FREQUENTLY ASKED QUESTIONS

Suboxone/Buprenorphine

1) How many times per day should buprenorphine be dosed in order for it to be effective?

Buprenorphine can be given in a single daily dose for opioid use disorder. Pregnant women require more frequent dosing (see pregnancy questions below). When used for chronic pain it should be dosed multiple times per day. After a period of stabilization buprenorphine for OUD can be given every other day at twice the daily dose, although dose should never exceed 32 mg in one day. For all clinical indications the amount prescribed per dose should be individualized to each patient's clinical presentation and need.

References:

- https://www.suboxone.com/pdfs/prescribing-information.pdf
- Lawrence A Haber, MD, Triveni DeFries, MD, MPH, Marlene Martin, MD, Things We Do for No Reason™: Discontinuing Buprenorphine When Treating Acute Pain. *J. Hosp. Med* 2019;10;633-635. Published online first August 21, 2019. doi:10.12788/jhm.3265
- Amass, L, Kamien, J B, Mikulich, S K. Efficacy of daily and alternate day dosing regimens with the combination buprenorphine-naloxone tablet. (200) Drug Alcohol Depend. 58(1-2):143-52. doi: 10.1016/s0376-8716(99)00074-5.

2) What is the target maintenance dose for buprenorphine for treatment of opioid use disorders (OUD)?

Evidence suggests that 16 mg per day or more of buprenorphine may be more effective than lower doses and equally effective to moderate doses of methadone (85mg/ day). Although there is no maximum dose of methadone, there is a maximally approved dose of buprenorphine of 32 mg in one day; this maximum buprenorphine dose is based not only on the FDA approved package insert but also based on the pharmacology of buprenorphine. Since buprenorphine has a ceiling effect, not seen with other opioids, there is no clinical or pharmacological benefit to increasing the dose above 32mg/ day.

If started during withdrawal then a "dose of buprenorphine sufficient to suppress withdrawal symptoms should be given."

References:

- https://www.asam.org/Quality-Science/quality/2020-national-practice-guideline
- Hillhouse, M., Canamar, C. P., Doraimani, G., Thomas, C., Hasson, A., & Ling, W. (2011). Participant characteristics and buprenorphine dose. *The American journal of drug and alcohol abuse*, *37*(5), 453–459. https://doi.org/10.3109/00952990.2011.596974
- Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD002207. DOI: 10.1002/14651858.CD002207.pub4.Parran TV et al. Drug Alcohol Depend 2010
- Jacobs, P., Ang, A., Hillhouse, M. P., Saxon, A. J., Nielsen, S., Wakim, P. G., … & Blaine, J. D. (2015). Treatment outcomes in opioid dependent patients with different buprenorphine/naloxone induction dosing patterns and trajectories. *The American Journal on Addictions*, *24*(7), 667-675.

3) Which medication for OUD should be given to someone with abnormal liver functioning?

FDA approved medications for OUD have been associated with rare liver function elevations; however, there are many reasons for elevated liver function test (LFT) in patients with OUD and AUD and a hepatitis panel should be obtained to rule out other causes. Although these medications haven't been well studied in patients with severe LFT elevations, they have been used safely in populations with Hepatitis C and liver inflammation for more than a decade.

References:

- https://pcssnow.org/wp-content/uploads/2014/10/PCSS-MAT-NTX-Liver-Safety-Guideline1.pdf
- https://pcssnow.org/wp-content/uploads/2014/03/PCSS-MATGuidanceMonitoringLiverFunctionTests-and-HepatitisInBupPatients.Saxon_.pdf
- NIDA. (2013, December 6). Medications That Treat Opioid Addiction Do Not Impair Liver Health. Retrieved from https://archives.drugabuse.gov/news-events/nida-notes/2013/12/medications-treat-opioid-addiction-do-not-impair-liver-health
- Nasser AF, Heidbreder C, Liu Y, Fudala PJ. Pharmacokinetics of Sublingual Buprenorphine and Naloxone in Subjects with Mild to Severe Hepatic Impairment (Child-Pugh Classes A, B, and C), in Hepatitis C Virus-Seropositive Subjects, and in Healthy Volunteers. *Clin Pharmacokinet*. 2015;54(8):837-849. doi:10.1007/s40262-015-0238-6

4) **We have a pregnant patient on 10 mg buprenorphine three times per day; is that ok?**

During pregnancy patients will require more frequent dosing and higher doses of methadone and buprenorphine because of increased volume of distribution of medication and increased liver enzyme activity. These changes are evident by the second trimester; therefore, pregnant patients will need to be seen more frequently and likely require dose adjustments that would not be required in nonpregnant patients.

References:

- https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/08/opioid-use-and-opioid-use-disorder-in-pregnancy
- Zhang H, Kalluri HV, Bastian JR, Chen H, Alshabi A, Caritis SN, Venkataramanan R. Gestational changes in buprenorphine exposure: A physiologically-based pharmacokinetic analysis. Br J Clin Pharmacol. 2018 Sep;84(9):2075-2087. doi: 10.1111/bcp.13642. Epub 2018 Jun 21. PMID: 29873094; PMCID: PMC6089832. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6089832/

5) Patient comes in on 32 mg per day, we don't ever give more than 16mg per day; what should we do?

Abruptly decreasing from 32mg per day to 16mg per day will result in opioid withdrawal symptoms and a risk for increased cravings and return to illicit substance use.

Verify patient was taking the entire dose and talk to their provider about how this dose was determined to be the right dose for the patient.

Should you determine the patient does not require 32 mg per day or 32 mg per day was not achieving the desired outcome of decreased illicit substance use, you may gradually taper the amount of medication over time.

Do you have arbitrary limits on other medications? If not, then consider a policy or guidelines change to support medication dosing determinations made by providers or a nonformulary review committee.

6) Many jails are working on changing their opioid withdrawal protocols from medications to treat symptoms only to buprenorphine. What is the best way to change withdrawal protocols?

Buprenorphine should be started when objective evidence of withdrawal is present. An adequate dose of buprenorphine should be given to relieve withdrawal symptoms. When this approach is taken, additional medications are not required to treat withdrawal symptoms as the withdrawal symptoms will be treated with buprenorphine. Patients can be stabilized within 1-24 hours, depending on how your protocol is written.

7) What are some of the dangers/pitfalls in under-medicating someone with buprenorphine?

The most dangerous consequence of under-medicating someone with buprenorphine is death, which is associated with ongoing drug use due to undertreated withdrawal symptoms and/or cravings. Ongoing drug use is also associated with medical and mental health costs, such as those associated with infectious disease and suicide attempts, custody issues related to gang activity and violence, and recidivism.

8) Is there a risk of precipitated withdrawal when using Subutex® or buprenorphine, or is it only a risk when using medications that contain naloxone?

The presence of naloxone is not the only thing that determines or can cause precipitated withdrawal. Buprenorphine comes in many formulations, some include naloxone and others do not (the latter is referred to as the mono formulation, as it has only buprenorphine - the trade name of this formulation is Subutex®). If buprenorphine/naloxone is taken correctly, that is, under the tongue or placed inside the cheek, then the naloxone is not absorbed and therefore does not cause withdrawal. Buprenorphine is a partial agonist *AND* it binds very strongly to opioid receptors (mostly mu receptors). Because of that strong biding, buprenorphine can displace heroin or other opioids from the receptors and precipitate withdrawal. That happens because it is a *partial agonist.* Persons with active OUD have opioids such as heroin and fentanyl sitting on the opioid receptors, which fully activate the receptors; when buprenorphine sits on those receptors, it only partially activates the receptor. If a person with OUD has an opiate in their system and is given buprenorphine, that can kick the opioids off of the receptor and cause withdrawal symptoms.

Antagonists, such as naltrexone and naloxone sit on that receptor and BLOCK all activation. That's why sometimes individuals who are revived from an overdose with naloxone get upset; the naloxone revives them but puts them into withdrawal. In these cases, the naloxone is being injected or delivered intranasally and is absorbed from those routes. Although naloxone is not well absorbed when taken in the mouth or swallowed into the stomach, naltrexone is absorbed from the stomach and can also precipitate withdrawal if someone has used opioids recently.

<u>Diversion</u>

1) Patient was caught diverting their buprenorphine in the jail and the on-call provider stopped the medication. Was that the right thing to do?

Diversion has many reasons within a jail and should be addressed with a well thought out plan.

1. Talk with the patient about the incident; ensure the patient is safe from anyone coercing them to divert the medication. If this is a concern, an option may be to move the patient to a different yard or facility.
2. Adjustments may need made to the treatment plan; options include:
   2.1. Switch from oral to injectable buprenorphine; or switch from buprenorphine to methadone
   2.2. If buprenorphine is abruptly stopped, this likely will lead to a return to illicit opioid use and/or opioid withdrawal, neither of which helps the patient or the jail.

It is also important to distinguish between "diversion" and "misuse" of medication. *Diversion* is when a patient gives their prescribed medication to someone else; *Misuse* is when a patient may cheek or otherwise avoid taking the medication at the time it is administered which may be for their own use at another time. In the case of misuse, talk with the patient about why they are seeking to take the medication at another time. They may be experiencing symptoms that are leading to this behavior that can be addressed by adjusting how their medication is administered.

Jail and MAT

1) Is there research that demonstrates the effectiveness of implementing a MAT program in jail?

Yes, several studies have demonstrated positive outcomes of providing MAT in custody:

- The number of post-incarceration fatal overdoses went down significantly after implementation of a MAT program in Rhode Island Department of Corrections: https://jamanetwork.com/journals/jamapsychiatry/article-abstract/2671411
- Incarcerated persons provided with methadone received fewer disciplinary tickets compared to those forced into withdrawal. https://pubmed.ncbi.nlm.nih.gov/29341974/

2) If a patient is sentenced to jail, can a provider advocate for MAT to be continued in jail?

All providers should contact their jail to find out what their protocol is, and how clients can make sure MAT is continued. Some jails will want clients to bring in all medications with them to make sure there is no delay in the medication being dispensed. It is important to remember that a MAT program does not always mean the same thing. Some jails will withdraw clients who are incarcerated for more than brief periods but allow them to restart a few days before release. Other jails will maintain them on Suboxone® if they bring in a valid prescription, and other jails will start clients who are in withdrawal. A provider can always advocate for their clients who go to jail, but it is important to understand the jails' current protocol so it can be explained to clients before they are incarcerated.

3) What is the best medicine to start in the jail for an inmate who has OUD?

There are three medicines used for Medication Assisted Treatment (MAT): methadone, buprenorphine, and naltrexone extended-release injection (Vivitrol®). Several factors should be considered in selection of the best treatment agent for each patient. Like any other condition, therapy should be tailored to the individual patient and patient choice of medication contributes to successful outcomes with medication (Nunes 2021). Naltrexone cannot be used to manage acute withdrawal, so for inmates in acute withdrawal, use methadone or buprenorphine and then transition to maintenance MAT therapy. There is a higher relapse rate with naltrexone than buprenorphine or methadone; this has to do with an increase in getting patients started on naltrexone, as that requires complete resolution of withdrawal symptoms and being off all opioids. In order to select between buprenorphine and methadone, consider history of past use and success or failure. Consider methadone for patients with past history of successful treatment with methadone or

failure on buprenorphine. Finally, while all treatment should be optimized for each patient, whether an inmate or not, practical factors such as cost, continuity of treatment, etc. often play a role in prescribing. In the carceral environment, consider which medication may be more readily available both during incarceration and post release. The restrictions related to methadone administration are often more onerous for jails so buprenorphine may be preferred.

Naltrexone

1) When is naltrexone the best indicated medication?

Naltrexone does not treat opioid withdrawal and cannot be initiated until one has been off opioids for 7 days and completed withdrawal. Therefore, naltrexone is best utilized in someone who has been off opioids for some time and is having cravings and/or wants to take medication to increase the likelihood of remaining abstinent. It has significant data to support its use in persons involved in the criminal justice system and in healthcare and other professionals. Persons experiencing moderate to severe pain during withdrawal do not respond well to naltrexone (Nunes, 2021).

References:

Nunes, et al. (2021) Sublingual buprenorphine-naloxone compared with injection naltrexone for opioid use disorder: potential utility of patient characteristics in guiding choice of treatment. Am J of Psychiatry 178:7, 660-671.

Methamphetamine

1) Is there evidence-based medication assisted treatment for methamphetamine use?

At this time, there are no FDA approved medications for stimulant use disorders (methamphetamine or cocaine use disorder). Many medications have been tried in either methamphetamine use disorder or cocaine use disorder. Most studies have been small and have not generated positive results. Generally, studies with positive results have not yet been replicated. One such study utilized a combination of extended-release injectable naltrexone every three weeks with 450mg/day of bupropion (trade name Wellbutrin) compared to extended-release injectable naltrexone with placebo. The difference between the combination treatment and the single medication was 11% in favor of combination medication. This study requires replication and a longer duration of treatment to determine the lasting impact of this small percentage of improvement. The limited data does not support changes in prescribing practices. Robust evidence-based psychosocial interventions, such as contingency management, have solid data to demonstrate their efficacy with stimulant use disorders.

References:

- Lee, Nicole K. (2018) Drug and Alcohol Dependence 191 309-337. Pharmacotherapy for amphetamine dependence: A systematic Review.
- Trivedi, et al. (2021). Bupropion and Naltrexone in Methamphetamine Use Disorder. NEJM; 384:140-153.

Psychosocial Treatment

1) Is psychosocial treatment (therapy/counseling) a requirement of inmate participation in MAT?

The Substance Abuse and Mental Health Services Administration (SAMHSA) defines MAT as the “use of medications, in combination with counseling and behavioral therapies, to provide a ‘whole-patient’

approach to the treatment of substance use disorders." For inmates served by Opioid Treatment Programs (OTPs), including those who provide methadone for inmates, federal standards require the OTPs to provide "adequate substance abuse counseling to each patient as clinically necessary" and state standards, including any current COVID-related flexibilities, that apply to the OTPs would apply while the patient is a jail inmate. For individuals on buprenorphine, the Drug Addiction Treatment Act of 2000 (DATA 2000) requires that buprenorphine providers have the "capacity to provide directly" or "by referral … appropriate counseling and other appropriate ancillary services." The legislation also requires training for physicians on buprenorphine to address "counseling and recovery support services".

The definition of appropriate psychosocial treatment can vary broadly, however. The best available evidence suggests there is a valuable role for psychosocial supports, but current research does not clearly establish what models are most appropriate and effective in which settings and for which population, including individuals in jail. While there is no clear, validated model of care, best practice recommendations include:

- **Addiction as a Chronic Disease**: psychosocial support services that encourage self-management after initial patient stabilization.
- **Patient-Centered, Flexible Care:** a range of treatment options based upon needs, from intensive individual counseling to flexible psychosocial supports.
- **Stepped-Care or Phased Approach**: 1) Screening and Identification, 2) Assessment, 3) Medication Management, and 4) Referral to other psychosocial supports based upon need
- **Recovery Supports and Social Determinants**: Supports that address "whole person" needs, both in custody such as peer services, spiritual and faith-based support, and parenting education and supports upon reentry including housing, transportation and employment.

Since medications for addiction treatment are an evidence-based treatment demonstrated to reduce deaths due to overdose and since the incarcerated population is at much higher risk for overdose deaths post-release than the general population, addressing this risk through offering of medications then continuing to seek access to appropriate psychosocial interventions rather than making medication contingent upon access to behavioral health interventions is recommended. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder (2020 focused update) states that "because of the potential harm associated with untreated opioid use disorder, *a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of opioid use disorder*, with appropriate medication management. Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment or support services appropriate for addressing their individual needs. In the absence of added psychosocial treatment, clinicians may need to further individualize treatment plans to address the potential for issues related to adherence and diversion". **References:**

- Substance Abuse and Mental Health Services Administration. Medication and Counseling Treatment. 2015. Available from: https://www.samhsa.gov/medication-assistedtreatment/treatment.
- Appendix B of Psychosocial Supports in Medication-Assisted Treatment: Site Visit Findings And Conclusions https://aspe.hhs.gov/basic-report/psychosocial-supports-medication-assisted-treatment-site-visitfindings-and-conclusions
- The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder 2020 Focused Update https://www.asam.org/docs/default-source/quality-science/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2

MAT General

1) How do we determine who is appropriate for MAT for Opioid Use Disorder?

Evidence-based screening and assessment is necessary to accurately diagnose Opioid Use Disorders. Because treatment effectiveness for opioid use disorder, without medication, is roughly 15 percent at one year, medication for opioid use disorder is considered the standard of care. Therefore, medication should be offered to everyone with an OUD. Evidence-based screening and assessment will reveal which patients have an opioid use disorder and which patients have opioid withdrawal.

It is important to remember that not everyone who has opioid withdrawal has an opioid use disorder. Withdrawal occurs when the opioid is stopped or decreased in someone who is physiologically dependent on opioids; this can occur when taking medication as prescribed for a legitimate medical condition and can occur when taking medication or illegal opioids for other reasons. The issue is which medication is right for which patient at this time in their disorder. This issue is addressed in other questions (Mattick and Hall).

Treatment effectiveness for alcohol use disorder, without medication, is higher than for opioid use disorder; for this reason, the standard of care is to offer medication to people who have not responded to nonpharmacological treatment alone. (APA).

References:

- American Psychiatric Association. Practice Guideline Alcohol Use Disorder. http://psychiatryonline.org/doi/full/appi.books.9781615371969.alcohol03
- Mattick, RP & Hall W (1996). Are detoxification programmes effective? The Lancet 347: 8994, 97-100.