Considerations for Treatment of Opioid Use Disorder in Pregnancy

It is essential that patients be informed about the various risks of opioid use disorder (OUD) in pregnancy, including health consequences such as stillbirth as well as legal consequences such as involvement of Child Protective Services. This should be coupled with counseling about the treatment options including Medication Assisted Treatment (MAT) and behavioral therapies as well as support to realize their preferred treatment if they indicate willingness to start. A trauma-informed approach to the preceding counseling is strongly advised (see Best Practice #5).

Given that there is evidence that MAT achieves better maternal and neonatal outcomes, it should be strongly recommended over medically supervised withdrawal. However shared-decision making should be used to determine if patient would like to pursue abstinence from opioids with or without medication. The table below highlights information that can be helpful to provide patients who are considering whether or not to pursue MAT.

	Supervised Withdrawal	**Medication Assisted Treatment (MAT)**
Definition	Use of adjunctive therapies (e.g. behavioral therapies, antiemetics) while patients detox from opioids to help patients decrease/abstain from opioid use	Use of FDA-approved medications for treatment of OUD along with adjunctive therapies to help patients decrease/abstain from opioid use
Contraindications	Medically unstable	Medically unstable Allergy to both medications
Complicating Factors	Severe psychiatric illness	Severe psychiatric illness Acute pain Liver disease Heavy benzodiazepine and alcohol use
Benefits	Possibility of decreased opioid use and abstinence Avoid risks of MAT side effects Avoid ongoing need for opioid agonist if successful	Increased rates of opioid abstinence Reduction in illicit opioid use and injection drug use Reduction in overdose deaths and all-cause mortality Lower rates of stillbirth Lower risk of preterm birth Lower risk of growth restriction
Risks	Experience of withdrawal Higher risk of stillbirth Higher risk of relapse High risk of death seen in nonpregnant patients	Medication side effects Diversion of treatment (Note: no known increased risk of birth defects)

If patients express interest in MAT, shared-decision making should also take place to help them determine which medication to pursue. Methadone has been studied more extensively in pregnancy and approved for use accordingly, Buprenorphine is reasonable given a growing

body of evidence of safety though longitudinal impact on children is more limited compared to Methadone.

Prior experiences with MAT are important to elucidate. Patients who have previously been on Buprenorphine/Naloxone (Suboxone) should be made aware that Buprenorphine without Naloxone (Subutex) is considered standard of care in pregnancy given limited data on the safety of Naloxone in pregnancy and decision of how to proceed should be patient-centered. Switching between different types of MAT is not advised in pregnancy given limited data and concern for high relapse rates.

The table below highlights key similarities and differences between the two MAT options that should be leveraged in the counseling of patients.

	Buprenorphine	**Methadone**
Withdrawal Considerations	Need to be in mild to moderate withdrawal to initiate Can cause withdrawal if opioids are still in patients' system	Do not need to be in withdrawal to initiate
Dispensing Considerations	Must be dispensed by provider with an X license Variable frequency of visits depending on clinical need	Must be dispensed by Opioid Treatment Program (OTP) Typically daily visits but potential for take-homes after 3 months
Treatment Retention[1]	Lower than Methadone	Higher than Buprenorphine
Diversion Potential	Low for directly observed therapy High for take-homes	Low for directly observed therapy High for take-homes
Overdose Risk	Low Increased with sedating medications	Low-moderate Increased with treatment induction
Contraindications	Allergy to Buprenorphine Severe liver impairment	Allergy to Methadone Respiratory depression or hypercarbia Paralytic ileus Prolonged QTc (>500)
Warnings/Precautions	Medications with interactions Concomitant substance use Concomitant psychiatric illness Severe cardiovascular disease and/or hypotension Difficulty in engaging in care	Medications with interactions Concomitant substance use Concomitant psychiatric illness Decompensated liver disease
Maternal Outcomes	Increased rates of opioid abstinence Reduction in illicit opioid use and injection drug use Reduction in overdose deaths and all-cause mortality, though may be higher than with buprenorphine	Increased rates of opioid abstinence Reduction in illicit opioid use and injection drug use Reduction in overdose deaths and all-cause mortality, though may be higher than with buprenorphine
Neonatal Outcomes[2]	Later average gestational age than untreated OUD and methadone	Later average gestational age than untreated OUD

	Higher average birthweight than untreated OUD and methadone Less severe neonatal abstinence syndrome (NAS) than untreated OUD and methadone Dose does NOT affect NAS severity	Higher average birthweight than untreated OUD Less severe than NAS than untreated OUD Dose does NOT affect NAS severity
Lactation Considerations	Considered safe and advisable provided no concern for other contraindications (Limited data for Naloxone however) If not breastfeeding, appropriate to switch to Buprenorphine/Naloxone combination postpartum	Considered safe and advisable provided no concern for other contraindications

1. In the MOTHER Study, retention in treatment with Buprenorphine was 88% vs 67% with Methadone.
2. In the MOTHER Study, average NAS treatment for patients on Buprenorphine was 10 inpatient days and 1.1mg of Morphine vs 17.5 inpatient days and 10.4mg morphine for patients on Methadone.

Once patients determine which MAT option they would like to pursue, a decision needs to be made regarding where to initiate treatment. In contrast to non-pregnant patients, pregnant patients have obstetric risks that often make inpatient induction more desirable.

Outpatient induction of MAT is reasonable if the following conditions are met:

- ☐ Gestational age less than 20 weeks
- ☐ No other significant co-existing substance use, medical or psychiatric diagnosis
- ☐ Stable housing
- ☐ Ability to comply with frequent visits initially
- ☐ Outpatient infrastructure to allow for prompt enrollment in a Methadone Opioid Treatment Program or access to provider who can prescribe Buprenorphine within 3 days (see Appendix B: Sample Outpatient Buprenorphine Induction Algorithm)
- ☐ Ability to realize comprehensive "Plan of Safe Care" (see Best Practice #38)
- ☐ Informed consent for outpatient Buprenorphine induction, including recognition that there is limited data investigating this approach compared to inpatient induction

If the preceding conditions cannot be met, inpatient MAT induction is advisable (see Appendix B: Sample Inpatient Medication-Assisted Treatment Induction Algorithms).

Resources/References

1. Providers' Clinical Support System's Guidance on Buprenorphine Induction
2. ZSFG Inpatient Protocols
3. VCMC Protocols
4. SAMSA 2018 Clinical Guidelines
5. Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. N Engl J Med. 2010;363(24):2320-31. [MOTHER Trial]