Medications to Treat OUD in Pregnancy

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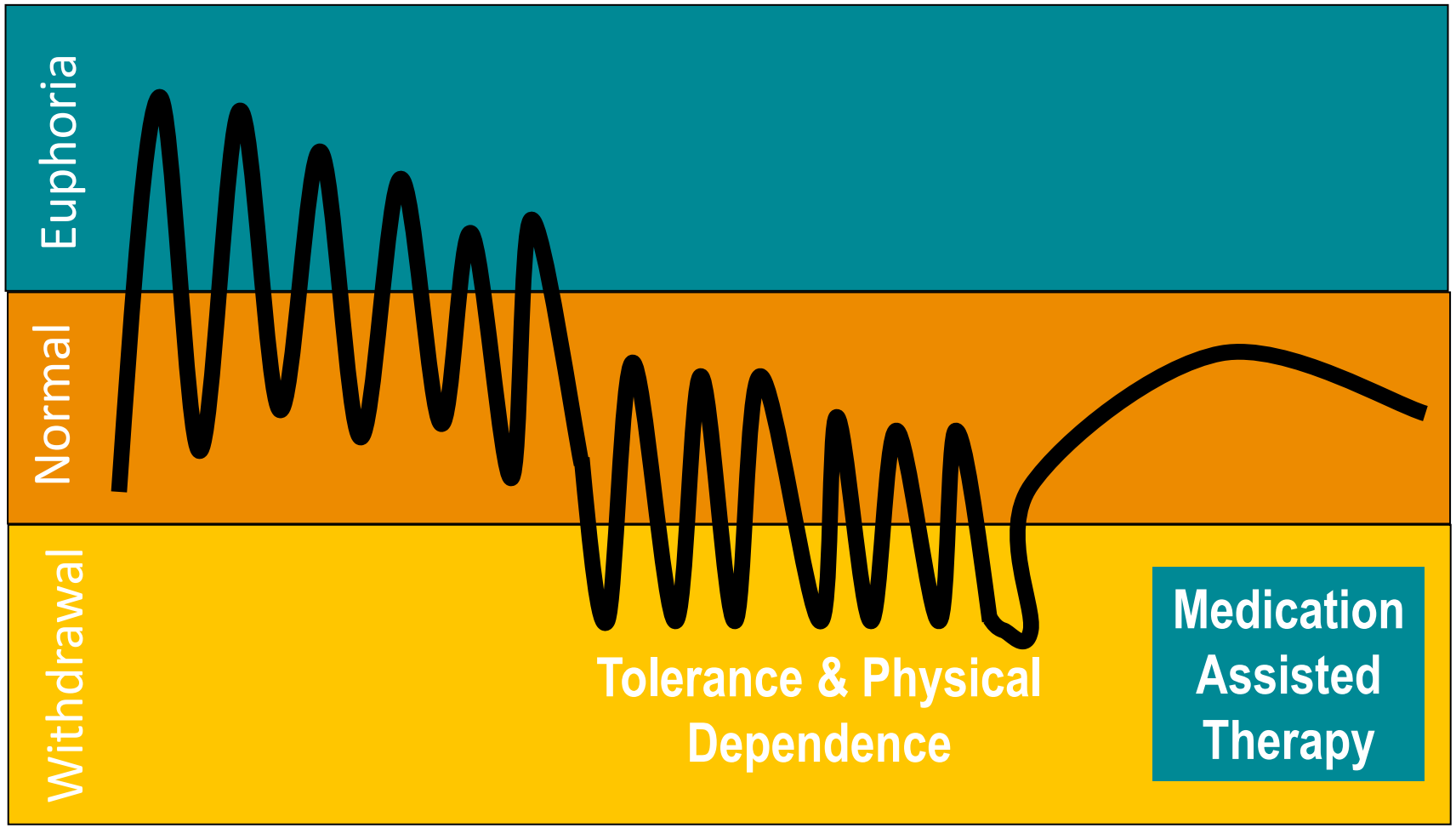
Disclosures

I have no relevant disclosures

Learning Objectives

- Identify appropriate MAT drug therapy for pregnant women
- Discuss the standard of care and timing for initiation of MAT for pregnant women
- Describe appropriate initiation and maintenance dosing of MAT for pregnant women



Acute Use

Chronic Use

Alford, Boston University, 2012

Naltrexone

- Opioid antagonist that blocks other opioids
- Does not lead to physical dependence, or to withdrawal when stopped
- Causes acute withdrawal in opioid-dependent patients
- Can be used in office-based settings without added training
- Effective in alcohol use disorder treatment
- Two formulations available:
  - 50 mg tablet
  - 380 mg long-acting injection

Methadone

- Most effective
  - ⬆ survival, treatment retention, employment
  - ⬇ illicit opioid use, hepatitis and HIV infections, criminal activity
- Highly regulated, dispensed at Opioid Treatment Programs (OTP)
  - Supervised daily dosing with take-home doses if stable
  - Counseling, urine testing
  - Psychiatric, medical services often not provided
  - **Illegal** to prescribe methadone **for addiction** in general practice
- Pregnant women can be admitted to OTPs without meeting the one-year OUD diagnosis criteria

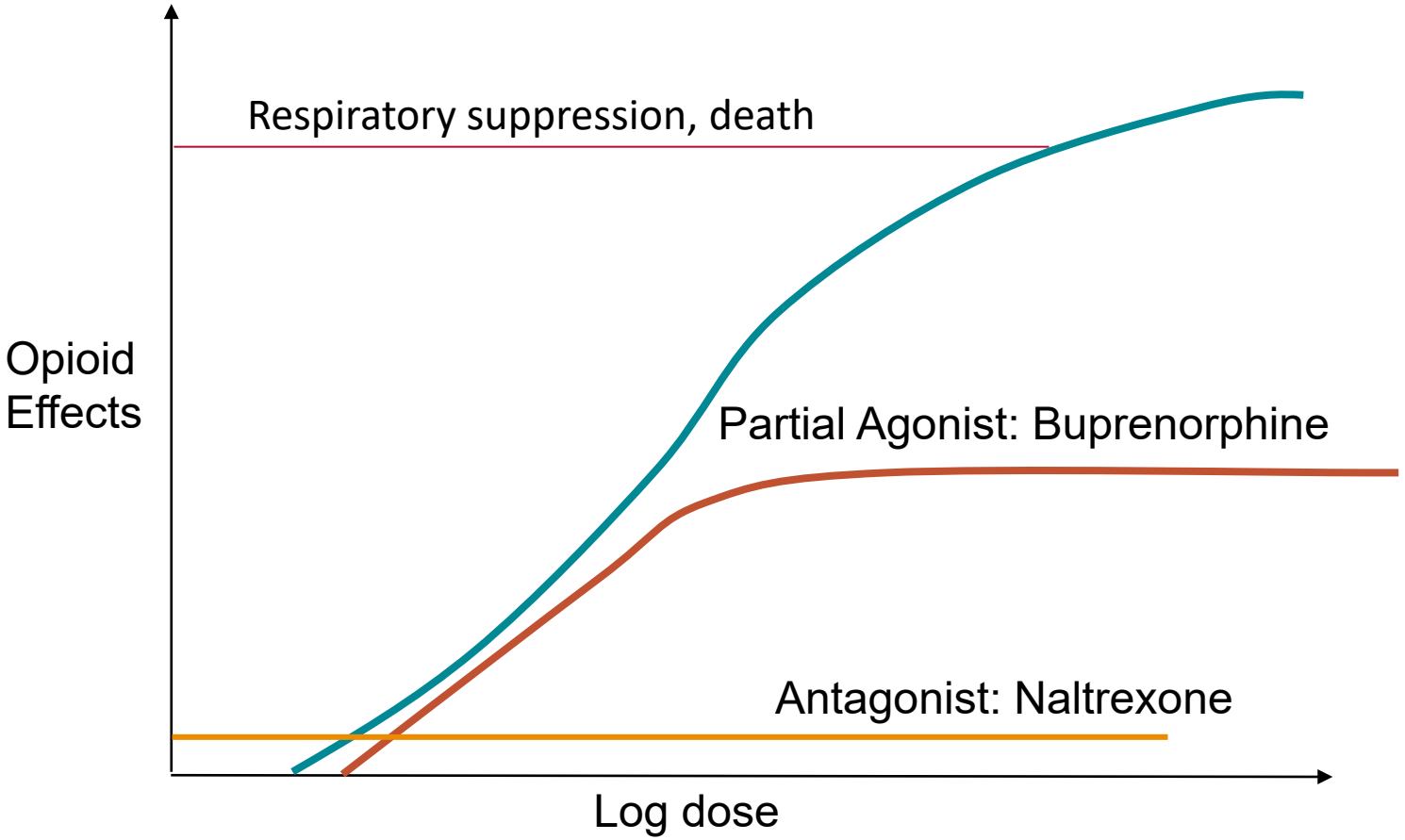
Buprenorphine

- 2000 Federal Drug Addiction Treatment Act ("DATA-2000"):
  - Made office-based addiction treatment by physicians legal
  - Must complete 8-hour training and obtain federal waiver
- 2002: Suboxone (buprenorphine/naloxone) FDA approved
  - Outcomes much superior to psychosocial treatment alone
  - Longer treatment duration is more effective
- Compared to methadone (general patients):
  - Similar abstinence from illicit opioids and decreased craving
  - Lower retention in treatment
  - Can be prescribed in general practice, lowering barriers to treatment

Buprenorphine

- Partial opioid agonist, so safer than methadone
- High mu receptor affinity, so blocks other opioids
- Formulated with naloxone - abuse deterrent
- Sublingual dosing because of reduced oral bioavailability
- Can precipitate withdrawal in tolerant patients
- Requires induction after patient enters mild-moderate withdrawal
- Extended release subcutaneous injectable approved in those initiated on transmucosal buprenorphine 8-24mg/day after a minimum of 7 days

Why is Overdose Potential Low with Buprenorphine?



Agonist: Methadone, Heroin, etc.

MAT in Pregnancy

- Buprenorphine vs Buprenorphine/naloxone
  - Buprenorphine has traditionally been preferred in pregnancy due to theoretical risks to the fetus
  - This has changed in recent years as a growing number of studies do not support a risk for naloxone
- Methadone
  - Pregnant women who receive methadone may have fewer setback to drug use and be retained in treatment longer
  - A history of IV drug use or severe OUD may benefit from the structure of an OTP
- Naltrexone
  - Should not be initiated in pregnancy due to a lack of safety data
  - Continuation of naltrexone for a woman who becomes pregnant while on treatment should be carefully assessed and informed consent of risks, as well as the risk of inadequate pain management during labor and delivery

Treatment Guidance

- Pregnant women with active OUD should be treated with methadone or buprenorphine as the standard of care.
- Pregnant women with a history of OUD may be candidates for treatment if a return to opioid use is possible
- Psychosocial needs should be assessed and patients should be offered or referred to psychosocial treatment
- A woman's choice to decline psychosocial treatment **should not delay** opioid agonist therapy

Methadone Initiation and Dosing

- Initiation:
  - Early initiation for longer gestation time and higher birth weight
  - Dose range 10 – 30 mg
  - 5 – 10 mg given every 3 – 6 hours as needed to treat withdrawal symptoms – max first day dose = 30 – 40 mg
  - Increase dose by no more than 10 mg about every 5 days
- Dosing during Pregnancy:
  - Doses may need to be increased in the 2nd and 3rd trimester due to increased metabolism and circulating blood volume
  - Half-life falls from ~ 24 hours to ~ 8 hours in pregnant women
  - Increased or split dosing (every 12 hours) may be needed to maintain effect

Buprenorphine Initiation

- Initiation:
  - Initiation may lead to withdrawal symptoms
  - Begin dosing when there are objective, observable signs of withdrawal
    - 6 – 12 hours after last short-acting opioid dose, 24 – 48 hours after last long-acting opioid
  - Hospitalization may be considered during initiation, especially during the 3rd trimester
  - If concern for fentanyl use (short-acting with a long half-life of 8 – 10 hours and high affinity for the mu opioid receptor), may wait until COWS score is 13 or higher (moderate withdrawal)

Buprenorphine Dosing

- Initiation dosing same as non-pregnant patient:
  - 2 – 4 mg, observe for signs of withdrawal, after 60 – 90 minutes without withdrawal symptoms, repeat dosing in increments of 2 – 8 mg
  - Repeat COWS during initiation to assess effect of buprenorphine dose
  - Determine dose needed to provide effects for 24 hours
- Buprenorphine dosing may not need to be adjusted in pregnancy
- Split dosing may be considered as pregnancy progresses to address afternoon/evening increase in craving
- Dosing adjustments post-partum are generally not required
- May continue buprenorphine post-partum without a need to switch to buprenorphine/naloxone if the patient prefers.

Naloxone in Pregnancy

- Naloxone should not be used to evaluate opioid use in pregnant women in a clinical setting
- May induce withdrawal that may precipitate preterm labor or fetal distress
- Naloxone SHOULD be used in the case of maternal overdose
- Naloxone SHOULD be provided to pregnant women and family/friends for emergency use

NOWS (Neonatal Opioid Withdrawal Syndrome)

- NOWS is a term that in gaining increased use in place of NAS (neonatal abstinence syndrome)
- There is a risk of NOWS when using opioid agonists for the treatment of OUD in pregnant women
- No evidence that methadone or buprenorphine have a higher risk of NOWS than use of illicit opioids
- The risk of untreated OUD to the mother and infant is much higher than the risk of NOWS
- Pregnant women should be encouraged to continue MAT while pregnant and post-partum to decrease the risk of setbacks.
- Stopping smoking can reduce the severity of NOWS

Indiana Medicaid Coverage

- Buprenorphine/naloxone and buprenorphine are covered by Indiana Medicaid for the treatment of OUD in pregnant women
- Recently, prior authorization has been relaxed for the use of buprenorphine without naloxone in post-partum women
- The preferred drug list for buprenorphine products will continue to prefer the tablet dosage form due to significant cost issues
- If a pregnant woman has been stabilized on the film dosage form, there should not be a requirement for the patient to try the tablet dosage form in order to have the film covered by Indiana Medicaid

References:

- Ecker J, Abuhamad A, Hill W, Bailit J, Bateman BT et al. Substance use disorders in pregnancy: clinical, ethical, and research imperatives of the opioid epidemic: a report of a joint workshop of the Society for Maternal-Fetal Medicine, American College of Obstetricians and Gynecologists, and American Society of Addiction Medicine. SMFM Special Report (smfm.org). March 2019.
- ACOG Committee Opinion. Committee on Obstetric Practice. American Society of Addiction Medicine. Number 711. August 2017.
- Substance Abuse and Mental Health Services Administration (SAMHSA). Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. HHS Publication No. (SMA) 18-5054. January 2018.
- Crotty K, Freedman KI, Kampman KM. Executive Summary of the Focused Update of the ASAM National Practice Guideline for the Treatment of Opioid Use Disorder. J Addict Med 2020;14:99-112.
- American Society of Addiction Medicine (ASAM) National Practice Guideline for the Treatment of Opioid Use Disorder. 2020 Focused Update. doi: 10.1097/ADM.0000000000000633.