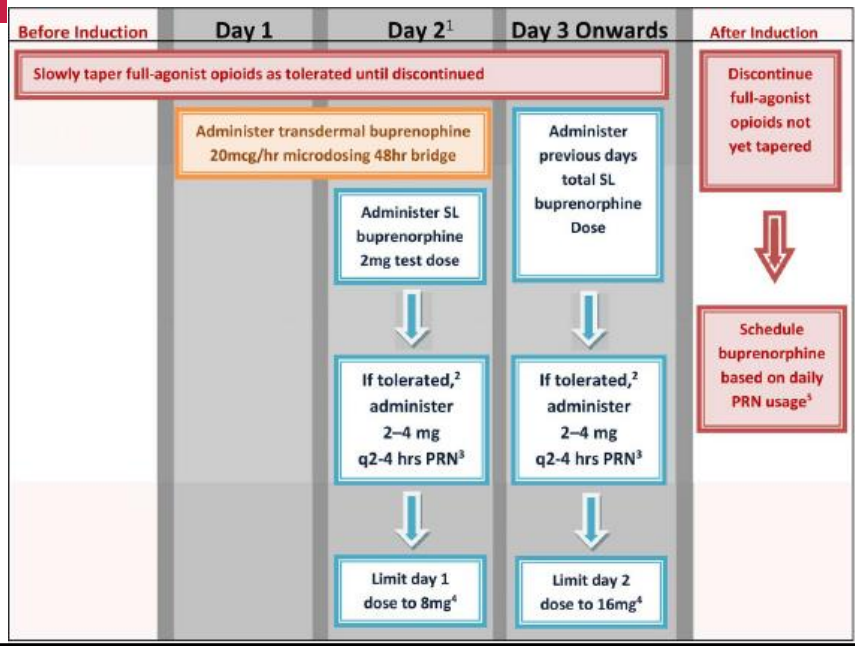
BUPRENORPHINE TRANSDERMAL METHOD



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Resources

SAMHSA publications TIP 63: Medications for Opioid Use Disorder- Introduction to Medications for Opioid Use Disorder Treatment

https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Introduction-to-Medications-for-Opioid-Use-Disorder-Treatment-Part-1-of-5-/BackInStock/SMA18-5063PT1

COWS for opioid withdrawal:

http://www.mdcalc.com/cows-score-opiate-withdrawal/

- Robohm JS. Training to reduce behavioral health disparities: How do we optimally prepare family medicine residents for practice in rural communities? Int J Psychiatry Med. 2017 Jan 1:91217417730294. doi: 10.1177/0091217417730294.
- Wakeman SE. Medications For Addiction Treatment: Changing Language to Improve Care. J Addict Med. 2017 Jan/Feb;11(1):1-2. doi: 10.1097/ADM.0000000000000275
- Livingston JD, et al. The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. Addiction 2011. 107:39-50.

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Resources

- Vogel M et al., Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. Substance Abuse and Rehabilitation, 2016:7, 98-105
- Sandu R et al., Buprenorphine/naloxone induction for treatment of acute on chronic pain using a micro-dosing regimen: A case report. Canadian Journal of Pain, 2019 (3), issue 1
- Sukhpreet K et al., Rapid Micro-induction of Buprenorphine/Naloxone for Opioid Use Disorder in an Inpatient Setting: A case series. The American Journal of Addictions (28)issue
- Transitioning Hospitalized Patients with Opioid Use Disorder from Methadone to Buprenorphine without a Period of Opioid Abstinence Using a Microdosing Protocol. Pharmacotherapy: The J of Human Pharm and Drug Therapy 2019

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