

Pharmacological Treatment of Substance Use Disorders in The Perinatal Period

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Disclosures

I do not have any relevant financial relationship
with a commercial interest to disclose.

Objectives

- case
- barriers to care
- assessment and diagnostic work-up
- pharmacological treatment of SUDs in the perinatal period
 - General guidelines for pharmacology for SUD and other comorbid mental health disorders (dual diagnosis)
 - Opioid Use Disorder (OUD)
 - Alcohol Use Disorder (AUD)
 - Cocaine/Meth/Stimulant UD
 - Tobacco/Nicotine UD
 - Marijuana (Cannabinoid) UD
 - Prescribing controlled substances: Stimulants & Benzodiazepines
 - Medications for sleep and insomnia

Case:

- 23 year old female with history of **Hepatitis C** and **Borderline Personality Disorder**, chief complaint: Fatigue, anxiety and insomnia.
- 8 weeks pregnant, found out week 4 (G4P111)
- Discontinued all psych medications 4 weeks ago
- Smokes some marijuana at night to sleep
- ‘No illicit drugs’
- **Marijuana** is ‘prescribed’.
- Utox positive for **Buprenorphine and Fentanyl?** Yes.
- Qualitative and Quantitative measures: **negative for norbuprenorphine, extremely high levels of naloxone, buprenorphine, positive for fentanyl, cocaine, THC**
- **Medication list:** clonazepam 0.5 mg BID, quetiapine 100 mg qhs, escitalopram 10 mg qd, gabapentin 600 mg TID, lamotrigine 50 mg qd, clonidine 0.1 TID, buprenorphine/naloxone 8mg/2mg TID.



Low barrier perinatal psychiatric care for patients with substance use disorder: meeting patients across the perinatal continuum where they are

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ABSTRACT

Pregnant and postpartum patients with substance use disorders (SUD) often have other co-occurring mental health disorders. Complications of substance use and mental health conditions, such as overdose and suicide, are a significant contributor to maternal morbidity and mortality. For individuals dually diagnosed with SUD and other mental health disorders, the perinatal period can be both a motivating and a vulnerable period for care. Barriers to optimal care include, but are not limited to, lack of screening, lack of referrals for care, a limited number of psychiatric providers available to care for pregnant patients, and stigma around mental health and addiction care in pregnancy. In this review, we discuss approaches to low-barrier perinatal psychiatric care for women with SUD to promote engagement in care. We review (1) appropriate psychiatric assessment and diagnostic work-up; (2) treatment planning incorporating shared-decision making, non-punitive and culturally sensitive patient-centred care, and principles of harm reduction with a focus on psychopharmacology, and (3) the benefits of an integrated and collaborative multidisciplinary care model for this subpopulation of vulnerable patients.

ARTICLE HISTORY

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Barriers to Care

- **Stigma:** SUD and Other Mental Health Diagnoses
 - Over, under and misdiagnosis
- **Lack of**
 - Trauma informed care
 - Employing Harm Reduction
 - Patient centered care
 - Culturally sensitive care
 - Addressing disparities (racial, financial, sex & gender identity etc.)
 - Evidence based care
 - Insurance and/or access to care
 - Resources to further access other needed care, integrated care, collaborative care.
 - Sufficient or appropriate screening, assessment and planning >>> attrition, increased no-shows
 - **Need for Multitude of Specialties**
 - (e.g. obstetrics and gynecology, substance use disorders care, pediatrics, primary care, psychology or therapy, case management, recovery coaching and psychiatry)
 - Technology
 - **Education/ comfort for clinicians to treat including psychopharmacology**

Barriers to Care

- **Dual Diagnosis** in Perinatal Period:

- Complications of substance use and mental health conditions, including **relapse, overdose and suicide**, are a significant contributor to the rising maternal morbidity and mortality rate in the United States

(Faherty et al 2020, Mangla et al. 2019, Gemmill et al 2019)

- ~ delayed perinatal care
- ^^^antepartum hospitalizations
- Poor outcomes for the mother and fetus/infant

(Dworkin et al. 2017)

Barriers to Care

- Common mental health comorbidities
 - trauma and trauma related disorders
 - mood disorders
 - anxiety related disorders
 - attention deficit disorder

Assessment & Diagnosis

- Vulnerable Time
 - pregnancy, peripartum, postpartum
- Motivating Time
 - Motivation for change = basis of recovery

Assessment & Diagnosis

- Create a therapeutic relationship
 - Trauma informed care
 - Employing Harm Reduction
 - Patient centered care
 - Culturally sensitive care
 - Addressing disparities (racial, financial, sex & gender identity etc.)
 - Evidence based care
 - need to cultivate trust !
- Hx of Trauma = Projection of mistrust
- Lack of trust = loss to follow up

Assessment & Diagnosis

- Structured, yet flexible & negotiated care planning
- ‘meeting patients where they are’ :
 - Flexibility beyond boundaries expected in traditional psychiatry
 - Gradually organize patient as they advance in recovery, introduce and expect structure

Pharmacology for Tx of SUD

- **~45% of all pregnancies in the US are unplanned**
- Pick meds with well-studied reproductive safety profile
- If possible, make changes prior to pregnancy
(important for newly postpartum patients too, as they can get pregnant again !)
- Limit number of Rxs. to decrease exposure of infant
(maximize one med prior to adding a second)
- **>80% of pregnancies in SUD (OUD) are unplanned**
- **Discuss contraception & pregnancy planning**
(including for the newly postpartum)

(Finer et al 2016, Terplan et al 2015)

“New” Rule

The FDA published the “Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling, referred to as the:

“Pregnancy and Lactation Labeling Rule” (PLLR)



(i.e. No more letter categories – A, B, C, D and X)

(FDA.gov ,2014)



Treatment Strategies



Clinics in Perinatology
Volume 46, Issue 2, June 2019, Pages 215-234



Safety of Psychotropic Medications During Pregnancy

Edwin R. Raffi MD, MPH  , Ruta Nonacs MD, PhD, Lee S. Cohen MD

Medication Assisted Treatment (MAT) for treatment of Substance Use Disorders (SUD)

- patient's history of use and treatment
- patient's preference for treatment
- history of relapse
- need for closer monitoring.



Opioid Use Disorder (OUD)

Between 2018 and 2021, pregnancy-associated overdose mortality rates increased among all women in all age groups.

Among pregnant and postpartum women 35 to 44 years of age, the mortality rate more than tripled, increasing from 4.9 (95% CI, 3.0-8.0) per 100,000 mothers in January to June 2018 to 15.8 (95% CI, 12.3-20.4) in July to December 2021.

- This increase parallels the sharp increases in overdose deaths seen across US populations.
- Data from MA:
 - Between **2005 and 2014**, approximately **one in five pregnancy-associated deaths (20.6%)** were related to substance use.
 - Researchers observed an increasing trend in the proportion of substance use-related deaths over the study period, rising from 8.7% in 2005 to 41.4% in 2014.
 - **More than a third** (38.3%) of the deaths among women delivering a live birth between 2011 and 2015 were **fatal opioid-related overdoses**.

ACOG released recommendations regarding universal screening for opioid use disorders in women during the perinatal period

Han B, Compton WM, et al. JAMA Psychiatry. 2024



Medication Assisted Treatment (MAT): Options for Opioid Use Disorder (OUD)

- **Methadone**
 - full agonist, daily dosing
- **Buprenorphine products**
 - PO, IM
 - w/ or w/o naloxone
 - partial agonist/antagonist
- **Naltrexone (PO and IM)**
 - PO or IM
 - full blocker
- **Abstinence**



Medication Assisted Treatment (MAT):
Options for Opioid Use Disorder (OUD)

The Maternal Opioid Treatment: Human Experimental Research (MOTHER) project

eight-site, randomized, double-blind, double-
dummy, flexible-dosing, parallel-group clinical
trial **compared** treatment with **methadone** to that
of **buprenorphine**.



(Jones et al 2010)

Medication Assisted Treatment (MAT): Options for Opioid Use Disorder (OUD)

MOTHER project:

- **neonates treated with buprenorphine required...**
 - shorter hospital stays,
 - lower morphine requirements
 - average of 4.1 days of tx for NAS vs. 9.9 days for methadone ($p < 0.01$).



(Jones et al 2010)

Medication Assisted Treatment (MAT): Options for Opioid Use Disorder (OUD)

MOTHER project:

However, 33% of women on buprenorphine therapy stopped treatment as vs. 18% of the methadone group ($p=0.02$).

(Full agonists >>>less cravings)

Moreover, women in both groups had to present to a clinic daily
(vs. buprenorphine prescribed weekly+)



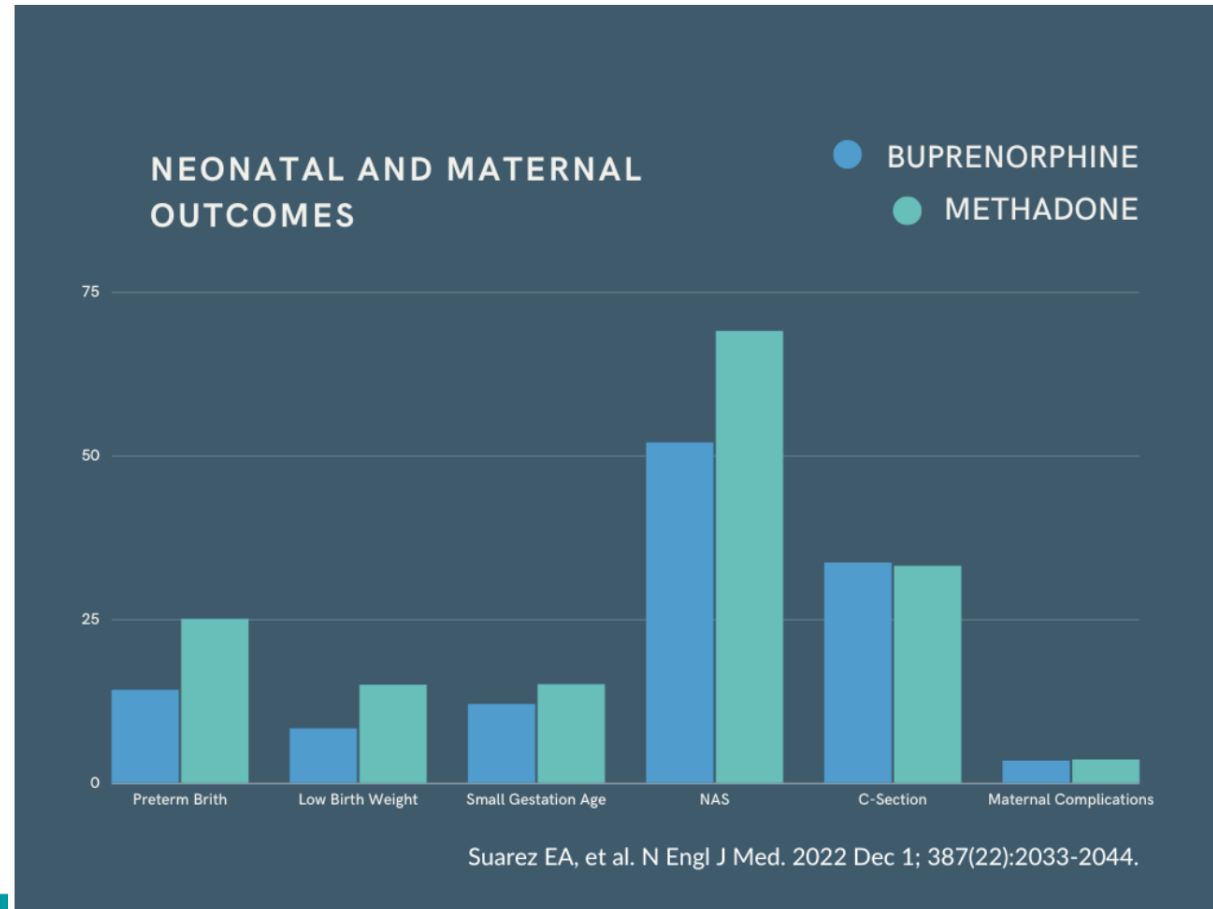
(Jones et al 2010)

Medication Assisted Treatment (MAT): Options for Opioid Use Disorder (OUD)

nationwide Medicaid
data, pregnancies from
2000 -2018.

2.5 million pregnancies
resulting in a live birth

In early pregnancy
10,704 were exposed to
buprenorphine and
4,387 to methadone; in
late pregnancy (week 20
or later), 11,272 and
5,056 were exposed,
respectively



Medication Assisted Treatment (MAT):
Options for Opioid Use Disorder (OUD)

- **Methadone vs. buprenorphine products**

- Deciding on inpatient vs. outpatient for initiation, induction or titration
- Consider risk of withdrawals / overdose / treatment compliance

(Debelak et al. 2013, Wiegand et al 2015)

Medication Assisted Treatment (MAT): Options for Opioid Use Disorder (OUD)

Medication assisted treatment (MAT) for substance use disorders (SUD)

- patient's history of use and treatment
- patient's preference for treatment
- history of relapse
- need for closer monitoring.



Medication Assisted Treatment (MAT): Options for Opioid Use Disorder (OUD)

- **Buprenorphine vs. Buprenorphine/Naloxone ? Can use either**
- **(actually the combo might be better!)**
 - Buprenorphine alone: higher potential for abuse or diversion
 - Buprenorphine/Naloxone: minimal risk of fetal exposure
 - Debelak et al 2013, Wiegand SL 2015
 - Ordean A et al 2023
 - Straub et al, 2024
- **Injectable buprenorphine :**
 - no formulation with enough reproductive data currently.
 - Trial of a long acting injectable [weekly (Brixadi with no NMP solvent) & monthly (eg. Sublocade with NMP solvent)] is ongoing

Important for patients with Opioid Use Disorder (OUD)

- **naloxone**

limited to cases of maternal overdose only in order to save the mother's life.



Medication Assisted Treatment (MAT): Option for Opioid and/or Alcohol Use Disorder

- **Naltrexone (PO or IM)**

- opioid antagonist: tx of OUD & Alcohol Use Disorder (AUD).
- short term PO and long term IM
- not first line tx during pregnancy, especially for initiation of care.

- **Not enough reproductive safety data....but**

- Consider risk of no treatment
- E.g. consider risk of relapse or overdose if you stop the medication, withdrawals if you start the medication



Medication Assisted Treatment (MAT): Options for Alcohol Use Disorder (AUD)

- **Not enough reproductive safety data....but may utilize (naltrexone and gabapentin) given risk stratification and severity of disease**
 - Naltrexone for AUD
 - Disulfiram (Antabuse) for AUD
 - Acamprosate for AUD
 - Gabapentin? for recent discontinuation of AUD

Anton et al 2020, Desrochers B 2024



Medication Assisted Treatment (MAT): Options for Tobacco Use Disorder

- **bupropion, varenicline, Nicotine Replacement Therapy (NRT) for smoking cessation.**
- no information regarding the reproductive safety of varenicline; generally not used in pregnancy.
- ACOG recommends caution on NRT as unclear about safety of nicotine during pregnancy
- data reassuring for use of bupropion in pregnancy (especially for multiple comorbidities E.g. depression, or off label use for ADHD)



Options for treatment of Cocaine/Stimulants/Meth Use Disorder in Pregnancy

- **cocaine/stimulant use disorder /meth**
- medications aimed at curbing cravings (e.g. topiramate, naltrexone, baclofen should likely be avoided during pregnancy)
- Data on mirtazapine (reproductive safety and treatment of stimulant use) approaching
- Screen and consider treatment of comorbid ADD?

Ostenfeld, Petersen et al 2022



Marijuana (Cannabinoid) Use Disorder

In Pregnancy

- ‘Prevalence of past-month cannabis use, daily/near daily cannabis use, and number of days of cannabis use, all increased among pregnant and nonpregnant women aged 12 to 44 years’

(Volkow 2019) National Survey of Drug Use and Health 2002-2014

- Associated with increased risk of preterm births

(Daniel et al 2019)

- Drop in IQ in adolescents?

- Animal studies show disruption in brain development

(Campolongo et al 2011)

- prenatal marijuana exposure is associated with decreased attention span and behavioral problems

- An independent predictor of marijuana use by age 14 years

(Fried PA et al. 2001, Day NL et al. 2006, Goldschmidt L et al 2000)

Marijuana (Cannabinoid) Use Disorder

In Pregnancy



ABCD study: prenatal cannabis use associated with

- behavioral issues
- lower birth weight
- lower brain volume and lower white matter volume

September 12, 2022

Association of Mental Health Burden With Prenatal Cannabis Exposure From Childhood to Early Adolescence

Longitudinal Findings From the Adolescent Brain Cognitive Development (ABCD) Study

David A. A. Baranger, PhD¹; Sarah E. Paul, MA¹; Sarah M. C. Colbert, BA²; [et al](#)

» [Author Affiliations](#)

JAMA Pediatr. 2022;176(12):1261-1265. doi:10.1001/jamapediatrics.2022.3191

 [Related Articles](#)

Dramatic increases in cannabis use during pregnancy are alarming because of evidence that prenatal exposure may be associated with a host of adverse outcomes.¹ We previously found that prenatal cannabis exposure (PCE) following maternal knowledge of pregnancy is associated with increased psychopathology during middle childhood using baseline data from the Adolescent Brain Cognitive Development (ABCD) study.² Here, leveraging longitudinal ABCD study data (data release 4.0), we examined whether associations with psychopathology persist into early adolescence.

Baranger et al. ABC, JAMA 2022
Volkow et al JAMA. 2019

Marijuana (Cannabinoid) Use Disorder

In Pregnancy

- Inquire about
 - Type of Cannabinoid (indica ? sativa?)
 - Method and amount of use (Smoke? Plant or Vape? Edibles? Gummies? Cookies?)
 - How it is obtained (dispensary, dealer, home-grown?)
- Discuss conflict with diagnostic work-up and treatment planning
 - Mood disorders, attention deficit disorder, anxiety disorder, etc.
- Discuss lack of data to want to prescribe in pregnancy or otherwise for MH disorders despite the name “medical” used in other settings:
 - dosing, types of MJ (indica, sativa, etc.), routes of taking it, medication-medication interactions, etc.
- Possibility of slowing down of fast dividing cells such as a fetus
- Inquire benefits from use (anxiety, insomnia, trauma related issues, appetite, nausea) : offer alternative evidence-based treatments

(Barbosa-Leiker, et al 2020)

Prescribing Controlled Substances:

The Art & Science of handling Rx of Stimulants & Benzodiazepines



- **stimulants, benzodiazepines & other controlled prescribed medications**
- If thinking of starting patients on these medications
 - discussion around alternative non-habit-forming medications, including reproductive safety data
 - providing the patient a chance to treat these disorders with non-habit-forming medications
 - E.g. 2nd generation antipsychotics for off label treatment of anxiety
 - E.g. atomoxetine for ADD --data re pregnancy emerging (Bröms G,et all 2023) , or bupropion for attention deficit disorder and/or comorbid smoking cessation and depression
 - During trial period with non-habit-forming medications patient-provider duo get to set treatment expectation and visit routines prior to starting other controlled substances, should it become necessary in the future
 - Get to set expectations
 - Monitor severity of illness

Prescribing Controlled Substances:

The Art & Science of handling Rx of Stimulants & Benzodiazepines



- **stimulants, benzodiazepines & other controlled prescribed medications**
 - Anxiety and attention related issues = comorbid or exist as a measure of symptoms of use or remission
- meet with patients regularly to discuss titrations and/or tapers as needed
- when prescribing controlled substances to patients in need of closer care:
 - shorter prescriptions
 - increase touch points with patients
 - prevent medication loss /diversion.
 - Check Prescribing Monitoring Program (PMP, state or federal) at every visit
- educate patients about the non-punitive nature of such an approach:
 - providing them more structure and touch-points with the provider
 - Offer them a way to manage their visits and their medications.
 - non punitive urine toxicology testing to help objectively measure improvement and also help you safely prescribe
 - Treatment planning /contracts/ agreements as way of providing education and setting boundaries and expectations

Prescribing Controlled Substances:

The Art & Science of handling Rx of Stimulants & Benzodiazepines



- **Stimulants, benzodiazepines & other controlled prescribed medications**
- Controlled substances can be utilized depending on the patient's pathology and the provider-patient relationship and agreement
- Discussion of risks, benefits, alternatives and risk of no treatment to the mother and the fetus, safe dosing strategies, etc.
- Outpatient tapering of controlled substances, when appropriate, should happen gradually and over time. Providers should recommend inpatient taper and detox when appropriate (eg. Severe and complicated AUD or benzodiazepine use disorder, hx of seizures, black outs, DTs).

Sleep

SUD /Trauma/Anxiety/Mood disorder/ADHD:
Where can you start?



Medications for Treatment of Insomnia in Pregnancy

- Diphenhydramine or doxylamine
- Very low dose TCAs (desipramine, nortriptyline, doxepin)
- Quetiapine, Olanzapine
- Low dose ?Benzodiazepines?
- Clonidine?, Prazosin ?
- Discontinue melatonin, trazodone, hydroxyzine
- Weigh risks, benefits, alternatives, including risk of no treatment with medications
 - e.g. prazosin vs. quetiapine and connection to possible relapse.
 - Consider patient's history
 - Negotiate care and patient preferences

Other Treatment Strategies:

- Biological (family history, medications, genetics, other physical ailments, etc.)
- Psychological (cogn. & behav. routines, coping mech., etc.)
- Social-Environmental (spouse, children, dog, car, finances, etc.)

Other Treatment Strategies: Psychological Treatment

Massachusetts General Hospital
Founding Member, Mass General Brigham
Psychiatry Academy

- Seeking Safety (non-exposure-based)
 - Dialectical Behavioral Therapy (none-exposure based)
 - Cognitive Behavioral Therapy (none-exposure based)
 - **Motivational Interviewing (none-exposure based)**
-
- Prolonged Exposure Therapy (exposure-based)
 - Cognitive Processing Therapy (exposure-based)
 - Eye Movement Desens. & Reprocessing (exposure-based)



Other Treatment Strategies:
Social / Environmental Factors

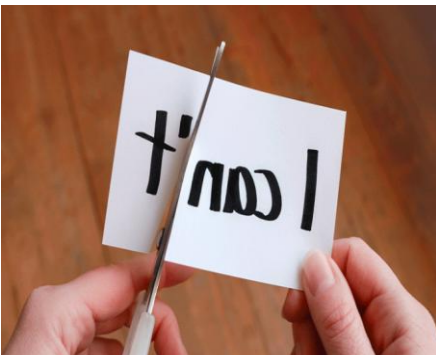


- Finances
- Housing
- Food
- Transportation
- Ongoing/ past trauma
- Access to pharmacy
- Access to phone
- Legal Issues
- Education
- Ability to maneuver the healthcare system
- Health Insurance
- Child and Family Services
- Relationship/Partner
- Partner's SUD
- Military Connection

& collaborative and/or integrated care to the extent possible

- need for multitude of specialties

(e.g. Ob Gyn, SUDs care, pediatrics, primary care, psychology or therapy, case management, recovery coaching and psychiatry)



Case

- 23 year old female with history of **Hepatitis C** and **Borderline Personality Disorder**, chief complaint: Fatigue, anxiety and insomnia.
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The End.



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