Medical Management of Alcohol Use Disorder in Pregnancy and the Peripartum Period

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Disclosure Information

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Workshop Learning Objectives

- Review the epidemiology of alcohol use during pregnancy.
- Identify maternal and fetal complications of perinatal alcohol use disorder.
- Apply evidence-based strategies for managing acute alcohol withdrawal in pregnancy.
- Evaluate the safety and efficacy of medications for alcohol use disorder (MAUD) during pregnancy, considering potential fetal risks and maternal/fetal benefits.
- Explore the ethical considerations of clinical decision-making for pregnant individuals with AUD, including the implications of forgoing MAUD.
- Identify barriers to care and strategies to improve access to treatment for this population.

Principles of Prescribing in Pregnancy

- Accepting limitations: on available data, definitive answers, known outcomes
- Risk-risk analyses
- Shared decision making
- Harm reduction
- Dose adjustments

Lack of Data in Pregnant Populations

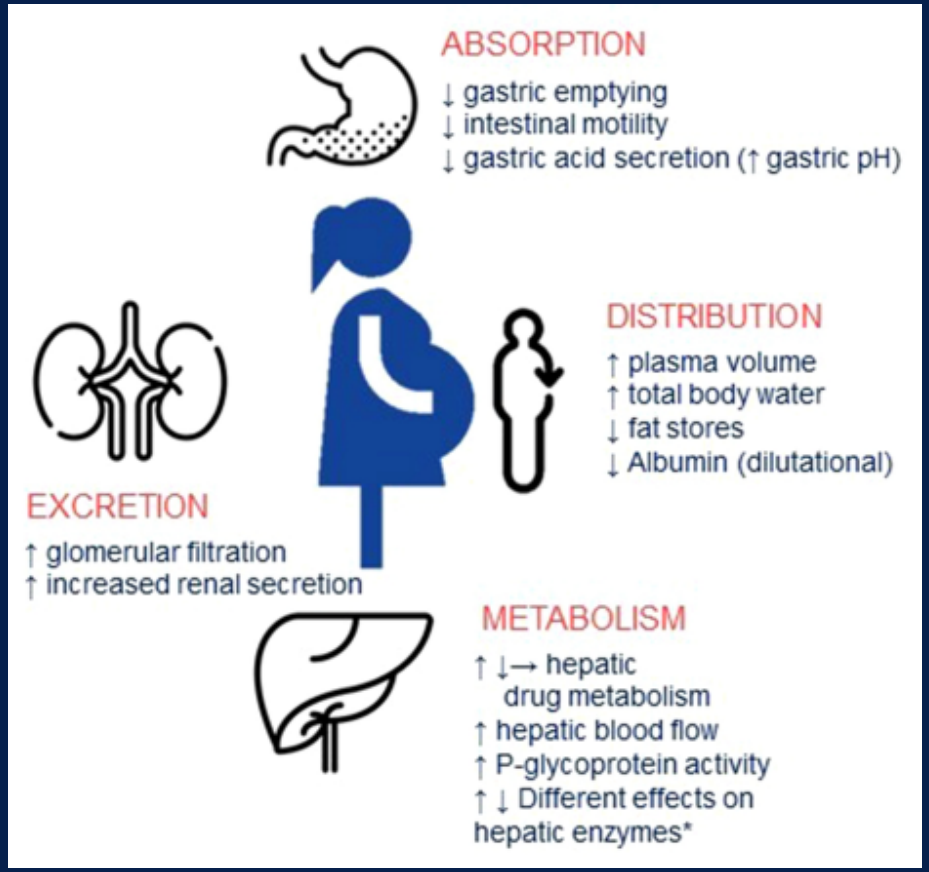
- 2009 Cochrane review of ~800 citations found NO RCTs evaluating the effectiveness of pharmacotherapy to improve maternal, birth, or infant outcomes in pregnancy
- 2014 WHO review also did not identify RCTs - only observation studies and retrospective data
- Ethical limitations in randomization of treatments of unknown risks when considering maternal and fetal health
- Biological changes during pregnancy can complicate trial design and data interpretation
- Without comparison to a control group, difficult to determine outcome differences to medication
  - ex. Is congenital malformation due to naltrexone versus alcohol exposure?

Smith and Terplan 2009

Counseling in Pregnancy

- Considerations in pregnancy can be more complicated

- Physiologic changes
  - Hormone changes affecting physical and emotional symptoms
  - Increased volume of distribution
  - Increased enzyme efficacy --> faster metabolism
  - Changes in protein binding affect medication and drug distribution



Hesse 2023

Counseling in Pregnancy, Continued

- Many recommendations have weak support, so definitive recommendations may not be available
- Different patients may weigh values differently, so individual tailoring is often necessary

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"Risk-Risk" Discussion

- Risk-benefit discussion is typical in medication prescription, in which the pros and cons of a medication are weighed before deciding to prescribe
- Risk-risk discussion is often more helpful
  - Medications carry risks
  - Not treating with medication carries risks
- Particularly helpful in pregnancy where the risks of untreated or undertreated substance use can have serious consequences

Image generated using ChatGPT

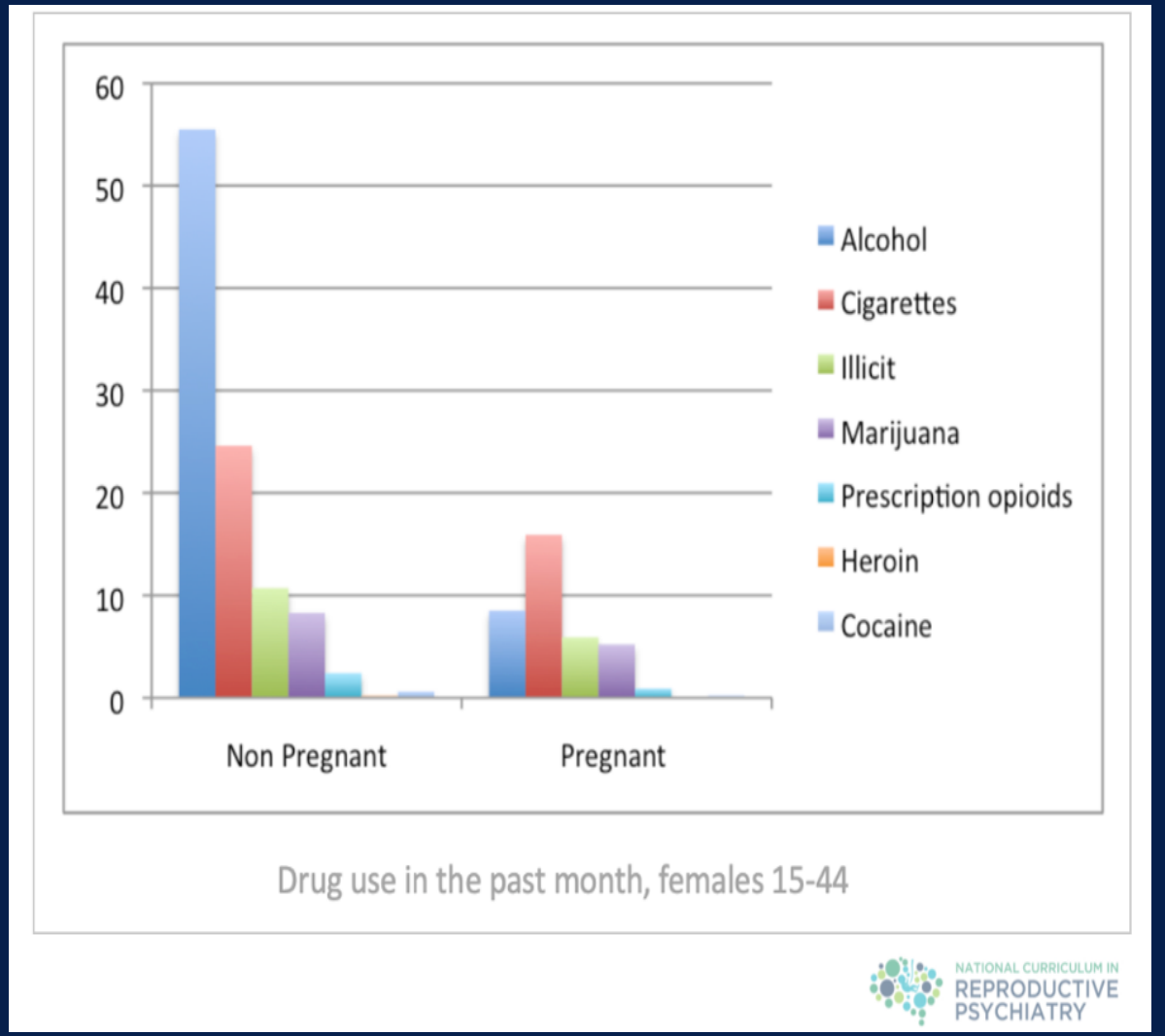
Prevalence of Alcohol Use in Pregnancy

- From 2011 to 2018, alcohol use among pregnant adults **increased** from 9.2% to 11.3%
- In 2020, **13.2%** of pregnant adults reported current alcohol use, with 5.2% engaging in binge drinking within the last 30 days
- Pregnant adults with frequent mental distress have 2x the prevalence of any drinking and 3x the prevalence of binge drinking compared to those without such distress
- Likely underreported due to stigma, fear of repercussions, and the desire to be perceived as a “good” parent

Denny et al. 2020, Gosdin et al. 2022, Frazer et al. 2019, Gunnarsson et al. 2013

A Time to Intervene

- Pregnancy is a unique motivator for individuals to adopt healthier lifestyles
- The perinatal period usually involves increased interactions and follow up with medical providers



NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

Fergie et al. 2019

Treatment Gaps

Table 1 Guidelines for the pharmacological treatment of pregnant women with an alcohol use disorder

Group	Recommendations
The American Psychiatric Association [64]	"APA recommends that for pregnant or breastfeeding women with alcohol use disorder, pharmacological treatments not be used unless treating acute alcohol withdrawal with benzodiazepines or unless a co-occurring disorder exists that warrants pharmacological treatment" "For individuals who become pregnant while taking a medication to treat AUD, the risk of continuing or stopping pharmacological treatment should be individualised to the patient and discussed with the patient, her obstetrician, and, if applicable, her partner. Potential risk to the fetus from medication should be balanced against the risk of relapse to alcohol use, which itself carries teratogenic risk"
British Association for Psychopharmacology [9]	"Pregnant women with symptomatic withdrawal should be offered medical cover for their detoxification, ideally as an inpatient" "Starting relapse prevention medication should be avoided, although if already successfully established on relapse prevention medication, patients' needs should be assessed on a case-by-case analysis"

Kelty et al. 2021

Treatment Gaps

The French Alcohol Society in partnership with the European Federation of Addiction Societies [16]	"No treatments other than those for alcohol withdrawal should be initiated in pregnant or breastfeeding women "In the event of a pregnancy occurring in a patient obviously stabilised by a medication for supporting abstinence, the continuation of the drug should be considered on a case by-case basis, weighing up the benefit/risk ratio" "Disulfiram is an exception, and it should be always stopped during pregnancy, to the unknown risks on the fetus of the Antabuse [disulfiram] effect"
International Task Force of the World Federation of Societies of Biological Psychiatry and the International Association for Women's Mental Health [10]	"If medically assisted withdrawal is necessary, benzodiazepines may be used at the lowest dose for the shortest duration" "Due to the low level of evidence or to their low benefit/risk ratio, pharmacological treatment for maintenance of abstinence should not be used during pregnancy"
World Health Organization [72]	"Pregnant women who develop withdrawal symptoms following the cessation of alcohol consumption should be managed with the short-term use of a long-acting benzodiazepine" "Given that the safety and efficacy of medications for the treatment of alcohol dependence has not been established in pregnancy, an individual risk benefit analysis should be conducted for each woman"

Kelty et al. 2021

Alcohol as an Abortifacient

- EtOH exposure during pregnancy is associated with greater risk of miscarriage, compared to no exposure
  - Meta-analysis of data from >200,000 pregnant individuals suggests odds ratio 1.19

- For EtOH use of ≤5 drinks/week, each additional drink/week was associated with a 6% increase in miscarriage risk

- Each additional week of EtOH exposure during the 1st trimester increases risk of spontaneous abortion, even at low levels of consumption

Sundermann et al. 2019, 2021

Consequences of Alcohol Use in Pregnancy

- **Fetal and Delivery Complications:**
  - Highest teratogenic risk is with >4 drinks/day but assume no safe level
  - Miscarriage, stillbirth, intrauterine growth restriction, neonatal abstinence syndrome (not just with opioids!), preterm labor
- **Pediatric Complications:**
  - Fetal Alcohol Spectrum Disorders (FASD) - leading cause of preventable disability in U.S.
  - Neurodevelopmental disorders, behavioral dysregulation throughout life, sudden infant death syndrome (SIDS)
- **Maternal Complications:**
  - Hepatic/pancreatic toxicity, carcinogenic, falls, cognitive decline, mood + anxiety disorders, life-threatening withdrawal
- Other:
  - Behavioral risks – ex. driving while intoxicated
  - Risk of removal of child from parental custody (state-dependent laws)

Sundermann et al. 2019; Denny, Coles, and Blitz 2017; Smid and Terplan 2022; Bay and Sokol 2011; Popova et al. 2023

Treatment Centers

Treatment Settings for Substance Use Disorders		
Level of Care	**Services Offered**	**Additional Notes/Perinatal Options**
Outpatient	Counseling	• Individual or group • Facilitated by social workers or mental health/drug and alcohol counselors
	Medication management	• Methadone needs to be administered by a federally licensed facility. • Buprenorphine can only be prescribed by a waivered provider. • Naltrexone, acamprosate, disulfiram, or medications for smoking cessation can be prescribed by any provider *(see SUD4, SUD5)*.
Intensive Outpatient	Group and Individual Counseling +/- medication	• Can be used for direct admission or as a step-down from a higher level of care • Can vary in length and frequency of sessions • Examples include: Intensive Outpatient program (IOP), Structured Outpatient Addiction Program (SOAP), and Partial Hospital Program (PHP)
Acute Treatment Services (a.k.a. "Detox")	Medically Supervised Withdrawal (Inpatient)	• Indicated for physiological dependence on alcohol or benzodiazepines • Difficult to access during pregnancy • Tapering opioids is not recommended during pregnancy.
Short-Term Residential (under 30 days)	Step-down and non-pharmacologic "detox"	• Examples include Clinical Stabilization Services (CSS) and Transitional support Services (TSS) or "holding." • Some treat co-morbid psychiatric and substance use disorder (dual-diagnosis) and include: Individual, group, family therapy, case management, and linkage to aftercare, and medication. • Some programs admit pregnant women and coordinate with prenatal care providers.
Long-term Residential (over 30 days)	Structured group living with supervision and treatment provided by addiction professionals	• Examples include 4-6 month recovery homes or "halfway houses" and specialized residential programs for women, families, and youth. • Many programs assist with employment, parenting skills, and retaining/regaining custody of children. • Some have enhanced services for pregnant/post-partum women and their infants, which include the coordination of perinatal/pediatric care. • Individual, group therapy, case management
Involuntary Commitment/ Section 35 (up to 90 days)	Court-ordered treatment for medically supervised withdrawal and step-down services	• Family/providers can petition the local court with evidence that the patient is a danger to self/others due to substance use. • The patient is brought before the judge, who decides if commitment is warranted.

BARRIER:
MANY programs have exclusion criteria for pregnant people or do not cater to people caring for children

Mittal et al 2019

Acute Withdrawal Management

- Limited literature for alcohol withdrawal management in pregnancy

- **Pregnant patient experiencing withdrawal should consider hospitalization**
  - even when at low or medium risk of complicated withdrawal
    - particularly if CIWA > 10
  - Different from non-pregnant populations!
  - Considered a "community standard," although not necessarily evidence-based

- Consult obstetrician/maternal fetal medicine and addiction medicine
- Inform patient of risks of alcohol use and benefits of treatment
- Benzodiazepines >> barbiturates are preferred; valproate contraindicated
  - Special consideration for third trimester: short term benzo preferred and dose adjustments to limit fetal exposure

ASAM – Clinical practice guideline on alcohol withdrawal management, 2020

Risks of Alcohol Withdrawal

- Limited data; reports include:
  - 37.5% had loss of conception; low birth weight, length and head circumference
    - 4/5 neonates with complication, 1 required NICU admission, 1 had respiratory distress and required intubation; 1 neonatal abstinence syndrome and another with respiratory distress syndrome 2/2 meconium aspiration
  - Developmental problems
    - Speech delay, seizure disorder, autism spectrum disorder
  - ICU admissions
    - Median duration 45 hours
  - Seizures
    - Fetal mortality increases for 10% for every minute of maternal seizure activity
- Limitations: overlap of findings from withdrawal + withdrawal management

ASAM – Clinical practice guideline on alcohol withdrawal management, 2020; Daidone et al 2024

Risks of Alcohol Withdrawal

- Uncomplicated alcohol withdrawal: dysautonomia, anxiety, insomnia
- Complicated alcohol withdrawal:
  - Hallucinosis
  - Seizures
  - Delirium Tremens
- Risks in pregnancy related to the known symptoms of alcohol withdrawal favor treatment

ASAM – Clinical practice guideline on alcohol withdrawal management, 2020; Daidone et al 2024

Risk of Withdrawal Medications to Fetus

- Mixed evidence of risk from benzodiazepine use
  - Neonatal benzodiazepine intoxication/withdrawal
  - Teratogenicity – mixed evidence
  - Floppy baby syndrome - hypotonia, hypothermia, lethargy, respiratory difficulties, and sucking difficulties

- Fetal monitoring appropriate to the stage of pregnancy may be warranted due to risk of abruption, preterm delivery, and fetal distress or demise

ASAM – Clinical practice guideline on alcohol withdrawal management, 2020; Daidone et al 2024

Lorazepam

MOA: binds to benzodiazepine receptors on postsynaptic GABA-A neurons at multiple sites within the central nervous system (CNS) --> enhancing the effect of GABA

Dosing: variable; 2 mg q4-6h with CIWA triggered PRN vs loading dose

Contraindications: acute angle closure glaucoma

Efficacy: moderate with moderate quality of evidence vs placebo, high quality of evidence vs antipsychotics; most effective agent for prevention of seizures and delirium tremens (Amato et al. 2011)

* off label use

Lorazepam

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category D - some evidence of human fetal risk, but potential benefits may warrant use 1st trimester: evidence is mixed, case-control studies suggest teratogenicity but no risk in cohort studies 3rd trimester: floppy baby syndrome (Bhat et al 2015)	Mixed evidence- some studies have shown increased risk of preterm delivery and decreased birth weight; other studies have yet to find this association May have withdrawal symptoms but self-limited and resolve with time	Excreted in breast milk; low levels found in infant serum, one of the safest (along with oxazepam and temazepam) *(LactMed)*
1st line for alcohol withdrawal		

* off label use

Phenobarbital

MOA: binds to GABA-A receptor subunits --> increasing duration chloride channels are open --> depressing the central nervous system

Dosing: 260 mg IV followed by 130-mg doses every 15–30 minutes PRN up to 15 mg/kg of ideal body weight

Contraindications: latent porphyria, liver failure, nephritic syndrome

Efficacy: similar efficacy to benzodiazepines but with increase risk of respiratory depression (Martin et al. 2017)

* off label use

Phenobarbital – stat pearls from NCBI

Phenobarbital

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category D - reported to cause fetal damage; higher than expected incidence of fetal abnormalities in mother's who were administered phenobarbital	Limited data on impact If used in 3rd trimester need to monitor for withdrawal symptoms	Excretion is highly variable and dependent on other medications (e.g. other antiepileptics) Can contribute to sedation, poor sucking *(LactMed)*
Recommendation: Second line for alcohol withdrawal; counsel on risks to fetus		

* off label use

Acute Withdrawal Management

- Standard protocol recommended by ASAM
  - Clinical institute withdrawal assessment alcohol (CIWA) monitoring

TABLE 1. Alcohol Withdrawal Severity.

Severity Category	Associated CIWA-Ar Range*	Symptom Description
Mild	CIWA-Ar < 10	Mild or moderate anxiety, sweating and insomnia, but no tremor
Moderate	CIWA-Ar 10-18	Moderate anxiety, sweating, insomnia, and mild tremor
Severe	CIWA-Ar ≥19	Severe anxiety and moderate to severe tremor, but not confusion, hallucinations, or seizure
Complicated	CIWA-Ar ≥19	Seizure or signs and symptoms indicative of delirium – such as an inability to fully comprehend instructions, clouding of the sensorium or confusion – or new onset of hallucinations

ASAM – Clinical practice guideline on alcohol withdrawal management, 2020

Acute Withdrawal Management – Risk Stratification

- PAWSS > 4
  - Elevated risk for complicated withdrawal
  - "Front loading" recommended
    - Loading with benzodiazepine (e.g. lorazepam 1-2mg or diazepam 10-20 mg IV q 10-15 minutes until patient calm); if symptoms not controlled can consider switch to phenobarbital + continued monitoring with CIWA q4h for breakthrough

- PAWSS < 4
  - Lower risk for complicated withdrawal
  - Symptom triggered withdrawal (e.g. CIWA); optimize non-benzodiazepine medications (gabapentin, clonidine)

ASAM – Clinical practice guideline on alcohol withdrawal management, 2020

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al., 2014

Part A: Threshold criteria: **(1 point each)**

1. Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days? OR did the patient have a "+" BAL upon admission? _____

IF the answer to either is YES, proceed with test:

Part B: Based on patient interview: **(1 point each)**

2. Have you ever experienced previous episodes of alcohol withdrawal? _____
3. Have you ever experienced alcohol withdrawal seizures? _____
4. Have you ever experienced delirium tremens or DTs? _____
5. Have you ever undergone of alcohol rehabilitation treatment? (i.e., in-patient or out-patient treatment programs or AA attendance) _____
6. Have you ever experienced blackouts? _____
7. Have you combined alcohol with other "downers" like benzodiazepines or barbiturates during the last 90 days? _____
8. Have you combined alcohol with any other substance of abuse during the last 90 days? _____

Part C: Based on clinical evidence: **(1 point each)**

9. Was the patient's blood alcohol level (BAL) on presentation > 200? _____
10. Is there evidence of increased autonomic activity? (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea) _____

Total Score: _____

- PAWSS > 4
  - Elevated risk for complicated withdrawal
  - "Front loading" recommended
- PAWSS < 4
  - Lower risk for complicated withdrawal
  - Symptom triggered withdrawal (e.g. CIWA)

Acute Withdrawal Management

- Limited literature for alcohol withdrawal management in pregnancy
- Standard protocol recommended by ASAM
  - Clinical institute withdrawal assessment alcohol (CIWA) monitoring
  - Risk stratification
  - Monitoring for extended duration

ASAM – Clinical practice guideline on alcohol withdrawal management, 2020

Case Presentation #1

28-year-old G2P1 woman at 28 weeks gestation with history of alcohol use disorder, anxiety presents to ED with complaints of tremors, restlessness, nausea. She reported using 6–8 standard drinks daily until three days prior when she decided to stop drinking due to concerns for her baby. Symptoms began 12 hours after cessation and progressively worsened. BAL < 10, UDS negative.

She has a history of uncomplicated withdrawal, blackouts; denies struggling with use of other substances and doesn't combine alcohol with other substances. No previous substance rehab treatment.

Case presentation written with assistance of chat GPT

Case Presentation #1

Physical Examination

- General Appearance: Anxious, restless, diaphoretic.
- Vital Signs: BP 142/88 mmHg, HR 108 bpm, RR 20/min, Temp 37.5°C, SpO2 98% on room air.
- Neurological: Coarse tremors in both hands, hyperreflexia, no nystagmus, no signs of focal neurological deficits.
- Abdominal Exam: Non-tender, gravid uterus consistent with 28 weeks gestation. Normal fetal heart rate (FHR) at 145 bpm.

Next steps in management?

Audience participation – placeholder slide

What else do you want to know?

Audience participation – placeholder slide

Case Presentation #1

- Risk stratification:
  - CIWA 24 (severe withdrawal)
  - PAWSS 4 (moderate to severe risk of complicated withdrawal)
- Admit to high dependency monitor unit, consider ICU admission
- Vital signs, mental status, and CIWA scores assessed hourly
- Continuous fetal heart monitoring to detect any distress
- Informed her of risks of medication to fetus
  - Lorazepam 2 mg IV q2hr CIWA >10; monitor every 1-4 hours for the first 24 hours and titrate to control for agitation vs. loading with diazepam + CIWA triggered diazepam q4h
- Give IV fluids (0.9 %NaCl), replenish electrolytes (K+ and Mg2+), and IV thiamine and folate

Case Presentation #1

Management considerations

- Obstetrics consult
  - No indication for further management at this time due to reassuring ultrasound
- Continue to observe patient
  - When CIWA < 10, can space out monitoring to 4-8 hours for 24 hours, or as clinically indicated
- Consult perinatal social worker support
  - Partner enrolled in counseling sessions to promote supportive home environment
  - Patient enrolled in pregnancy focused AUD program

Case Presentation #1

- Hospital course
  - Received an additional 6 mg of lorazepam and after 24 hours symptom improved
  - Transitioned to oral lorazepam q4h PRN for CIWA >10 and received total 4 mg in 24 hours; she was then transitioned to gabapentin 1200 mg TID and decreased to 900 mg TID. She was started on guanfacine 2 mg BID. She met criteria for generalized anxiety disorder and found gabapentin and guanfacine to be helpful for this. She was discharged home on day #4 and provided with referral for psychiatry and for therapy.

- Two week follow up
  - Continued to maintain sobriety and attending AA meetings weekly
  - Discussed medications for AUD in pregnancy
  - Established care with psychiatrist and has started individual psychotherapy and considering couple's therapy

What are your biggest concerns as a provider?

Audience participation – placeholder slide

Case Presentation #1 – Key Takeaways

- Monitor vital signs frequently (of both mother and fetus); supportive care including IV fluids and multivitamins (thiamine and folate)
- Benzodiazepines 1st line; phenobarbital second line if contraindication to benzos
  - Must counsel patient on risks of use to fetus
- CIWA to monitor for alcohol withdrawal symptoms with risk stratification to determine management of alcohol withdrawal
  - If PAWS > 4, would recommend front loading
- Beyond acute management
  - Should be linked with SW and case management for additional social support
  - Discuss AA meetings and other programming to help support sobriety
  - Medication management of alcohol use disorder

Maintenance Medications for AUD

- FDA approved:
  - Naltrexone (oral or long acting injectable)
  - Acamprosate
  - Disulfiram
- Other agents with efficacy:
  - Gabapentin*
  - Topiramate*
  - Baclofen*
- Emerging treatments:
  - Prazosin*
  - Ondansetron*

* indicates off-label use

Medications for AUD

- Medications for Alcohol Use Disorder (MAUD) are frequently underutilized
- MAUD are generally safe, effective, and efficacious, and should be considered for patients with AUD and at-risk drinking

Weighing the options for MAUD

- Claim #1: alcohol use in pregnancy, and alcohol use disorder especially, poses health and safety risks to both patient and fetus/baby
- Claim #2: medications for alcohol use disorder are available and underutilized for the treatment of AUD
- Corollary: medications for alcohol use disorder should be considered in pregnancy despite a lack of data

Naltrexone

MOA: opioid antagonist

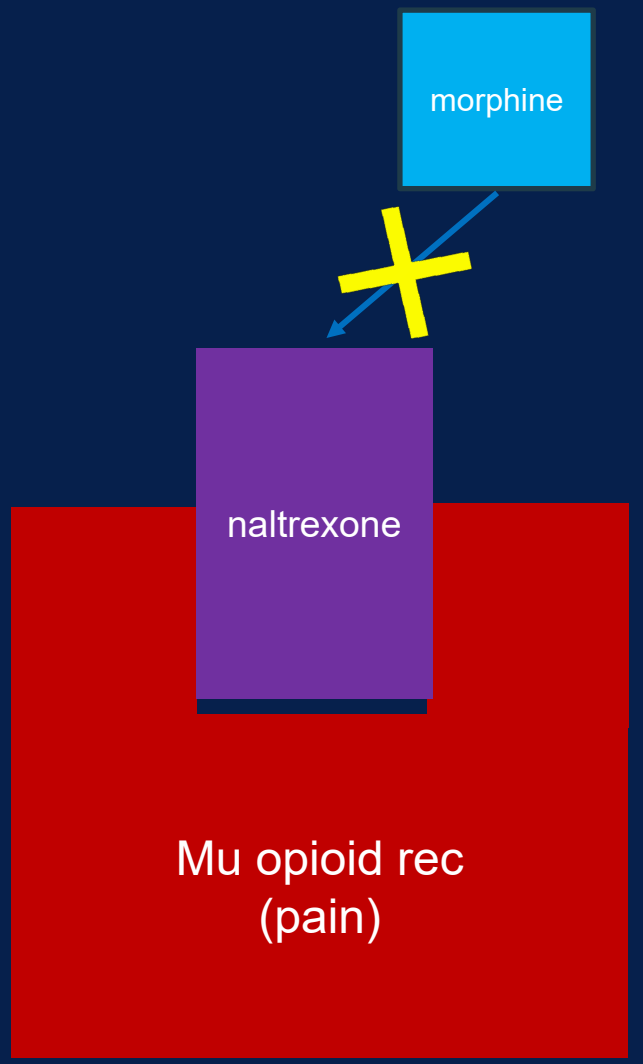
Dosing: 50mg PO daily or 380mg IM q4wk

Contraindications: acute liver failure; concurrent opioid use

Efficacy: **high** relative efficacy (strength of evidence is moderate); most helpful for individuals w/ binge-pattern of use; NNT = 11 for return to heavy drinking, 16 for return to any drinking (McPheeters et al. 2023)

Naltrexone

- May complicate post-operative pain management
  - Discuss stopping at ~36 weeks
- For elective C-section, may need to do washout period then restart 3-7 days after opioid abstinence
- If on long acting injectable, may need to transition to oral formulation in later stages of pregnancy in anticipation of delivery or procedures



Akbar et al. 2018

Context of Opioid Use Disorder

Home > Drugs > Article

A Retrospective Cohort Study of Obstetric Outcomes in Opioid-Dependent Women Treated with Implant Naltrexone, Oral Methadone or Sublingual Buprenorphine, and Non-Dependent Controls

Original Research Article | Published: 23 May 2017

Volume 77, pages 1199–1210, (2017) Cite this article

ORIGINAL RESEARCH | OBSTETRICS · Volume 222, Issue 1, P83.E1-83.E8, January 2020 Download Full Issue

Use of naltrexone in treating opioid use disorder in pregnancy

Craig V. Towers, MD · Emily Katz, CPRS · Beth Weitz, WHNP · Kevin Visconti, MD

Naltrexone

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category C - potential teratogenic effects in animals but very limited human data Appears to be well-tolerated at typical doses *(Center for Substance Abuse Treatment)* Abortive effects in animal studies at 5-18x the MHRD *(MIMS Online 2020, Kelty 2021)*	May complicate post-operative pain management *(Akbar et al. 2018)*	Minimally excreted into breast-milk; considered to be safe *(LactMed, Harris 2023, Raffi 2019)*
Recommendation: first-line therapy for pregnant populations, benefit likely outweighs the risk		

Acamprosate

MOA: GABA analog and NMDA receptor modulator

Dosing: 666mg po TID

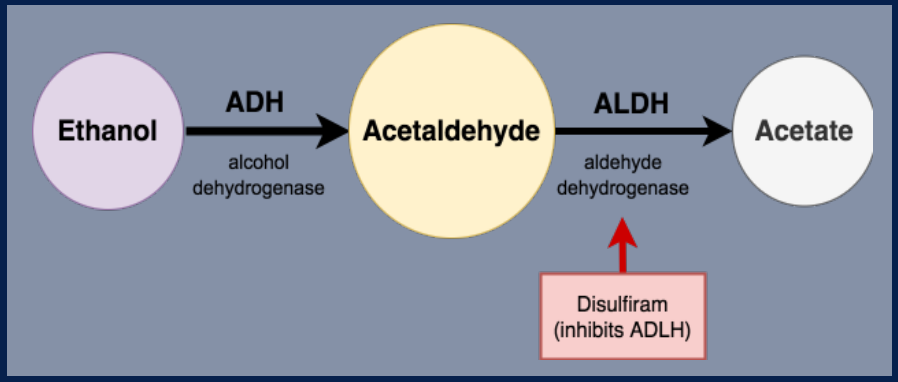
Contraindications: renal failure

Efficacy: **high** relative efficacy (strength of evidence is moderate); most helpful in setting of abstinence; NNT = 11 for return to any drinking (McPheeters et al. 2023)

Acamprosate

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category C - potential teratogenic effects in animals but very limited human data Possible hydronephrosis, malformation of subclavian artery and eyes in rats and rabbits but not reproducible *(Forest Pharmaceuticals 2012)* 2019 human study without clear link to negative outcomes (N=54) *(Kelty 2019)*	Limited data available, but no significant complications reported	Unknown excretion; low risk expected due to low oral bioavailability; some diarrhea reported *(LactMed)*
Recommendation: second-line therapy for pregnant populations, benefit likely outweighs the risk		

Disulfiram



MOA: irreversibly inhibits acetaldehyde dehydrogenase, causing buildup of acetaldehyde and unpleasant symptoms when alcohol is consumed

Dosing: 125 to 500mg daily

Contraindications: liver failure, ongoing alcohol use

Efficacy: limited to high-supervision settings; must have good adherence and complete abstinence; strength of evidence is low (McPheeters et al. 2023)

Image from PsychDB

Disulfiram

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category C - potential embryocidal effects in animals *(Salgo and Oster, 1974)* but very limited human data Risk of **cardiovascular collapse** with alcohol use *(Lanz 2023)* May amplify the teratogenic effects of alcohol mediated by acetaldehyde if ongoing use *(Lee 2005)* On its own, not well-established as a teratogen; data is limited to small case studies (N=38) *(Briggs 2011)*	Limited data available, but no significant complications reported	Drug labeling by the manufacturer recommends against breastfeeding while taking this medication Based on molecular structure, likely is excreted into breast milk No major adverse events recorded *(LactMed)*

Recommendation: **AVOID in pregnancy** due to high-risk side effects with return to use

Gabapentin*

MOA: modulates GABA and glutamate activity; reduces CNS hyperexcitability

Dosing: 300-3600 mg/day, divided into TID

Contraindications: acute renal failure

Efficacy: moderate relative efficacy (strength of evidence is low); most helpful in patients with concurrent anxiety, insomnia, withdrawal (McPheeters et al. 2023)

* off label use

Gabapentin*

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category C - possible association with defects although human data is limited Chronic exposure in 1st, 3rd trimesters may be associated with slight increase in cardiac defects and decreased birth weight, respectively *(Patorno 2020)* All AEDs have potential to affect folate metabolism and result in neural tube defects	Limited data on impact, but potential risk of preterm birth *(Patorno 2020)* If concurrently on buprenorphine for opioid use disorder, may increase risk of complex / prolonged NOWS	Excreted in breast milk; low levels found in infant serum, considered safe *(LactMed)*
Recommendation: third-line; supplement with high dose folic acid		

* off label use

Topiramate*

MOA: modulates GABA and glutamate activity; reduces CNS hyperexcitability

Dosing: 25-300mg daily

Contraindications: nephrolithiasis

Efficacy: moderate relative efficacy (strength of evidence is moderate); increasing frequency of use in the VA system (McPheeters et al. 2023)

* off label use

Topiramate*

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category D – positive evidence of human fetal risk Dose-dependent risk of cleft lip / palate in 1st trimester • ≤100 mg daily RR 1.64 (95% CI 0.53–5.07) • >100 mg daily RR 5.16 (95% CI 1.94–13.73) *(Hernandez-Diaz et al. 2018)* IUGR, neural tube defects *(Hernandez-Diaz et al. 2014, North American Antiepileptic Drug Pregnancy Registry)*	Limited data available, but no significant complications reported	Low levels in infant serum; generally well-tolerated with mild, self-limited effects (diarrhea, sedation) *(LactMed)*

Recommendation: fourth-line (third-line if past organogenesis); supplement w/ high dose folic acid

* off label use

Baclofen *

MOA: GABA(B) receptor agonist; reduces CNS hyperexcitability and alcohol cravings

Dosing: 15-80 mg/day

Contraindications: renal failure

Efficacy: moderate relative efficacy (strength of evidence is low); most helpful in highly dependent individuals (McPheeters et al. 2023)

* off label use

Baclofen *

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category C – possible teratogenic effects in animals but limited human data; considering route of admin in studies is vital as oral vs intra-thecal administration result in different levels of fetal exposure Animal studies are mixed but neural tube defects *(Briner 1995)*, omphalocele *(Saol Therapeutics 2019)* have been observed	Limited data available, late onset infant withdrawal possible *(Ratnayaka 2001, Duncan 2013, Freeman 2016)*	Some animal studies suggested baclofen inhibits prolactin release which could interfere with milk production (Lux 1986) Relative infant dose <5% *(Eriksson 1981, Lin 2014)*; there is no evidence of infant toxicity Withdrawal is possible with abrupt discontinuation
Recommendation: fourth-line; supplement with high dose folic acid		

* off label use

Ondansetron*

MOA: Serotonin 5-HT3 receptor antagonist; reduces alcohol-stimulated dopamine release

Dosing: 4 mcg/kg twice per day

Contraindications: congenital long QT syndrome

Efficacy: most helpful for populations with early onset AUD (<25 years old) (Bankole 2000) and with LL 5'HTTLPR genotype (Kenna 2014); most effective in combination with naltrexone

* off label use

Ondansetron*

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category B – preclinical trials do not demonstrate a risk to a fetus Considered safe – used frequently to treat pregnancy-associated nausea *(Anderka 2012, Kaplan 2019)*	Considered safe	Limited data but generally considered safe *(Job 2022)*
Recommendation: adjunct to naltrexone or fifth-line monotherapy – considered safe but efficacy limited to early onset AUD		

* off label use

Prazosin*

- MOA: Alpha-1 adrenergic receptor antagonist; reduces noradrenergic activity
- Dosing: 1 mg to 20 mg/day
- Contraindications: persistent hypotension
- Efficacy: most helpful for populations engage in stress-induced alcohol use (Fox 2012) or have severe withdrawal; strength of evidence is low

* off label use

Prazosin*

Fetal Development	Labor and Delivery	Breastfeeding
FDA Category C – possible teratogenic effects in animals but limited human data No evidence of teratogenicity was observed in reproduction studies with rats, rabbits, and monkeys at doses more than 225x, 225x, and 12x, respectively, the usual MRHD *(Pfizer 2018)*	Limited data available, but no significant complications reported May mask hypertensive disorders in pregnancy, such as pre-eclampsia, so use with caution or avoid if patient has risk factors	Limited data available, but expected to be excreted in breast milk *(LactMed)*
Recommendation: fifth-line; consider for individuals with PTSD or stress-related alcohol use who are not at high risk of pregnancy-associated hypertensive disorders		

* off label use

Case Presentation #2

A 33-year-old woman with a history of alcohol use disorder and generalized anxiety disorder currently on escitalopram 10mg presents to the office as a hospital discharge referral. She reports she was recently hospitalized for observation for 24hrs due to alcohol withdrawal; she had uncomplicated symptoms and has no history of complicated withdrawal. She reports a binge-pattern of use starting in adolescence, usually drinking 5-10 glasses of wine at a time a few nights per week. She reports a stretch of sobriety of about 1 mo in her 20s and otherwise 2-3 week stretches a few times per year; in the last 4 months she has been drinking daily. She has never tried to quit or had treatment, and she reports she is very scared by the withdrawal.

She reports a desire for treatment but plans to become pregnant soon and is wondering about her options for treatment.

Image generated using ChatGPT

How would you counsel this patient?

Audience participation – placeholder slide

Rank the medications from most to least likely to offer this patient.

Audience participation – placeholder slide

Case Presentation #3

A 36-year-old female is admitted to the medical floor for management of alcohol withdrawal. Her admission CIWA was 16 and she received 20 mg of IV diazepam in the emergency room, now improved to a CIWA of 8. A urine hcg suggests pregnancy, which she was not aware of. Her kidney and liver function are wnl.

Chart review suggests a ~7-year history of alcohol use disorder, severe, with several prior admissions for complicated withdrawal, including ICU stay for seizure and autonomic instability ~2 years ago.

She has intermittently engaged with outpatient addiction treatment. She has had trials of both naltrexone (including vivitrol) and acamprosate without significant benefit.

What would you like to do to manage alcohol withdrawal? Select all that apply.

Audience participation – placeholder slide

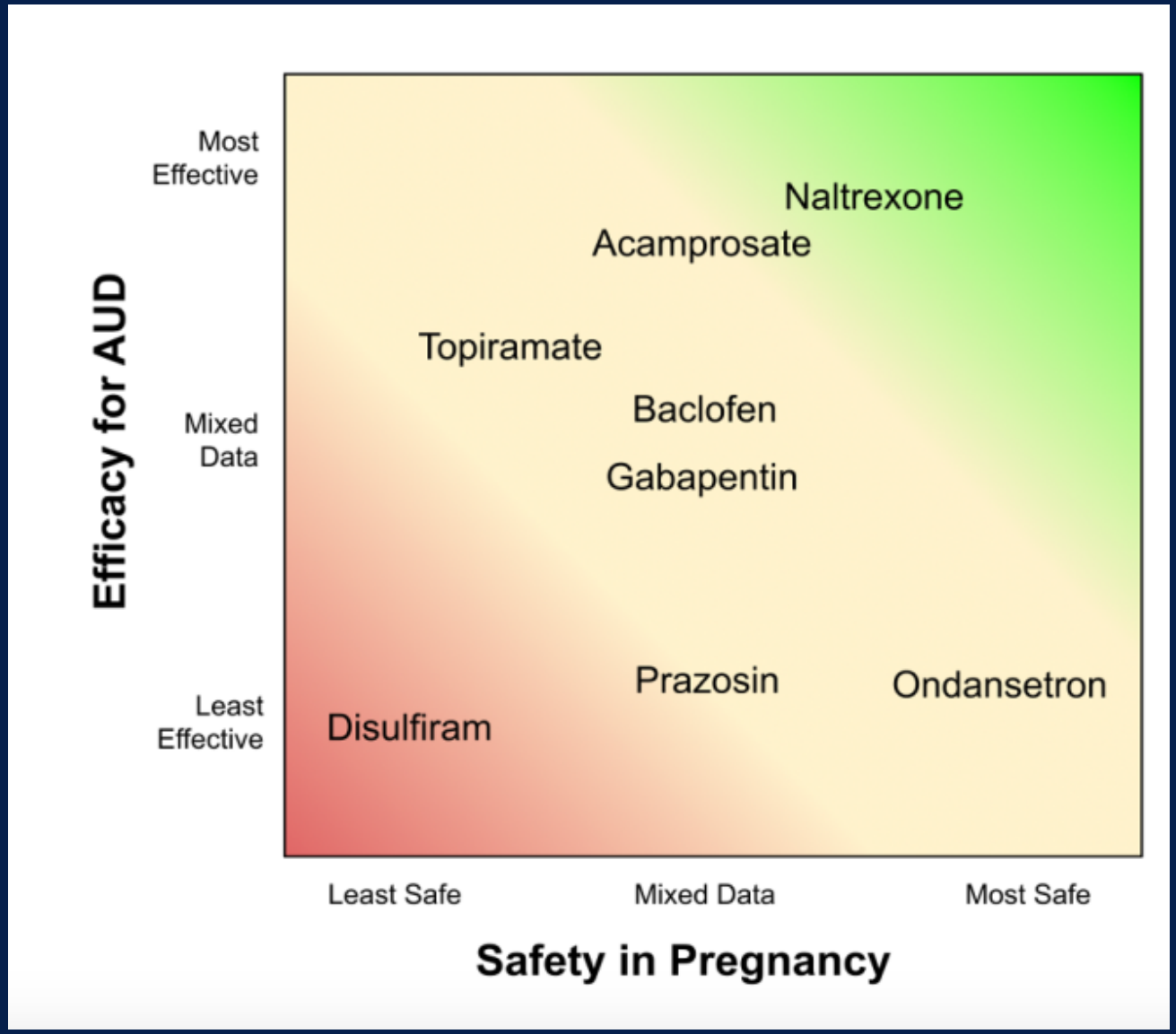
How do your recommendations differ from your standard approach?

Audience participation – placeholder slide

Final Takeaways

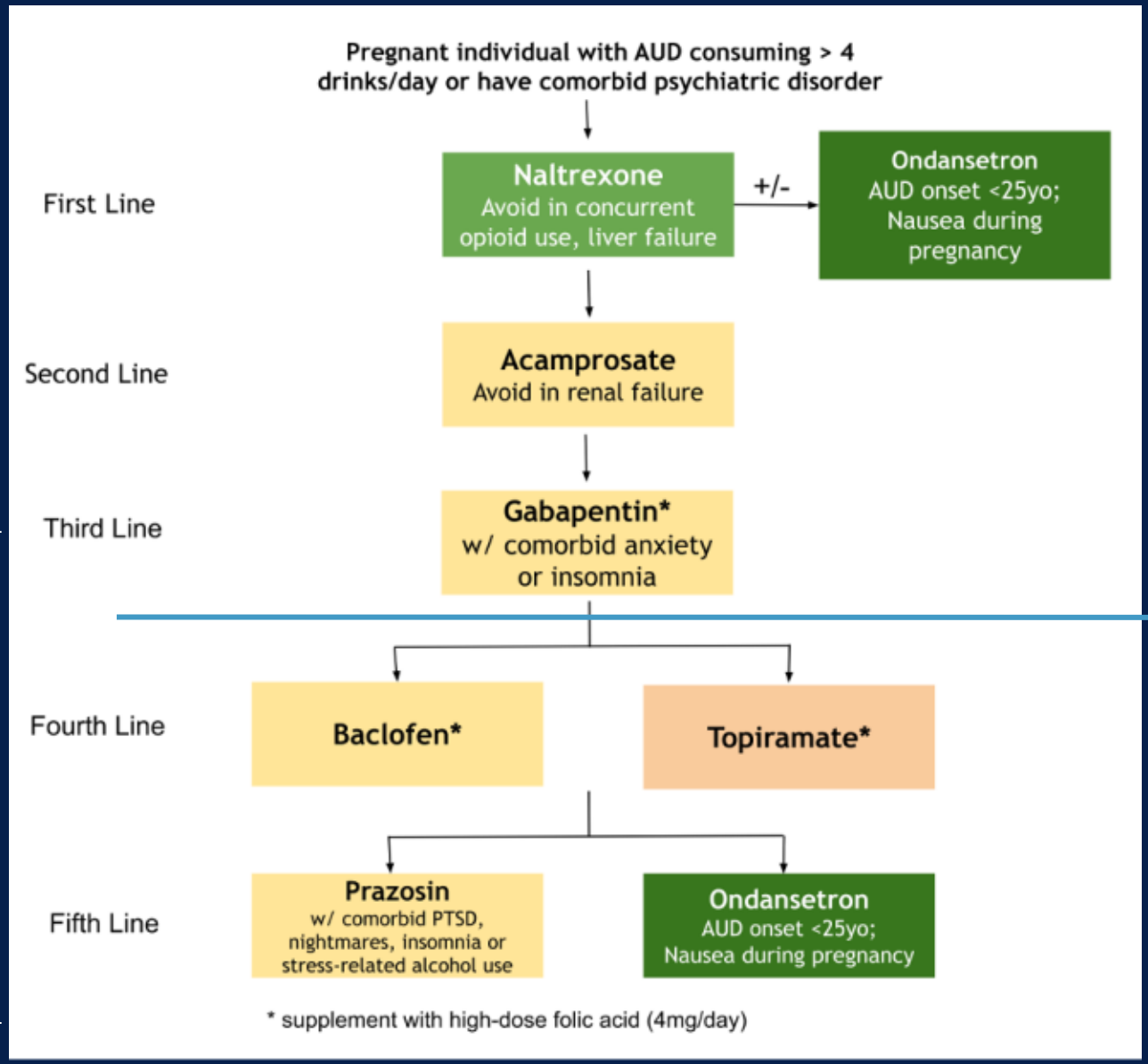
- Reconsidering professional society recommendations and standard of care treatments
- In pregnancy, evaluating risks and benefits is an individualized process with less available and lower-quality evidence
- Shying away from treatment of pregnant individuals due to lack of available evidence and/or discomfort has potential to significantly increase harm

Final Takeaways



Archer and Schnipke 2024

Final Takeaways



Off label

Typical cutoff where risks may outweigh benefits

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Provider Resources

- Massachusetts Child Psychiatry Access Program - Summary tables for Substance Use Disorders
  - https://www.mcpapformoms.org/Toolkits/Toolkit.aspx#Substance
  - https://www.mcpapformoms.org/Docs/SUD7,8.10.10.19.pdf
- Mother to Baby – Rx information for patients
  - https://mothertobaby.org/fact-sheets/
  - https://www.ncbi.nlm.nih.gov/books/NBK582980/
- LactMed – Rx information for providers for breastfeeding
  - https://www.ncbi.nlm.nih.gov/books/NBK501922/
- FindTreatment.gov - database of treatment centers by location

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Questions?

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