2017
Florida Best Practice Recommendations for
Women of Reproductive Age
with Serious Mental Illness and
Comorbid Substance Use Disorders

Florida Medicaid Drug
Therapy Management
Program for
Behavioral Health

medicaidmentalhealth.org
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Introduction and Purpose

Introduction

The National Institute of Mental Health (NIMH) reports the prevalence of women with serious mental illness (SMI) in the United States is around 4% (NIMH, 2015), and the National Survey on Drug Use and Health found that in 2014, close to 7.9 million adults in the United States had both a behavioral health and substance use disorder (SAMHSA, 2015). Women with SMI—including schizophrenia, schizoaffective disorder, bipolar disorder and major depressive disorder—are equally likely as women without serious mental illness to have children; yet, they are more likely to experience pregnancy complications (e.g., gestational diabetes, pre-eclampsia), negative birth outcomes (e.g., preterm birth, low-birth-weight infants), and substance use disorders (e.g., alcohol use, marijuana use). Individuals with SMI are 4 times more likely to drink four or more drinks per day, 3.5 times more likely to use marijuana regularly (21 times per year) and 4.6 times more likely to use other drugs at least ten times in their lives compared to those without SMI (SAMHSA 2015; DeCesaris 2013; Nguyen et al 2013; Jablensky, et al 2005). Metabolites of drugs, including alcohol, opioids, cocaine, marijuana, and tobacco enter the fetal bloodstream and cause multiple adverse effects, including physical abnormalities, neuronal cell death, problems with attention and cognition, fetal vasoconstriction, and neonatal abstinence syndrome (Minnes, et al 2011). Although there are multiple health risks associated with SMI and substance use, according to the National Institute on Drug Abuse (NIDA), only 7.9% of people with dual diagnoses of SMI and substance use received treatment for both conditions, and 53.7% of people received no treatment at all. Given these data, timely, integrated mental health care that addresses substance use issues in women who are pregnant or of childbearing age is crucial to improving pregnancy and neonatal outcomes. Early detection and prevention of substance use disorders through screening, education, and prompt intervention are key to minimizing adverse health outcomes on the mother and child.

Purpose

The purpose of the **2017 Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders** is to provide a guide to clinicians who treat women that are pregnant or of childbearing age with substance use problems. The recommendations also address use of long-acting contraceptives in women of childbearing age. These recommendations are intended as a starting point and provide rational approaches to help address some very challenging conditions. As always, the clinician and patient partnership prevails in the choice of treatment.

The recommendations cover a range of conditions that providers may encounter in their clinical practice including: alcohol use disorder, opioid use disorder, disorders of other drugs of abuse, and comorbid SMI and substance use. The recommendations also provide information about the use of long-acting contraceptives in women of childbearing age.
Process for Creating the Recommendations

The Florida Medicaid Drug Therapy Management Program brought together a diverse array of stakeholders to produce the 2017 Florida Best Practice Recommendations for Women with Serious Mental Illness and Comorbid Substance Use Disorders. This year’s group of stakeholders, known as the Florida Expert Panel, was composed of nationally recognized experts, academicians, obstetricians-gynecologists, substance abuse specialists, medical directors of Florida Medicaid programs and community mental health centers (CMHCs), child and adolescent psychiatrists, pediatricians, primary care providers, and pharmacists.

The 2017 Florida Expert Panel met on March 18, 2017 at the Renaissance International Plaza Hotel in Tampa, Florida to create the 2017 Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders. After a thorough literature review, the panel discussed the recommendations, proposed revisions, and reached a consensus about whether or not to adopt a particular set of recommendations. Thus, the final recommendations are a product of an in-depth review of the literature with an emphasis on the highest level of clinical evidence (e.g., randomized controlled trials, systematic reviews) and expert consensus on the strength of the evidence. The names of the meeting attendees and meeting presentations are available on the program website at http://medicaidmentalhealth.org. Financial disclosures are available upon request.

We are grateful to our dedicated panel of experts who have provided their expertise, editorial comments, and invaluable advice. We also would like to thank all external reviewers who took the time to make comments and point out areas needing clarity. The Florida Agency for Healthcare Administration (AHCA) is to be commended for its pursuit of providing evidence-based treatment recommendations.
**Organization**

The 2017 Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders are based on a thorough review of the research literature and consensus by the expert panel. When the scientific literature is absent or findings are mixed, the recommendations note and explain the absence of clear findings, and advise caution in treatment. Clinical tools recommended in these recommendations are available at http://www.medicaidmentalhealth.org. Recommended clinical rating scales are available in the public domain; those that are not are specifically noted.

The recommendations are organized by “levels” of treatment recommendations, beginning with Level 0, which involves a thorough clinical assessment. Subsequent levels (Levels 1, 2, 3, etc.) are based on the strength of the scientific evidence and expert consensus regarding a particular agent or treatment option. The expert panel considered both safety and efficacy when assigning a treatment option to a level. Thus, a Level 1 treatment option has the strongest clinical and scientific evidence and safety profile compared to subsequent levels.

The clinician is encouraged to begin treatment at Level 1. However, in some cases (e.g., severe symptoms), the clinician may choose to initiate treatment at a different level as appropriate based on clinical judgment in conjunction with the best evidence and guideline recommendations. Any decision regarding treatment should be based on clinical judgment that takes into account patient symptoms/needs and family treatment preferences as clinically appropriate.
The 2017 Florida Best Practice Recommendations for Women of Reproductive Age with Serious Mental Illness and Comorbid Substance Use Disorders are based on current scientific knowledge and clinical consensus at the time of publication for office-based treatment of alcohol and other substance use disorders in women with severe mental illness of childbearing age. These recommendations may not apply to all women of childbearing age with SMI and/or substance use disorders. Therefore, the recommendations should be adapted and tailored to the characteristics and needs of the individual. The use of these recommendations in whole or in part is also entirely the responsibility of the clinician. The authors bear no responsibility for treatment decisions and outcomes based on the use of these recommendations.
### Overview of Fetal Development and Critical Periods

#### Figure 1.

<table>
<thead>
<tr>
<th>Period Zygote</th>
<th>Age of Embrya</th>
<th>Fetal Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>20-36</td>
</tr>
<tr>
<td></td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

**Weeks**

- Week 1: Zygote
- Week 2: Early Embryo
- Week 3: Mid-Embryo
- Week 4: Late Embryo
- Week 5: Early Fetal
- Week 6: Mid-Fetal
- Week 7: Late Fetal
- Week 8: Early Neonate
- Week 9: Mid-Neonate
- Week 16: Late Neonate
- Week 20-36: Toddler
- Week 38: Preschooler

- **Central Nervous System**

- **Heart**

- **Upper Limbs**

- **Eyes**

- **Lower Limbs**

- **Teeth**

- **Palate**

- **External Genitalia**

- **Ears**
Principles of Practice

Level 0 - Screening, Brief Intervention, and Collaborative/Integrated Care.

Screen all women for alcohol use and use of other substances (marijuana, cocaine, methamphetamine, opioids, benzodiazepines) as early as possible during the pregnancy (initial contact) and during each trimester. Pregnant women and women who plan to breastfeed or are breastfeeding should be advised of the potential health risks of alcohol and other substance use to themselves and their babies.

Screen with an evidence-based screening tool and obtain urine drug screen (UDS) with recipient consent.

Provide brief intervention. Refer to Appendices A and B on pages 75-77. For those with a positive screen, consider referral to a specialist (e.g., substance use treatment specialist) and comprehensive assessment.

Comprehensive assessment includes a thorough history, physical exam, appropriate laboratory evaluations (CBC, CMP, urine drug screen), behavioral health assessment of the mother, and assessment of fetal health status. Refer to Appendix B on pages 76 and 77 for detailed components of comprehensive assessment.

Use validated measures to assess psychiatric symptoms, substance use, and impairment. For acute signs of alcohol or substance intoxication or withdrawal, women dependent on alcohol or drugs should be referred to the Emergency Department (ED) for immediate evaluation and detoxification services under medical supervision.

Notes:
• Facilitate communication and integrate care.
• Facilitate shared decision making and patient engagement.

Level 1 - Evidence-Based Psychosocial Intervention with a Qualified Therapist.

See Table 2 on pages 10-13 for evidence-based psychosocial interventions for substance use disorders.

- Monitor response to treatment using reliable and valid measures of changes in the target symptoms.
- In mild cases, psychosocial intervention is recommended as the initial step.
- In moderate to severe cases, a higher level of intervention may be appropriate as the initial step. Be sure to carefully weigh the risks and benefits of treatment to the mother and, if pregnant or breastfeeding, to the fetus or infant.

There are no strong studies for treatment with medication in pregnancy or during lactation.

Table 1.
Pre-Screening and Screening Tools for Substance Use Disorders

<table>
<thead>
<tr>
<th>Tool</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIAAA/NIDA Pre-Screening Questions</td>
<td>“How many times in the past year have you had 4 or more drinks in a day?” (NIAAA) “How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?” (NIDA)</td>
</tr>
<tr>
<td>Drug Abuse Screening Test (DAST-10)</td>
<td>The DAST-10 is a 10-item yes/no self-report questionnaire used to screen for substance use disorders other than alcohol use disorder in older youth and adults.</td>
</tr>
</tbody>
</table>

Note: For recommended screening tools for specific substance use disorders, refer to the appropriate sections in these guidelines.
Level 2 - Reassessment:

If psychosocial interventions have failed, carefully weigh the risks and benefits of initiating treatment with medications to maintain abstinence from substance use, including the effects of medications on the fetus or infant if pregnant or breastfeeding. As noted previously, there are no strong studies for treatment with medication in pregnancy or lactation. Consider referral to experienced outpatient substance use treatment specialists in cases of severe substance use.

Notes:
- Effort should be made to communicate between obstetrician-gynecologists, primary care providers, psychiatrists, addiction medicine specialists, case workers, and other team members to ensure integrated care.
- Prior to initiating any intervention (e.g., psychosocial, medication), assess the risks/benefits of treatment to the mother and fetus/infant.
- Individuals should be educated about the risks and benefits of treatment, including review of boxed warnings.
- Education should be targeted to the condition and potential effects to the fetus or infant.
- Written informed consent should be obtained from the parents/legal guardian if appropriate (e.g., the individual legally able to consent to medical interventions) and documented in the chart.

If a decision is made to initiate medication after careful consideration of the risks and benefits:

- Continue evidence-based psychosocial treatment during treatment with medication.
- Use monotherapy. Start low, go slow.
- Use the lowest effective dose to minimize potential adverse effects to the mother and if pregnant or breastfeeding, to the fetus/infant.
- Monitor for suicidality.
- Monitor for adverse effects of medications on both mother and child.
  - Closely monitor for pregnancy complications.
  - Closely monitor fetal or infant health status.
  - Closely monitor for adverse effects to fetus/infant if pregnant or breastfeeding.
- Use of a single medication at a higher dose is preferred over multiple medications. It is also preferable to use medications with fewer active metabolites, higher protein binding, and fewer interactions with other medications (ACOG Guidelines on Psychiatric Medication Use During Pregnancy and Lactation, 2007).
### Evidence-Based Psychosocial Interventions for Substance Use Disorders

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Motivational Enhancement Therapy (MET)/Motivational Interviewing (MI)** | - Time-limited, evidence-based variation of motivational interviewing  
- Provides feedback about attitudes and behaviors  
- Focuses on motivation to change based on feedback  
  **Components:**  
  - Examines individuals’ ambivalence to change  
  - Plans for and begins the process of change  
  - Enhances confidence in taking action  
  - Strengthens individuals’ commitment to change  
  **Core principles:**  
  - Expressing empathy  
  - Rolling with Resistance  
  - Developing Discrepancies  
  - Supporting Self-Efficacy |
| **Cognitive Behavioral Therapy (CBT)** | - Focuses on developing skills to cope with problematic substance use  
  **Specific techniques:**  
  - Exploring positive and negative consequences of continued drug use  
  - Self-monitoring to recognize cravings early  
  - Identifying situations that put one at risk for substance use  
  - Developing strategies to cope with cravings  
  - Avoiding high-risk situations |
| **Mutual Help Groups [e.g., 12-step facilitation, Alcoholics Anonymous (AA)]** | - Include organizations such as Alcoholics Anonymous  
  - Involve individuals with a common experience or problem (e.g., alcohol use disorders) who come together to share experiences and provide help/support to one another |
### Evidence-Based Psychosocial Interventions for Substance Use Disorders (continued)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Reinforcement</td>
<td>✦ Based on idea that environment of an individual has a powerful impact on encouraging or discouraging behavior (e.g. substance use)</td>
</tr>
<tr>
<td></td>
<td>✦ Involves extensive support through social and family networks and work experiences</td>
</tr>
<tr>
<td></td>
<td>✦ Individuals receive services including job counseling, lifestyle planning, and family counseling</td>
</tr>
<tr>
<td>Contingency Management (CM)</td>
<td><strong>Principles:</strong></td>
</tr>
<tr>
<td></td>
<td>✦ Based on theory that substance use disorders develop through operant conditioning (behavior is controlled or shaped by its consequences)</td>
</tr>
<tr>
<td></td>
<td>✦ Non-drug reinforcement should decrease substance use if available according to a schedule and in enough magnitude that is incompatible with substance use</td>
</tr>
<tr>
<td></td>
<td><strong>Voucher-Based Reinforcement Therapy:</strong></td>
</tr>
<tr>
<td></td>
<td>✦ Type of contingency management</td>
</tr>
<tr>
<td></td>
<td>✦ Individuals receive vouchers for positive behaviors (e.g., voucher given for negative urine drug screen)</td>
</tr>
<tr>
<td></td>
<td>✦ Vouchers are exchanged for goods or services compatible with a drug-free lifestyle</td>
</tr>
<tr>
<td>Coping-Skills Training (CST)</td>
<td>✦ Teaches variety of methods to deal with urges caused by cues that trigger substance use cravings</td>
</tr>
<tr>
<td></td>
<td><strong>Commonly used techniques in coping skills training:</strong></td>
</tr>
<tr>
<td></td>
<td>✦ Relapse prevention training – each therapy session focuses on specific situation that puts individual at high risk for relapse; teaches skills to prevent relapse in that situation</td>
</tr>
<tr>
<td></td>
<td>✦ Social or communication skills training – each session focuses on a general interpersonal skill to improve social relationships, reduce conflict, improve support systems not associated with substance use, and change individual lifestyles</td>
</tr>
<tr>
<td></td>
<td>✦ Cognitive-behavioral mood management training – each session focuses on skills to manage specific moods and emotions</td>
</tr>
<tr>
<td>Intervention</td>
<td>Description</td>
</tr>
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</tr>
</tbody>
</table>
| **Relapse Prevention Therapy (RPT)** | **Goals of treatment:**  
- Enhance self-control  
- Achieve abstinence from substance use through:  
  - Identifying high-risk situations for relapse  
  - Implementing effective coping strategies  
**Specific techniques:**  
- Exploring positive and negative consequences of continued use  
- Self-monitoring to avoid high-risk situations for relapse  
- Developing strategies to cope with and avoid high-risk situations for relapse |
| **Cue Exposure Therapy (CET)** |  
- Based on classical learning theory model – environmental cues associated with problem behavior (e.g., substance use) can lead to responses that may result in relapse  
- Focuses on repeated exposure to cues that may have led to substance use  
- Focuses on prevention of substance use as a response to cues/triggers  
- Variations of CET also incorporate coping-skills training (see page 11) in the presence of substance use-related cues |
| **Psychodynamic Therapy** |  
- Focuses on unconscious processes as they manifest in an individual’s current behavior  
**Goals:**  
- Self-awareness  
- Understanding influence of past on present behaviors  
- Goal of brief psychodynamic psychotherapy: explore unresolved conflicts from past dysfunctional relationships that manifest as need to use substances |
### Evidence-Based Psychosocial Interventions for Substance Use Disorders (continued)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
<th>Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interpersonal Therapy</td>
<td>✦ Type of short-term supportive psychotherapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✦ Focuses on connection between interactions, people, and development of psychiatric symptoms</td>
<td></td>
</tr>
<tr>
<td>Behavioral Couples Therapy (BCT)/Marital Therapy</td>
<td>✦ Designed for married or cohabiting individuals</td>
<td>✦ Build support for abstinence</td>
</tr>
<tr>
<td></td>
<td>✦ Both the individual with the substance use disorder and the spouse or live-in partner are seen together</td>
<td>✦ Improve relationship functioning</td>
</tr>
<tr>
<td>Goals:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Therapy</td>
<td>✦ Refers to a collection of therapeutic approaches that examines the family as a system and relationship of each individual to other individuals</td>
<td>✦ Strengthen family resources to live without substances use</td>
</tr>
<tr>
<td></td>
<td>✦ Based on theory that change in any part of the system brings change to other parts of the system</td>
<td>✦ Ameliorate impact of substance use on the individual and family</td>
</tr>
<tr>
<td>Goals:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Breastfeeding and Substance Use: General Considerations

Breastfeeding has proven benefits for both the infant and child. However, use of illicit substances and misuse of prescribed substances can have adverse effects on the breastfed infant.

**Women Should be Supported in the Decision to Breastfeed Their Infants If:**

- Women with substance use or misuse are engaged in substance use treatment and have provided consent to discuss progress in treatment and plans for post-partum treatment with substance use treatment counselors.
- Counselors can endorse that the woman has achieved and maintained sobriety prenatally.
- Women have been abstinent from illicit drug use or licit substance misuse for 90 days prior to delivery and have maintained sobriety in an outpatient setting. Note that women on opioid medication-assisted therapy should be encouraged to breastfeed.
  - **Note:** There is more limited evidence on the safety of buprenorphine in breastfed infants, but some recent studies indicate potential advantages of buprenorphine over methadone. See section on Opioid Use Disorders on pages 41-52.
- Women have negative maternal urine toxicology screens at delivery except for prescribed medications.
- Women have received consistent prenatal care.
- There is no contraindication to breastfeeding (e.g., HIV or use of medications contraindicated during breastfeeding).

**Women Require Careful Evaluation for Suitability to Breastfeed If:**

- Women relapse to illicit substance use or licit substance misuse 30 to 90 days prior to delivery but maintained abstinence within 30 days prior to delivery.
- Women have concomitant use of prescription medications. Evaluate safety of prescription medications in breastfed infants and weigh risks/benefits of breastfeeding.
- Women engaged in prenatal care and/or substance use treatment during or after the second trimester.
- Women attained sobriety only in an inpatient setting.

**Women Should be Strongly Discouraged from Breastfeeding If:**

- Women have established breastfeeding and subsequently relapse to illicit drug or alcohol use. There is a lack of pharmacokinetic data for most drugs of abuse in recently postpartum women to recommend a safe interval after use when breastfeeding after relapse can be re-established for specific drugs of abuse.

*Adapted from Academy of Breastfeeding Medicine, Protocol #21 (2014).*
Alcohol Use and Pregnancy

Box 1.

**DSM-5 Diagnosis: Alcohol Use Disorder**

*A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:*

- Alcohol is often taken in larger amounts or over a longer period than was intended
- There is a persistent desire or unsuccessful efforts to cut down or control alcohol use
- A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects
- Craving, or a strong desire or urge to use alcohol
- Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home
- Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol
- Important social, occupational, or recreational activities are given up or reduced because of alcohol use
- Recurrent alcohol use in situations in which it is physically hazardous
- Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol
- Tolerance, as defined by either of the following:
  - A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
  - A markedly diminished effect with continued use of the same amount of alcohol
- Withdrawal, as manifested by either of the following:
  - The characteristic withdrawal syndrome for alcohol
  - Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.
### Alcohol Use Definitions

**One standard drink equals 15 mL of pure ethanol:**
- 12 ounces of beer or wine cooler
- 5 ounces of table wine
- 8 to 9 ounces of malt liquor
- 1.5 ounces of 80-proof spirits

**Binge drinking:**
- Originally defined as 5 or more standard drinks per occasion (usually within 2 hours). Current definition is a pattern of drinking that raises a person’s blood alcohol concentration to 0.08% or greater (NIAAA).
- The National Institute on Alcohol Abuse and Alcoholism (NIAAA) defines binge drinking in women as the ingestion of 4 or more drinks per occasion to account for physiologic gender-related differences affecting alcohol absorption.

**At-risk or “heavy” drinking women:**
- More than 3 drinks on any day or 7 drinks per week (NIAAA).

**Moderate drinking in women:**
- 1 drink per day (but less than 7 drinks per week)

**Excessive alcohol consumption:**
- Binge drinking
- Heavy drinking
- Any drinking by pregnant women or those under 21 years of age

### Notes:
- All states have set a blood alcohol concentration (BAC) of 0.08% as the legal limit for driving under the influence (DUI) or driving while impaired (DWI).
- No amount of alcohol use during pregnancy is considered safe.

See Table 3 on page 17 for a list of blood alcohol concentration-specific effects on the individual.
Table 3. Blood Alcohol Concentration (BAC)-Specific Effects on the Individual.*

<table>
<thead>
<tr>
<th>BAC (%)</th>
<th>Dose-Specific Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.020-0.039%</td>
<td>Slight euphoria</td>
</tr>
<tr>
<td>0.040-0.059%</td>
<td>Lowered inhibitions, euphoria, impaired memory and judgement</td>
</tr>
<tr>
<td>0.060-0.099%</td>
<td>Slightly impaired balance, speech, vision, reaction time, and hearing; euphoria, reduced judgment, and self-control, impaired memory and reasoning</td>
</tr>
<tr>
<td>0.100-0.129%</td>
<td>Significant impairment of motor coordination and loss of good judgment, slurred speech; impaired balance, peripheral vision, reaction time, and hearing</td>
</tr>
<tr>
<td>0.130-0.159%</td>
<td>Lack of physical control, gross motor impairment, blurred vision, major loss of balance; less euphoria, increased dysphoria</td>
</tr>
<tr>
<td>0.160-0.199%</td>
<td>Dysphoria, nausea, severe lack of coordination</td>
</tr>
<tr>
<td>0.200-0.249%</td>
<td>Dysphoria, nausea, vomiting, disorientation, blackouts</td>
</tr>
<tr>
<td>0.250-0.399%</td>
<td>Loss of consciousness</td>
</tr>
<tr>
<td>≥0.40%</td>
<td>Coma, possible death due to respiratory arrest</td>
</tr>
</tbody>
</table>

*Note: These effects are may occur at lower BACs depending on the individual.
### Table 4.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description and Signs/Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol Intoxication</td>
<td>Disinhibition of normal social functioning, euphoria (initially), dysphoria (as BAC increases), ataxia, poor judgment, memory loss, slurred speech, nystagmus, vomiting, confusion/disorientation, progressive lethargy, coma, respiratory depression, and death.</td>
</tr>
<tr>
<td>Alcohol Withdrawal</td>
<td>Alcohol withdrawal symptoms can occur as early as two hours after the last drink and may persist for weeks. Symptoms range from mild anxiety and tremors to severe complications such as seizures, confusion, rapid heart rate, and fever. Signs and symptoms of alcohol withdrawal include fatigue, headache, insomnia, irritability or excitability, appetite loss, nausea and/or vomiting, palpitations, mood fluctuations, tremors, sweats, and delirium tremens.</td>
</tr>
<tr>
<td>Delirium Tremens</td>
<td>Delirium tremens (DTs) is a potentially life-threatening condition that occurs after abruptly reducing or abstaining from alcohol after years of heavy drinking. Symptoms of delirium tremens occur 48 to 96 hours after the last drink but may occur up to 7 to 10 days after the last drink. Seizures, most often generalized tonic-clonic seizures, occur with or without other symptoms of delirium tremens and occur most commonly within the first 12 to 48 hours after the last drink. Signs and symptoms of DTs: Fluctuations in mental status; agitation, irritability; loss of attention span; hallucinations; fluctuations in mood; sensitivity to light, sound, or touch; seizures (most often tonic-clonic seizures); fatigue or stupor</td>
</tr>
</tbody>
</table>

### Potential Adverse Effects of Alcohol Consumption During Pregnancy

Alcohol exposure in utero has been linked to negative birth outcomes in the mother and physical and behavioral health issues in exposed children. Examples of negative birth outcomes linked to in-utero alcohol exposure include increased risk of miscarriage, preterm delivery, babies that are small-for-gestational age or have low birthweight, stillbirth, and infant mortality. Effects on the fetus and infant include Fetal Alcohol Spectrum Disorders (FASD), neurocognitive impairments, and increased risk of mood disorders.
Working with Medicaid providers to:

- Improve behavioral health prescribing practices
- Improve patient adherence to medication
- Reduce clinical risks and medication side effects
- Improve behavioral and physical health outcomes

The following treatment guidelines are available on our website at medicaidmentalhealth.org.

- Autism Spectrum Disorder & Intellectual Developmental Disorder: Best Practice Psychotherapeutic Medication Recommendations for Target Symptoms in Children and Adolescents
- Best Practice Psychotherapeutic Medication Guidelines for Adults
- Monitoring Physical Health and Side-Effects of Psychotherapeutic Medications in Adults and Children: An Integrated Approach
- Best Practice Psychotherapeutic Medication Guidelines for Children and Adolescents

The Florida Clozapine Hotline and The Florida Pediatric Psychiatry Hotline are free services that provide consultation about medication management.

Florida Clozapine Hotline
1-727-562-6762

Florida Pediatric Psychiatry Hotline
1-866-487-9507

For more information, visit us at medicaidmentalhealth.org
### Conditions Associated with Alcohol Consumption During Pregnancy

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Diagnostic Criteria (American Academy of Pediatrics, 2016)</th>
</tr>
</thead>
</table>
| ✦ Documented maternal alcohol exposure | **Fetal alcohol syndrome is diagnosed when an individual meets all four diagnostic criteria:**  
1. Characteristic pattern of minor facial abnormalities, including two or more of the following: short palpebral fissures, smooth philtrum, thin upper vermillion lip border  
2. Prenatal and/or postnatal growth deficiency: height and/or weight ≤10th percentile  
3. Deficient brain growth, abnormal morphogenesis, or abnormal neurophysiology, including one or more of the following: head circumference ≤10th percentile, structural brain abnormalities, recurrent non-febrile seizures (other causes of seizures ruled out)  
4. Neurobehavioral impairment with or without cognitive impairment  
   **For children 3+ years:**  
   ✦ With cognitive impairment:  
     ✦ Evidence of global impairment [general conceptual ability or performance, verbal, or spatial IQ ≥1.5 standard deviations (SD) below the mean]  
     ✦ Cognitive deficit in at least one neurobehavioral domain (executive functioning, specific learning impairment, memory impairment, or visual-spatial impairment) ≥1.5 SD below the mean  
   ✦ Without cognitive impairment: evidence of behavioral deficit (impaired self-regulation) in at least 1 domain (mood or behavior regulation impairment, attention deficit, or impulse control) ≥1.5 SD below the mean  
   **For children <3 years:**  
   ✦ Evidence of developmental delay ≥1.5 SD below the mean  
   ✦ Other features often associated with fetal alcohol syndrome include abnormal facial features such as maxillary hypoplasia, cleft palate, or micrognathia. |
### Table 5. (continued)

<table>
<thead>
<tr>
<th>Conditions Associated with Alcohol Consumption During Pregnancy</th>
<th>Diagnostic Criteria (American Academy of Pediatrics, 2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Partial Fetal alcohol syndrome</strong> with or without documented prenatal alcohol exposure</td>
<td><strong>With documented maternal alcohol exposure (meets both criteria):</strong>&lt;br&gt;1. Characteristic pattern of minor facial abnormalities as noted in criteria for fetal alcohol syndrome&lt;br&gt;2. Neurobehavioral impairment as noted in criteria for fetal alcohol syndrome&lt;br&gt;<strong>Without documented prenatal alcohol exposure (requires all of the following):</strong>&lt;br&gt;1. Characteristic pattern of minor facial abnormalities as noted in criteria for fetal alcohol syndrome&lt;br&gt;2. Growth deficiency or deficient brain growth, abnormal morphogenesis, or abnormal neurophysiology as noted in criteria for fetal alcohol syndrome&lt;br&gt;3. Neurobehavioral impairment with or without cognitive impairment as noted in criteria for fetal alcohol syndrome</td>
</tr>
<tr>
<td><strong>Alcohol-Related Birth Defects (ARBD)</strong></td>
<td><strong>Requires both of the following:</strong>&lt;br&gt;1. Documented prenatal alcohol exposure&lt;br&gt;2. One or more major malformations demonstrated to be the result of prenatal alcohol exposure: cardiac (atrial septal defect, aberrant great vessels, ventricular septal defect, cotrunical heart defect); skeletal (radioulnar synostosis, vertebral segmentation defect, large joint contractures, scoliosis); renal (aplastic/hypoplastic/dysplastic kidneys, horseshoe kidney/ureteral duplication); eye (strabismus, ptosis, retinal vascular abnormalities, optic nerve hypoplasia); ears (conductive hearing loss, neurosensory hearing loss)</td>
</tr>
<tr>
<td><strong>Alcohol-Related Neurodevelopmental Disorder (ARND)</strong></td>
<td><strong>Requires both of the following:</strong>&lt;br&gt;1. Documented prenatal alcohol exposure&lt;br&gt;2. Neurobehavioral impairment&lt;br&gt;<em>Note: Diagnosis is not definitive in children &lt;3 years old.</em></td>
</tr>
</tbody>
</table>

**Definition of documented prenatal alcohol exposure:**<br>• \(\geq 6\) drinks per week for \(\geq 2\) weeks during pregnancy<br>• \(\geq 3\) drinks per occasion on \(\geq 2\) occasions during pregnancy<br>• Documentation of alcohol-related social or legal problems (e.g., driving under the influence of alcohol, DUI) before or during the index pregnancy<br>• Documentation of intoxication during pregnancy by blood, breath, or urine alcohol content testing<br>• Positive testing with established alcohol-exposure biomarker(s) during pregnancy or at birth (e.g., analysis of fatty acid ethyl esters, phosphatidylethanol, and/or ethyl glucuronide in maternal hair, fingernails, urine, or blood or in the placenta or meconium)<br>• Increased prenatal risk associated with drinking during pregnancy as assessed by validated screening tool (e.g., T-ACE or AUDIT)
### Neurobehavioral Disorder Associated with Alcohol Exposure

**Table 6.**

<table>
<thead>
<tr>
<th>Type of Impairment</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neurocognitive Domain</strong></td>
<td></td>
</tr>
</tbody>
</table>
| General cognitive impairment | • Mild or global developmental delay  
• Intellectual impairment |
| Executive function | • Poor planning/organization  
• Difficulty transitioning between activities  
• Problems learning sequential information |
| Learning | • Difficulty with early academic concepts (e.g., mathematic skills)  
• Requires repeated exposure to learn properly  
• Lower academic achievement than expected for intellectual level |
| Memory | • Difficulty with recall  
• Difficulty with multi-step verbal instructions  
• Difficulty remembering personal information (e.g., telephone number)  
• Frequently forgetful or misplacing possessions |
| Visual-spatial reasoning | • Difficulty copying simple visual patterns  
• Difficulty following a map/understanding directions  
• Difficulty solving puzzles |
| **Self-Regulation Domain** | |
| Mood/behavior | • Difficulty with sleep  
• Irritability/mood lability  
• Difficulty calming down |
| Attention | • Difficulty maintaining focus  
• Difficulty encoding new information  
• Difficulty sustaining mental effort |
| Impulse control | • Difficulty waiting  
• Chaotic/disorganized play  
• Difficulty following rules  
• Risky behavior  
• Difficulty delaying gratification |
### Neurobehavioral Disorder Associated with Alcohol Exposure (continued)

#### Table 6. (continued)

<table>
<thead>
<tr>
<th>Type of Impairment</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adaptive Domain</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Communication       | ✦ Delayed language acquisition  
                        | ✦ Difficulty following a conversation  
                        | ✦ Difficulty understanding jokes, idioms, or metaphors |
| Social              | ✦ Gullible or naïve  
                        | ✦ Overly friendly with strangers  
                        | ✦ Unaware of personal space  
                        | ✦ Difficulty understanding social consequences  
                        | ✦ Difficulty making/keeping friends |
| Daily Living        | ✦ Delay in early feeding  
                        | ✦ Delayed toileting, feeding, bathing  
                        | ✦ Difficulty managing daily schedule  
                        | ✦ Poor understanding of money/finances |
| Motor               | ✦ Delayed fine and gross motor skills  
                        | ✦ Frequent falls/loss of balance/poor coordination  
                        | ✦ Poor handwriting |

*Adapted from Hagan, et al., 2016*
Management of Alcohol Use During Pregnancy

Treatment of Acute Alcohol Withdrawal and Medication-Assisted Therapy for Alcohol Use Disorders

Benzodiazepines are first-line for treatment of acute alcohol withdrawal and have been shown to significantly decrease the risk of seizures (risk reduction of 7.72 seizures per 100 patients) and delirium tremens (risk reduction of 4.9 DTs per 100 patients) in individuals who are not pregnant (Asplund et al, 2004). Data on benzodiazepine use for the treatment of alcohol withdrawal in pregnant women is limited.

Disulfiram contraindicated during pregnancy for maintenance of abstinence in treating alcohol use disorders. There are insufficient data on the use of acamprosate in pregnant patients. Although preliminary data support use of naltrexone in maintenance of abstinence, there is currently insufficient data to make a recommendation for use during pregnancy for maintenance of abstinence for alcohol use disorders.

Treatment Goals for Alcohol Use During Pregnancy

Treatment goals for management of alcohol withdrawal syndrome are to reduce withdrawal symptoms, prevent seizures and delirium tremens, and encourage long-term abstinence from alcohol use. In the general adult population, up to one-third of individuals with alcohol withdrawal syndrome who have a related seizure will progress to developing delirium tremens.

Alcohol Consumption and Breastfeeding

Alcohol levels in breastmilk closely parallel blood alcohol levels in the mother. The highest alcohol levels in breastmilk occur approximately 30 to 60 minutes after an alcoholic beverage, but consuming alcohol with food delays the time to peak breastmilk alcohol levels. Some studies have also shown that blood alcohol levels had a later peak in lactating women than in non-lactating women. Alcohol has also been shown to decrease breastmilk production in lactating women.

Evidence shows that infant growth and motor function may be affected by 1 drink or more daily. Nursing after 1 or 2 drinks, including beer, can decrease the infant’s breastmilk intake by 20% to 23%, and can cause infant agitation and poor sleep patterns. Heavy alcohol consumption (3 or more drinks per day) may cause excessive sedation, fluid retention, and hormone imbalances in breastfed infants. Consuming 5 or more drinks decreases the milk letdown in the mother and disrupts nursing until blood alcohol levels decrease. The long-term effects of daily alcohol consumption on the breastfed infant are unclear (LactMed, 2017).

Women who consume an occasional single alcoholic beverage (as defined by a standard drink) should be advised to wait 3 to 4 hours (i.e., until alcohol clears from the maternal blood) before breastfeeding so that the infant’s exposure to alcohol is negligible. The American Congress of Obstetrics and Gynecology recommends that there is no need to pump and discard the breastmilk other than to maintain milk flow and prevent breast engorgement. Alcohol levels in breastmilk will decrease as blood alcohol levels decrease; pumping and discarding breastmilk does not affect alcohol levels in breastmilk (ACOG, Committee Opinion 496, 2011).
Level 0 - Pre-screening, screening, brief intervention, and collaborative/integrated care.

Comprehensive assessment of mother and baby’s health status. Refer to Principles of Practice on page 8 and 9. See Appendices A, B, and C on pages 75-78 for components of comprehensive assessment, types of brief intervention, and pre-screening algorithm for alcohol use disorders.

- The T-ACE, TWEAK, and AUDIT-C screening instruments with high specificity and sensitivity that can be used to identify at-risk alcohol consumption.

- For prenatal visits, the T-ACE a simple four-item screening instrument specifically for assessing prenatal alcohol consumption. The T-ACE is a valuable and efficient tool for identifying a range of alcohol use, including pre-pregnancy risk drinking (defined as more than two drinks per day), and lifetime diagnoses based on the Diagnostic and Statistical Manual of Mental Disorders (DSM). A score of 2 points or greater on the T-ACE is a positive screen.

- The CIWA-Ar and SAWS scales are used to assess alcohol withdrawal symptoms. The CIWA-Ar is recommended to assess alcohol withdrawal symptoms because of its well-documented reliability, validity and reproducibility, and ease of use in a range of clinical settings.

Rule out alternative diagnoses. Perform testing, including lumbar puncture and cranial CT as indicated to rule out medical causes of presenting symptoms.

*Note: Infection (e.g., meningitis), trauma (e.g., intracranial hemorrhage), metabolic abnormalities, drug overdose, liver failure, and gastrointestinal bleeding can mimic and/or coexist with alcohol withdrawal.*

Once alcohol withdrawal syndrome is diagnosed, initiate treatment promptly to prevent symptom progression to seizures and/or delirium tremens (DTs).
Level 1 - If no physical dependence, initiate psychosocial interventions.
See Table 2 on pages 10-13.
Evidence-based psychosocial treatments found to be effective in treating alcohol use disorders include:

- Motivational enhancement therapy (MET)
- Cognitive behavioral therapy (CBT)
- Other behavioral therapies such as community reinforcement and contingency management
- 12-step facilitation (e.g., Alcoholics Anonymous)
- Psychodynamic therapy/Interpersonal therapy, and
- Marital and family therapies

Note: Data do not show that one mode of behavioral intervention is superior to others in pregnant women with alcohol use disorders.

- Monitor response to treatment using reliable and valid measures of changes in the target symptoms.

Women identified to have heavy drinking patterns and who are unlikely to reduce their consumption should be referred to professional alcohol use treatment programs.

For at-risk (“heavy”) or chronic alcohol use, residential or intensive outpatient treatment may be appropriate prior to office-based care depending on the duration and severity use.

Level 2 - No recommendations.
There are no recommendations appropriate for Level 2 based on the evidence.

Level 3 - No recommendations.
There are no recommendations appropriate for Level 3 based on the evidence.

Level 4 - Lorazepam + folic acid supplementation are recommended for acute alcohol detoxification.
If physical dependence is present (e.g., signs/symptoms of alcohol withdrawal), initiate slow detoxification on an inpatient setting or at a substance use treatment facility in a quiet, protected environment using CIWA protocol with obstetrical (OB) support for a viable fetus and fetal heart tone monitoring in a non-viable fetus. Note that there are no studies of benzodiazepine use for alcohol detoxification during pregnancy. Recommendation is based on clinical consensus alone.
Level 5 - Medication management if benefits outweigh risks.

The safety and efficacy of medication management for long-term abstinence from alcohol has also not been well-established in pregnancy. In individuals who are not pregnant, naltrexone has been shown to decrease heavy drinking to 83% of the placebo group and decrease total drinking days by about 4% (Rösner S, et al, 2010). However, animal studies indicate potential adverse effects of naltrexone to the developing fetus, and there are no studies on the effects of naltrexone on pregnancy or the developing human fetus. Based on the evidence at this time, there are no recommendations for medication management for long-term abstinence from alcohol use.

Disulfiram (Antabuse®) is contraindicated during pregnancy. Disulfiram has been associated with serious birth defects, including club-foot, VACTERL syndrome (a pattern of congenital anomalies) and phocomelia of the lower extremities.

Not Recommended:

- Barbiturates (e.g., phenobarbital)
- Topiramate
- Disulfiram

Notes:

- Randomized controlled trials have shown that brief intervention is more effective than no intervention at all for alcohol use disorders, and is often as effective as more extensive intervention.
- Benefits of brief intervention include decreased alcohol consumption, decreased risk of alcohol-exposed pregnancy, higher rates of abstinence, and improvement in fetal and newborn outcomes.
- Maternal cessation of alcohol intake at any point during pregnancy is beneficial; children born to women who stop drinking late in gestation have better outcomes than those who continue to drink throughout pregnancy.
- Pregnant women experiencing alcohol withdrawal may be uniquely vulnerable to the effects of alcohol withdrawal.
- There are limited data on the effects of acute alcohol withdrawal during pregnancy.
Table 7. **Useful Initial Screening Tools for Alcohol Use Disorders**

<table>
<thead>
<tr>
<th>Screening Tool</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol Use Disorders Identification Test (AUDIT) Questionnaire</td>
<td>The AUDIT is a 10-item screening tool developed by the World Health Organization to assess alcohol consumption, drinking behaviors and alcohol-related problems. The AUDIT has been validated in a wide range of racial and ethnic groups as well as across genders.</td>
</tr>
</tbody>
</table>
| AUDIT-C Questionnaire                 | The AUDIT-C is a modified version of the AUDIT questionnaire. The AUDIT-C is 3-item alcohol screen to help identify individuals who are at risk for alcohol use disorders. Each question has 5 answer choices that are scored from 0-4 points. The total score on the AUDIT-C ranges from 0 to 12 points. The higher the score, the more likely it is that the individual’s alcohol consumption is affecting her safety. Questions on the AUDIT-C:  
  - How often do you have a drink containing alcohol?  
  - How many standard drinks containing alcohol do you have on a typical day?  
  - How often do you have six or more drinks on one occasion?  
In women, a score of 3 or more is considered a positive screen for hazardous alcohol consumption. |
| CAGE (Cut down, Annoyed, Guilty feelings, Eye-opener) Questionnaire | The CAGE questionnaire is a 4-item questionnaire that assesses for problems with alcohol use. It asks about the following in a yes or no format:  
  - C – Cut down – If individuals have ever felt the need to cut down drinking  
  - A – Annoyed – If individuals have ever felt annoyed with criticisms of their drinking  
  - G – Guilty – If individuals have ever felt guilty about drinking  
  - E – Eye-opener – If individuals they have ever felt the need to drink first thing in the morning (eye-opener).  
An answer of “yes” to two or more questions is considered a positive screen. A positive screen does not indicate a diagnosis of alcohol use disorder, but should signal the physician or other health care practitioner to discuss pregnancy at-risk drinking with the patient. |
Useful Initial Screening Tools for Alcohol Use Disorders

<table>
<thead>
<tr>
<th>Screening Tool</th>
<th>Description</th>
</tr>
</thead>
</table>
| CRAFFT Questionnaire (Adolescents) | The **CRAFFT** screening tool asks 6 questions to screen adolescents for high risk alcohol consumption and use of other substances:  
   - **C** – **Car** – “Have you ever ridden in a car driven by someone (including yourself) who was “high” or had been using alcohol or drugs?”  
   - **R** – **Relax** – “Do you ever use alcohol or drugs to relax, feel better about yourself, or fit in?”  
   - **A** – **Alone** – “Do you ever use alcohol/drugs while you are by yourself, alone?”  
   - **F** – **Forget** – “Do you ever forget things you did while using alcohol or drugs?”  
   - **F** – **Friends** – “Do your family or friends ever tell you that you should cut down on your drinking or drug use?”  
   - **T** – **Trouble** – “Have you gotten into trouble while you were using alcohol or drugs?” |
| T-ACE (Tolerance, Annoyed, Cut down, Eye-opener) Questionnaire | The **T-ACE** questionnaire is a 4-item questionnaire that asks the following:  
   - **T** – **Tolerance** – “How many drinks does it take to make you feel high?”  
   - **A** – **Annoyance** – “Have people annoyed you by criticizing your drinking?”  
   - **C** – **Cut Down** – “Have you felt you should cut down on your drinking?”  
   - **E** – **Eye Opener** – “Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?” |
| TWEAK Questionnaire | The **TWEAK** is a five-item questionnaire to screen for risky drinking behavior during pregnancy. The acronym stands for the questions below:  
   - **T** – **Tolerance** – “How many drinks can you hold?”  
   - **W** – **Worried** – “Have close friends or relatives worried or complained about your drinking in the past year?”  
   - **E** – **Eye Opener** – “Do you sometimes take a drink in the morning when you first get up?”  
   - **A** – **Amnesia (blackouts)** – “Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember?”  
   - **K** – **K/Cut Down** – “Do you sometimes feel the need to cut down on your drinking?” |
## Rating Scales to Assess Severity of Alcohol Withdrawal Symptoms

### Table 8.

<table>
<thead>
<tr>
<th>Rating Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Institute Withdrawal Assessment for Alcohol</strong></td>
<td>The CIWA-Ar is a self-report scale that measures 10 symptoms. Symptom categories are agitation, anxiety, and auditory disturbances, clouding of sensorium, headache, nausea/vomiting, paroxysmal sweats, tactile disturbances, tremor and visual disturbances. Scores range from 0 to 7 in each category. Scores of less than 8 indicate minimal to mild withdrawal. Scores of 8 to 15 indicate moderate withdrawal and scores of 15 or more indicate severe withdrawal. High scores, in addition to indicating severe withdrawal, are also predictive of development of seizures and delirium. The CIWA-Ar has well-documented reliability, validity and reproducibility and is easy to use in a range of clinical settings, including general medical/surgical wards and psychiatry units.</td>
</tr>
<tr>
<td><strong>Short Alcohol Withdrawal Scale (SAWS)</strong></td>
<td>The SAWS is a 10-item self-report scale that asks individuals to report on symptoms of anxiety, confusion, restlessness, misery, problems with memory, tremor, nausea, pounding heart, sleep disturbance, and sweating on a scale of 0-3 (none to severe) within the past 24 hours. The SAWS can be used to determine severity of alcohol withdrawal symptoms at first clinical presentation and in a variety of clinical settings. The scale has good validity, particularly in the outpatient setting, but can be used in a variety of clinical settings, including community, residential, and inpatient settings as a supplement to standard clinical assessment and observations. Higher scores indicate more severe symptoms, and individuals reporting scores of 12 or above likely require medication to reduce withdrawal severity.</td>
</tr>
</tbody>
</table>
Medications Used to Maintain Abstinence from Alcohol Use Disorders

Studies on the use of medications for maintenance of abstinence from alcohol use disorders are limited in women who are pregnant; therefore, no definitive evidence-based recommendations can be provided.

Table 9.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of Action</th>
<th>Dosing Recommendations</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naltrexone (Revia®)</td>
<td>Mu opioid receptor antagonist</td>
<td>50 mg/day orally starting 4-7 days after last drink; may begin at 25 mg by mouth one time daily for first 3-5 day to minimize adverse effects</td>
<td>Contraindicated in patients receiving long-term opioid therapy. Contraindicated in acute hepatitis or liver failure Monitor liver dysfunction.</td>
</tr>
</tbody>
</table>

*As previously noted, data on the use of naltrexone during pregnancy are lacking, and there are no studies on the effects of naltrexone on the human fetus.
Alcohol Use and Pregnancy: Summary

BACKGROUND

At-risk alcohol use by women of childbearing age has a disproportionate effect on reproductive function and pregnancy outcomes. Approximately half of all US women of childbearing age have reported alcohol consumption within the past month, with use ranging from sporadic intake to 15% reporting binge drinking (Williams, et al, 2015). The National Institute on Alcohol Abuse and Alcoholism defines at-risk alcohol use for healthy women as more than three drinks per occasion, more than seven drinks per week, or any amount of drinking for women who are pregnant or at risk of pregnancy (NIAAA, 2017). Moreover, the U.S. Preventive Services Taskforce (USPSTF) recommends that all adult patients in a primary care setting be screened for alcohol misuse and provided counseling for identified risky or harmful drinking (USPSTF, 2013).

No amount of alcohol intake during pregnancy is considered safe. The U.S. Surgeon General advises that pregnant women should not consume any alcohol. Women who have already consumed alcohol during a pregnancy should stop consumption to minimize further risk to the fetus. Women who are considering becoming pregnant or who are sexually active and do not use contraceptive methods proven effective should also remain abstinent from drinking alcohol.

SCOPE OF ALCOHOL USE DURING PREGNANCY

Prenatal exposure to alcohol is the leading preventable cause of birth defects as well as intellectual and neurodevelopmental disabilities.

- One in ten women report alcohol use, defined as at least one drink of any alcoholic beverage in the past 30 days (CDC, 2015).
- 7.6% of pregnant women report continued alcohol use (CDC, 2012).
- 1.4% report binge drinking despite the U.S. Surgeon General’s warnings to remain abstinent from alcohol due to potential risks of alcohol exposure to the fetus (CDC, 2012).

RISK FACTORS FOR ALCOHOL USE IN PREGNANCY

Poverty, homelessness, and substance use, particularly substance use prior to conception, are all risk factors for alcohol use during pregnancy. The greatest risks for alcohol use during pregnancy have been reported to be comorbid mental health problems and a personal history of physical or sexual abuse.

ALCOHOL USE AND COMORBID MENTAL HEALTH CONDITIONS

Between 56% and 92% of those who report alcohol use have a comorbid mental health diagnosis; up to 70% of those who report alcohol use have a personal history of childhood sexual abuse. Common psychiatric comorbidities include major depressive disorder independent of substance use, bipolar disorder, and anxiety disorders. Therefore, treatment of alcohol and other substance use problems requires a multidisciplinary, integrated approach that not only treats the substance use but also addresses underlying psychosocial problems and mental health conditions (Bhuvaneswar, 2007).
CONSEQUENCES OF ALCOHOL CONSUMPTION DURING PREGNANCY

According to the Centers for Disease Control and Prevention, experts estimate that the full range of Fetal Alcohol Spectrum Disorders (FASD) in the United States and some Western European countries may be as much as 2% to 5% of the general population (CDC, 2017).

Alcohol exposure in utero has been linked to negative birth outcomes in the mother and physical and behavioral health issues in exposed children.

Examples of negative birth outcomes linked to in-utero alcohol exposure:

- Increased risk of miscarriage
- Preterm delivery
- Babies that are small-for-gestational age
- Low birthweight
- Stillbirth and infant mortality

Negative consequences of in-utero alcohol exposure on the fetus include Fetal Alcohol Spectrum Disorders (FASD) and higher risk for behavioral health conditions and social problems.

- Fetal Alcohol Spectrum Disorders (FASD)
  - FASD is the general term that refers to a range of adverse effects associated with prenatal alcohol exposure.
  - FASD encompasses diagnoses such as:
    - Fetal Alcohol Syndrome (FAS)
    - Partial Fetal Alcohol Syndrome
    - Alcohol-Related Birth Defects (ARBD)
    - Alcohol-Related Neurodevelopmental Disorder (ARND)
    - Behavioral or other neurocognitive problems related to prenatal alcohol exposure
  - Increased rates of co-occurring behavioral health conditions in children and adolescents with a history of in-utero alcohol exposure include:
    - Anxiety disorders
    - Mood disorders, particularly depression and suicidal behavior
    - Attention-deficit hyperactivity disorder
    - Substance use disorders
  - Children with a history of prenatal alcohol exposure also have higher rates of school disruption, problems with the law, and under- or unemployment.

Epidemiological studies consistently show common risk factors associated with FAS, ARBD, and ARND. These include age older than 25 when a child with fetal alcohol syndrome is born; use of other drugs including tobacco and other illicit substances; premature morbidity or mortality from alcohol related causes; low socioeconomic status; early onset of regular drinking, frequent binge drinking, frequent drinking, high blood alcohol concentration and/or no reduction in drinking during pregnancy, low self-esteem or depression; alcohol misuse in family members; marital status (cohabitation, never married, separated or divorced); loss of children to foster or adoptive placement; and cultural or community background that is relatively tolerant of heavy drinking (May and Gossage, 2017).
**Fetal Alcohol Syndrome (FAS)**

First described in 1973, Fetal Alcohol Syndrome (FAS) is considered one of the most serious consequences of maternal alcohol consumption during pregnancy. Estimates of the prevalence of FAS range from 0.10 to 3.10 per 1000 births, depending on the method used. The lowest rates of fetal alcohol syndrome are reported with passive surveillance methods, and the highest rates are found through clinic-based methods, particularly in studies of high-risk populations (May and Gossage, 2017).

Fetal alcohol syndrome is characterized by a distinctive set of facial anomalies – specifically, short palpebral fissures, a flat midface, thin upper lip, and flat or smooth philtrum in children whose mothers drank heavily during pregnancy. Children with fetal alcohol syndrome also exhibit slowed growth and significant cognitive and/or behavioral problems. Many individuals with fetal alcohol syndrome have an intelligence quotient (IQ) less than 70. Although a substantial proportion of these children perform in the low average to average range on IQ tests, children with fetal alcohol syndrome have difficulty with complex language tests, tests of pragmatic language, arithmetic skills, and attentional function (e.g., executive skills, which includes ability to plan and coordinate appropriate responses, and to modify behavior flexibly in response to feedback).

**Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure**

Exposure to alcohol in-utero is associated with impairments in neurocognition, self-regulation, and/or adaptive functioning.

**Neurocognition**

Neurocognitive impairment is characterized by impairment in one of the following: global impairment, problems with executive function, learning deficits, memory problems, or difficulty with visual-spatial reasoning, as assessed by standardized testing, clinical observation and/or clinical history. Comprehensive standardized tests are the standard of care to assess global impairment.
SELF-REGULATION

Impaired self-regulation includes difficulty regulating mood or behavior, problems with attention, or poor impulse control. In younger children, mood or behavior problems may manifest as problems with sleep, severe reactions to discomfort, or extended tantrums. Moreover, attention problems are most commonly associated with prenatal alcohol exposure.

ADAPTIVE

Impaired adaptive functioning includes difficulty with communication, social interaction, daily living skills, and/or motor skills. Adaptive functioning is considered impaired if there are deficits across two of these domains. Individuals with neurobehavioral disorder associated with prenatal alcohol exposure may show difficulty with understanding figurative language, may be overly friendly or have difficulty learning social rules through experience, may have difficulty maintaining skills such as following household rules and organizing daily activities, and may have problems with gross motor (e.g., balance, coordination) or fine motor coordination (e.g., poor writing) (Hagan, et al., 2016).

TREATMENT OF ACUTE ALCOHOL WITHDRAWAL AND MEDICATION-ASSISTED THERAPY (MAT) FOR ALCOHOL USE DISORDERS

Benzodiazepines are considered first-line for treatment of acute alcohol withdrawal, although studies in pregnant patients are limited. Benzodiazepine dosing schedules for acute alcohol withdrawal are fixed-schedule, where medications are administered at regular intervals, or symptom-triggered dosing, where medications are administered based on reported symptoms using a validated self-report scale such as the CIWA-Ar. Symptom-triggered therapy has been shown to reduce the duration of therapy, benzodiazepine dose, and length of stay (Sachdeva, 2015). Naltrexone shows some promise for potential use in medication-assisted therapy for alcohol use disorders, but data on the effects of naltrexone administered during pregnancy are limited to animal studies, and no definitive recommendation for use during pregnancy can be made based on evidence alone.
### Sedative-Hypnotic Use and Effects of Prenatal Exposure

<table>
<thead>
<tr>
<th>Substance</th>
<th>Signs/Symptoms of Intoxication</th>
<th>Signs/Symptoms of Withdrawal</th>
<th>Effects of Exposure During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines (e.g., alprazolam, lorazepam, diazepam)</td>
<td>Slurred speech, nystagmus, hypotension, paradoxical agitation, altered mental status/impaired cognition (e.g., attention, memory difficulties), respiratory depression, stupor, coma</td>
<td>Irritability, psychomotor agitation, sleep disturbance, anxiety/panic attacks, hand tremor, sweating, difficulty with concentration, nausea, vomiting, weight loss, palpitations, increased heart rate (pulse greater than 100 bpm), headache, muscle stiffness, auditory or visual hallucinations or illusions, grand mal seizures.</td>
<td>Increased absolute risk of facial clefts with exposure to diazepam. Some studies have also reported increased risk of facial and cardiac malformations with chlordiazepoxide and cardiac malformations with diazepam exposure, but study results have been inconsistent. Late third-trimester exposure to benzodiazepines associated with floppy infant syndrome or neonatal withdrawal symptoms, including hypotonia, decreased suck reflex, apneic spells, cyanosis, and impaired response to cold stress.</td>
</tr>
</tbody>
</table>
### Sedative/Hypnotic Use and Effects of Prenatal Exposure

<table>
<thead>
<tr>
<th>Substance</th>
<th>Signs/Symptoms of Intoxication</th>
<th>Signs/Symptoms of Withdrawal</th>
<th>Effects of Exposure During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Z-drugs” (e.g., eszopiclone, zaleplon, zolpidem)</td>
<td>Nausea, vomiting, dizziness, drowsiness, dry mouth, headache, impaired cognition (e.g., amnesia, confusion), impaired psychomotor function, depression, and hallucinations have been reported. Adverse effects include daytime sedation, increased risk of motor vehicle accidents, increased falls, and dissociative states. Zaleplon may cause impairment of short-term memory at doses of 10 to 20 mg.</td>
<td>Withdrawal symptoms resemble those of benzodiazepine withdrawal symptoms.</td>
<td>Lack of well-controlled human studies. Some evidence of withdrawal symptoms, respiratory depression, and neonatal flaccidity.</td>
</tr>
</tbody>
</table>

**Abbreviations:** bpm = beats per minute
Benzodiazepines

All classes of benzodiazepines cross the placenta and are secreted in breastmilk, but data on the use of benzodiazepines in pregnant and breastfeeding women are limited. Prenatal exposure to diazepam increases the absolute risk of oral cleft by 0.01% (from 6 to 7 per 10,000 infants). Some studies have also reported increased risk of facial and cardiac malformations with chlordiazepoxide and cardiac malformations with diazepam exposure, but study results have been inconsistent (Belantuono, 2013).

Maternal use of benzodiazepines before delivery has also been associated with floppy infant syndrome and neonatal abstinence syndrome, particularly with late third-trimester exposure. Late third-trimester exposure to benzodiazepines has been associated with neonatal withdrawal symptoms, including hypertonia, decreased suck reflex, apneic spells, cyanosis, and impaired response to cold stress. Withdrawal syndromes may persist for several months after delivery in infants whose mothers received alprazolam, chlordiazepoxide, or diazepam.

Use of estrazolam, flurazepam, quazepam, temazepam, and triazolam are not recommended in pregnant women. If prescribed, benzodiazepines with a short or medium half-life (e.g., lorazepam) at the lowest effective dose are recommended with caution if the benefits outweigh the risks of treatment; however, cases of neonatal sedation and respiratory depression have also been reported (Belantuono, 2013).

Treatment of Benzodiazepine withdrawal During Pregnancy

- Individualized, gradual taper over several weeks with clonazepam with fetal monitoring (twice daily fetal heart tones) on an inpatient unit or substance use detoxification facility is recommended (based on clinical consensus).

Effects of Benzodiazepine Use on the Fetus/Infant During Pregnancy

- Floppy Infant Syndrome
  Floppy infant syndrome has been described after moderate benzodiazepine use during the last trimester of pregnancy or a single large benzodiazepine dose given prior to delivery. Symptoms include hypotonia (floppy appearance of muscles), lethargy, sucking difficulty, feeble cry, hypothermia, low APGAR scores and respiratory depression, particularly in infants of mothers who received high doses of diazepam (>30 mg) during labor (Harding and Timko, 2008).

- Neonatal Abstinence Syndrome (NAS)
  Exposure to high-dose benzodiazepines in utero has been associated with withdrawal symptoms such as irritability and restlessness, apnea, cyanosis, lethargy and hypoxia or hypertonia in the newborn. Symptoms of benzodiazepine withdrawal also include tremor, diarrhea, and vomiting. Benzodiazepine withdrawal syndromes have been described in neonates exposed to benzodiazepines in utero during the last several months of pregnancy. To avoid neonatal abstinence syndrome, it is recommended to gradually taper benzodiazepines during the last months of pregnancy, or sooner, if possible (Harding and Timko, 2008).
“Z-DRUGS”: ESZOPICLONE, ZALEPLON, ZOLPIDEM

There is a lack of well-controlled human studies with sedative hypnotic agents such as eszopiclone, zaleplon, and zolpidem. Some evidence of withdrawal symptoms and neonatal flaccidity have been found with these agents.

- Zaleplon
  
  One pre- and postnatal study in rats showed increased stillbirth and postnatal mortality, decreased growth and decreased physical development in offspring of females exposed during late gestation (FDA, 2007).

- Zolpidem
  
  Case reports have indicated severe respiratory depression in the neonate when zolpidem was used at the end of pregnancy, especially when used with other CNS depressants (FDA, 2008).
Benzodiazepines are excreted in breastmilk to varying degrees. Case reports have found that nursing infants of mothers taking diazepam or chlordiazepoxide had symptoms of lethargy, weight loss, and floppy infant syndrome. Literature reviews have recommended avoiding use of benzodiazepines in nursing women. If the benefits outweigh the risks and benzodiazepines are prescribed to nursing women, the recommendation is to forgo breastfeeding.

“Z-Drugs”: Eszopiclone, Zaleplon, Zolpidem

Extreme caution is advised in use of hypnotics in breastfeeding mothers, as there are limited data on the levels of zolpidem and zaleplon in breastmilk, no data on the levels of eszopiclone in breast milk, and no data on the effects of zolpidem, zaleplon, or eszopiclone in breastfed infants.

- Eszopiclone
  
  No published data is available on the use of eszopiclone during breastfeeding; therefore, eszopiclone is not recommended for use in breastfeeding mothers.

- Zolpidem and Zaleplon
  
  Due to low levels of zolpidem and zaleplon in breastmilk and the short half-life of these medications, the amounts ingested by breastfeeding infants is thought to be small, and no special precautions have been recommended. However, caution is advised when prescribing zolpidem or zaleplon as studies examining levels in breastfeeding mothers is limited, and no published data exist on levels in breastfed infants.

  One study was done in five nursing mothers who were 3-4 days post-partum and given a single oral dose of zolpidem 20 mg. Milk was collected 3 hours after the oral dose was administered and analyzed. Zolpidem levels in breastmilk were between 0.76 and 3.88 micrograms per liter after 3 hours, and levels were undetectable (<0.5 micrograms/L) in the milk 13 to 16 hours after the oral dose was administered.

  Another study of 5 nursing mothers who were at least 14 days post-partum and were given a single oral dose of zaleplon 10 mg found that peak zaleplon levels were an average of 14 micrograms/L 1.2 hours after the oral dose. The mean half-life in milk was 1.1 hours. According to LACTMED through the National Institute of Health, using the peak milk levels from this study, exclusively breastfed infants would receive an estimated maximum dose of 2.1 micrograms/kg daily (approximately 1.4% of the maternal weight-adjusted dose) (LactMed, 2017).
Box 3.

**DSM-5 Diagnosis: Opioid Use Disorder**

**A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:**

- Opioids are often taken in larger amounts or over a longer period than was intended.
- There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
- A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
- Craving, or a strong desire or urge to use opioids.
- Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
- Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
- Important social, occupational, or recreational activities are given up or reduced because of opioid use.
- Recurrent opioid use in situations in which it is physically hazardous.
- Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
- Tolerance, as defined by either of the following:
  - A need for markedly increased amounts of opioids to achieve intoxication or desired effect
  - A markedly diminished effect with continued use of the same amount of opioid

*Note:* This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.

- Withdrawal, as manifested by either of the following:
  - Characteristic opioid withdrawal syndrome
  - Opioids are taken to relieve or avoid withdrawal symptoms.
**Definitions: Terminology**

According to National Institute on Drug Abuse (NIDA), an opioid is a substance that binds to cells in the brain that impact functions such as pain control, digestion, and respiration. Opioid refers to prescription pain medications such as oxycodone, hydrocodone, and fentanyl as well as illicit synthetic substances such as heroin. Opioids are sometimes divided into categories based on naturally occurring opioids (sometimes referred to as opiates), semi-synthetic opioids, and fully synthetic (man-made) opioids. See Table 11 below.

**Table 11.**

<table>
<thead>
<tr>
<th>Type of opioid</th>
<th>How derived</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural opioid (opiate)</td>
<td>Alkaloid derived from plants such as opium poppy</td>
<td>Morphine, codeine</td>
</tr>
<tr>
<td>Semi-synthetic</td>
<td>Created in labs from natural opioids</td>
<td>Heroin, hydrocodone, hydromorphone, oxycodone, buprenorphine</td>
</tr>
<tr>
<td>Fully synthetic</td>
<td>Completely man-made</td>
<td>Fentanyl, levorphanol, meperidine, methadone, tramadol</td>
</tr>
</tbody>
</table>
Opioid Use Disorders and Pregnancy (continued)

**OPIOID PAIN MANAGEMENT AND TREATMENT PLANNING**

Treatment of chronic, non-cancer related pain should begin with non-pharmacological interventions. If pharmacological interventions are necessary, non-narcotic medications such as acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) should be tried first. Second-line pharmacological interventions include adjunctive therapy with anticonvulsants or antidepressants [tricyclic antidepressants (TCAs) or serotonin/norepinephrine reuptake inhibitor (SNRI) medications], as long as benefits outweigh risks and there are no contraindications to treatment in pregnancy (Kapman and Jarvis, 2015).

Special considerations are needed when treating pain in the context of opioid use disorder. Pregnant women with opioid use disorder are more likely to seek prenatal care late in pregnancy, miss appointments, experience poor weight gain, or exhibit signs of withdrawal or intoxication. Opioid agonists such as methadone and buprenorphine are the recommended treatments for medication-assisted therapy.

### Table 12.

**Signs and Symptoms of Opioid Intoxication and Withdrawal**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description and Signs/Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid Intoxication</td>
<td>Euphoria commonly followed by apathy, dysphoria, psychomotor agitation or retardation and impaired judgement during or shortly after opioid use. Pupillary constriction and one or more of the following: drowsiness/coma, slurred speech and impairment in attention or memory occur.</td>
</tr>
<tr>
<td>Opioid Withdrawal</td>
<td>Withdrawal is defined as cessation or reduction in opioid use that has been heavy and prolonged. Signs/symptoms of opioid withdrawal include dysphoric mood, nausea/vomiting, muscle aches, lacrimation or rhinorrhea, pupillary dilation, piloerection or sweating, diarrhea, yawning, fever, or insomnia.</td>
</tr>
</tbody>
</table>

**OPIOID USE DURING PREGNANCY: POTENTIAL PREGNANCY-RELATED COMPLICATIONS**

Opioid use during pregnancy is associated with increased risk of low birth-weight, respiratory issues, third trimester bleeding, toxemia, and mortality. Opioid exposure during pregnancy has also been associated with multiple complications, including preeclampsia, miscarriage, premature delivery, fetal growth restriction, fetal death, postnatal growth deficiency, microcephaly, neurobehavioral issues, and sudden infant death syndrome (SIDS).

It is difficult to ascertain whether these problems are due to opioid use, withdrawal, or co-occurring use of other drugs. Other factors that may contribute to obstetric complications include concomitant maternal medical, nutritional, and psychosocial issues, as well as comorbid psychiatric conditions or treatments.
Neonatal Abstinence Syndrome (NAS)

Opioid use during pregnancy is associated with pregnancy complications such as neonatal abstinence syndrome (NAS), where opiate exposure in-utero leads to a postnatal withdrawal syndrome. It is estimated that 45% to 94% of infants exposed in-utero can be affected by NAS, which is characterized by hyperactivity of the central and autonomic nervous systems. Signs and symptoms of NAS may include irritability, feeding difficulties, tremors, hypertonia, emesis, loose stools, seizures, and respiratory distress.

The appearance of NAS symptoms correspond with the half-life and duration of action of the opioid used. Treatment of NAS is considered adequate if the infant has rhythmic feeding and sleep cycles, as well as optimal weight gain.

Neurobehavioral Disorder Associated with Prenatal Opioid Exposure

Data on long-term outcomes of infants with in-utero exposure to opioids is limited. Earlier research studies have not found significant differences in the cognitive development of children up to 5 years old exposed to methadone in-utero compared to control groups. Control groups were matched for age, race, and socioeconomic status. Scores in the group of opioid exposed children were commonly lower when compared with population data (ACOG, 2012).

Opioid Agonist Treatment and Breastfeeding

Mothers receiving methadone or buprenorphine for treatment of opioid use disorders are encouraged to breastfeed. Additional precautions are warranted for women with concomitant medical or substance use disorders (Kapman and Jarvis, 2015).

There is some evidence of benefit in breastfeeding for women who are enrolled in methadone programs. Benefits include improved mother-infant bonding and positive effects on NAS.

One study examining buprenorphine in breastfeeding found that the level of buprenorphine metabolites secreted in breastmilk are so low that they pose little risk to the breastfeeding infant (LactMed, 2017).

Opioid Use Disorder Treatment: Medication-Assisted Therapy (MAT) with Opioid Agonists versus Withdrawal Management

Substitution treatment refers to transitioning opioid-dependent individuals to pharmacological management with an opioid agonist such as methadone, given in safe doses that are sufficient to prevent symptoms of withdrawal and reduce or eliminate drug cravings. Drug withdrawal treatment refers to slowly weaning the opioid agent until withdrawn completely.

Substitution treatment with opioid agonists is the standard of care pregnant women physically dependent on opioids. Pregnant women physically dependent on opioids should receive treatment using agonist medications rather than withdrawal management or abstinence as these latter methods may pose risks to the fetus.

Research has shown that withdrawal management is inferior in effectiveness to pharmacotherapy with opioid agonists. Withdrawal management increases the risk of relapse without concurrent benefit to mother or fetus.
Opioid Use Disorders and Pregnancy (continued)

- **Opioid Agonist Treatment in Pregnancy**
  - **Methadone**
    Methadone is the current standard of care for treatment of opioid use during pregnancy.
    Benefits include:
    - Improved newborn outcomes despite risk of Neonatal Abstinence Syndrome (NAS).
    - Improved maintenance of steady blood levels, leading to less withdrawal episodes that can be harmful to the fetus.
    - May reduce fetal exposure to illicit opioids.
  - **Buprenorphine**
    The evidence base for buprenorphine is less than that seen with methadone. However, some recent study results indicate potential advantages of buprenorphine (i.e., buprenorphine without naloxone) over methadone (Jones et al, 2010). These include:
    - Shorter hospital stays for infants born to buprenorphine treated mothers versus methadone treated mothers (10 days vs. 17.5 days, respectively)
    - Shorter treatment durations for NAS in buprenorphine treated mothers versus methadone treated others (4.1 days vs. 9.9 days, respectively)
    - Lower required cumulative dose of morphine for buprenorphine treated mothers versus methadone treated mothers (1.1 mg vs 10.4 mg, respectively).

- **Opioid Antagonist Use in Pregnancy**
  - **Naltrexone**
    It is appropriate to discontinue use of naltrexone if a woman becomes pregnant as long as the individual receiving treatment and clinician agree that the risk of relapse is low. If the individual receiving treatment is very concerned about relapse and wishes to remain on naltrexone, it is important to advise her of the associated risks of staying on naltrexone.
  - **Naloxone**
    Naloxone should only be used in case of maternal overdose to save the mother’s life. Naloxone or naltrexone may induce withdrawal, which may precipitate preterm labor or fetal distress.
NOT RECOMMENDED:

- Buprenorphine/Naloxone combination
  
  **Note:** There is insufficient evidence to recommend the combination of buprenorphine/naloxone formulation in pregnant patients. Buprenorphine without naloxone (i.e., buprenorphine monoprod) is recommended instead.

- Opioid Use During Breastfeeding
  
  - **Heroin**
    
    Case reports indicate that addiction can occur in breastfed infants of heroin-using mothers, and heroin can cause amenorrhea-galactorrhea syndrome in the mother. Use of heroin carries the additional risk of breastmilk contamination with a variety of chemicals that may be found in illicit heroin (Lactmed, 2017).

  - **Oral Opioids**
    
    Maternal use of oral opioids during breastfeeding can cause infant drowsiness, poor weight gain, hypotonia, central nervous system depression, and death in the breastfed infant. Newborn infants are particularly sensitive to the effects of even small doses of narcotic analgesics; therefore, it is best to provide pain control with a non-narcotic analgesic. Infants should be monitored for signs and symptoms of opioid intoxication, including sedation, poor weight gain, hypotonia, and breathing difficulties (LactMed, 2017).
### Medications Used for Opioid Withdrawal

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of Action</th>
<th>Dosing Recommendations</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Partial mu opioid receptor agonist</td>
<td>2 to 16 mg/day</td>
<td>Neonatal withdrawal is noted when used in pregnant patients. Neonatal abstinence syndrome is less severe with buprenorphine compared to methadone.</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Alpha-2 adrenergic agonist</td>
<td>0.1 to 0.3 mg every 6 to 8 hours. Max dose: 1.2 mg/day</td>
<td>Hypotensive effects limit dose.</td>
</tr>
<tr>
<td>Methadone</td>
<td>Mu opioid receptor agonist</td>
<td>Start taper at 20 to 30 mg/day up to a max of 60 to 120 mg/day</td>
<td>Monitor for QT prolongation and other arrhythmias. Neonatal withdrawal is noted when used in pregnant patients. Neonatal abstinence syndrome is less severe with buprenorphine compared to methadone.</td>
</tr>
</tbody>
</table>

Notes:

◊ Methadone and buprenorphine (i.e., buprenorphine without naloxone) have the most evidence for use in pregnant women who are physically dependent on opioids.

† Methadone dosing during pregnancy requires adjustment in the second and third trimesters due to increased metabolism and circulating blood volume. Therefore, increased or split methadone dosing is suggested as pregnancy progresses.

* Clonidine is not FDA-approved for opioid withdrawal. However, clonidine is recommended off-label in the British Association of Psychopharmacology (2012) guidelines and in the American Psychiatric Association Substance Use Treatment guidelines (2010) for treatment of opioid withdrawal. Other drugs in the same class such as guanfacine may also be used off-label to treat opioid withdrawal symptoms.
### Level 0 - Screening, brief intervention, and collaborative/integrated care.

Comprehensive assessment of mother and baby’s health status. Refer to *Principles of Practice* on pages 8 and 9.

Rule out alternative diagnoses.

Counseling and testing for HIV, hepatitis B and C, and liver function is suggested. Hepatitis A and B vaccination is recommended for those with negative serology.

*Note: At each level, coordinate care between all care providers (e.g., obstetrician, psychiatrist, addiction medication specialist).*

#### Useful tools for screening of opioid withdrawal:

- **Objective Opioid Withdrawal Scale (OOWS).** The Objective Opioid Withdrawal Scale (OOWS) relies on observation by the clinician and is useful when documenting the objectively measurable symptoms of opioid withdrawal.

- **Subjective Opioid Withdrawal Scale (SOWS).** The Subjective Opioid Withdrawal Scale (SOWS) relies on the patient’s rating of opioid withdrawal on a 16 item scale.

- **Clinical Opiate Withdrawal Scale (COWS).** The Clinical Opiate Withdrawal Scale is an 11 item, clinician-rated assessment tool. It is used clinically to follow course of withdrawal and effectiveness of medication treatment. It is a symptom triggered withdrawal rating scale, utilizing subjective and objective symptoms.

### Level 1 - Evidence-based psychosocial intervention with a qualified therapist if no evidence of chronic, repetitive substance use or physical dependence on opioids.

- Monitor response to evidence-based psychosocial treatments using reliable and valid measures of changes in the target symptoms.

- If pregnant and physically dependent on opioids, proceed to Level 2.
Management of Opioid Use Disorders and Opioid Withdrawal During Pregnancy (continued)

<table>
<thead>
<tr>
<th>Level 2 - Monotherapy with either buprenorphine without naloxone or methadone in conjunction with psychosocial treatment if pregnant and physically dependent on opioids.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication-assisted therapy (buprenorphine or methadone) is recommended over abstinence for individuals with severe, chronic opioid use due to potential adverse effects of opioid withdrawal such as increased risk of abortion and preterm birth, and potential risk of relapse.</td>
</tr>
<tr>
<td>Based on clinical consensus, buprenorphine is preferred over methadone due to evidence of improved neonatal outcomes with buprenorphine [e.g., milder neonatal abstinence syndrome (NAS), shorter duration of NAS treatment, higher average birth weights with buprenorphine treatment compared with methadone treatment] .</td>
</tr>
<tr>
<td>For highly motivated individuals, can attempt abstinence in the 2nd trimester under close supervision of an addiction medicine specialist.</td>
</tr>
<tr>
<td>Psychosocial treatments that may be effective in conjunction with methadone or buprenorphine monotherapy include cognitive behavioral therapy, contingency management, relapse prevention, and motivational interviewing. See table 2 on pages 10 through 13 for evidence-based therapies used in treatment of substance use disorders.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 3 - No recommendations.</th>
</tr>
</thead>
<tbody>
<tr>
<td>There are no recommendations appropriate for Level 3 based on the evidence.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 4 - No recommendations.</th>
</tr>
</thead>
<tbody>
<tr>
<td>There are no recommendations appropriate for Level 4 based on the evidence.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 5 - If no access to medication-assisted therapy with buprenorphine without naloxone or methadone, continue with current opioid regimen to prevent fetal withdrawal.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Recommended:</td>
</tr>
<tr>
<td>✦ Long-acting naltrexone (Vivitrol)</td>
</tr>
<tr>
<td>✦ Buprenorphine/naloxone combination</td>
</tr>
</tbody>
</table>

*Note: Level 5 recommendation based on expert consensus alone.*
### Methadone versus Buprenorphine for Medication-Assisted Therapy

#### Table 14.

<table>
<thead>
<tr>
<th></th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Full mu receptor agonist</td>
<td>Partial mu receptor agonist</td>
</tr>
<tr>
<td><strong>Use</strong></td>
<td>More effective for severe dependence</td>
<td>Used for mild to moderate dependence</td>
</tr>
<tr>
<td><strong>Half life</strong></td>
<td>24 to 36 hours</td>
<td>36 to 48 hours</td>
</tr>
<tr>
<td><strong>Route</strong></td>
<td>Oral</td>
<td>Sublingual</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>Daily dose</td>
<td>Daily to 3 times per week</td>
</tr>
<tr>
<td><strong>Accessibility</strong></td>
<td>Opioid treatment program</td>
<td>Physician’s office or opioid treatment program</td>
</tr>
<tr>
<td><strong>Abuse potential</strong></td>
<td>More abuse potential</td>
<td>Less abuse potential</td>
</tr>
<tr>
<td></td>
<td>Less risk of injection misuse with oral liquid</td>
<td>Risk of injection misuse with sublingual tablet preparation</td>
</tr>
<tr>
<td><strong>Overdose risk</strong></td>
<td>No protective overdose factors</td>
<td>Ceiling effect limits risk of overdose</td>
</tr>
<tr>
<td><strong>Withdrawal</strong></td>
<td>Moderate to severe, prolonged withdrawal</td>
<td>Mild withdrawal symptoms</td>
</tr>
<tr>
<td><strong>Common side effects</strong></td>
<td>Cardiac dysrhythmia, hypotension, diaphoresis, constipation, nausea, vomiting, dizziness, sedation</td>
<td>Headache, nausea, sweating, rhinitis, constipation</td>
</tr>
<tr>
<td><strong>Use in pregnancy</strong></td>
<td>Current standard of care in pregnancy</td>
<td>Combination buprenorphine/naloxone not recommended in pregnancy; use methadone or buprenorphine alone</td>
</tr>
</tbody>
</table>

Opioid Use Disorders: Summary

Background

Misuse of prescription and non-prescription opioids is a growing trend in the United States, leading to an unprecedented opioid epidemic. Since 1999, overdose deaths involving opioids have nearly quadrupled. Moreover, the Centers for Disease Control and Prevention reported that in 2015, drug overdose was a leading cause of accidental death in the United States; there were 52,404 lethal drug overdoses, of which 20,101 were due to prescription pain medications and 12,990 were from heroin use (CDC, 2016).

Opioid use during pregnancy occurs disproportionately in the Medicaid population. In 2012, 81% of babies with NAS were born to mothers enrolled in state Medicaid programs, reflecting a tendency of mothers with active opioid use during pregnancy to be from lower-income communities (NIDA, 2015). Use of prescription opioids has also increased since 2000; one study found that among Medicaid enrollees, between 2000 and 2005, prescription opioid use was three times higher in those with a dual diagnosis of non-cancer pain condition (NCPC) and a mental health or substance use disorder compared with a diagnosis of NCPC diagnosis alone. The study also found that enrollees with a NCPC diagnosis and mental health or substance use disorder diagnosis had a longer duration of opioid use and were prescribed more potent opioids than those with a NCPC diagnosis alone (Sullivan et al, 2008). Given the scope of the growing opioid epidemic, particularly among pregnant women and individuals with a dual diagnosis of non-cancer pain and mental health issues, early, integrated treatment is essential to preventing potential complications of opioid misuse and overuse.

Opioid Exposure During Pregnancy and Potential Complications

Opioid use during pregnancy has been associated with multiple pregnancy-related complications, effects on the fetus, and post-natal effects such as preeclampsia, fetal growth restriction, miscarriage, fetal death, premature delivery, postnatal growth deficiency, microcephaly, neurobehavioral problems, and sudden infant death syndrome (SIDS). In-utero exposure to opioids also leads to adverse neonatal outcomes, including low birth weight, respiratory complications, and neonatal abstinence syndrome (NAS). Between 2000 and 2009, there was a nearly five-fold increase in babies born with NAS related to opioid exposure in-utero (rate of 1.2 per 1000 births in the year 2000 versus 5.63 per 1000 births in 2009). The number of babies with NAS continues to rise; in 2012, an estimated 21,732 infants were born with NAS related to opioid exposure (NIDA, 2015).
MEDICATION-ASSISTED THERAPY (MAT) FOR OPIOID USE DISORDERS DURING PREGNANCY

Substitution therapy with long-acting opioid agonists is the standard of care in treating pregnant women who are physically dependent on opioids. Substitution therapy is preferred to abrupt cessation of or abstinence from opioids in physically-dependent pregnant women due to potential adverse effects such as premature labor, fetal distress, and miscarriage. Methadone, and more recently buprenorphine, are the two opioids commonly used for substitution therapy. While methadone has been more well-studied and is considered the current standard of care for opioid maintenance, studies done with buprenorphine indicate it is equally safe as methadone. Potential advantages of buprenorphine therapy include infants who experience less severe dependence after being exposed to buprenorphine versus methadone in-utero, less abuse potential with buprenorphine, a ceiling effect that limits risk of overdose with buprenorphine, and decreased hospital length-of-stay in infants of mothers treated with buprenorphine compared to methadone (Jones, 2010).
A problematic pattern of tobacco use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

- Tobacco is often taken in larger amounts or over a long period than was intended.
- There is a persistent desire or unsuccessful efforts to cut down or control tobacco use.
- A great deal of time is spent in activities necessary to obtain or use tobacco.
- Craving, or a strong desire or urge to use tobacco.
- Recurrent tobacco use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., interference with work).
- Continued tobacco use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of tobacco (e.g., arguments with others about tobacco use).
- Important social, occupational, or recreational activities are given up or reduced because of tobacco use.
- Recurrent tobacco use in situations in which it is physically hazardous (e.g., smoking in bed).
- Tobacco use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by tobacco.
- Tolerance, as defined by either of the following:
  - A need for markedly increased amounts of tobacco to achieve the desired effect.
  - A markedly diminished effect with continued use of the same amount of tobacco.
- Withdrawal, as manifested by either of the following:
  - The characteristic withdrawal syndrome for tobacco (i.e., four or more of the following signs/symptoms 24 hours after abrupt cessation or reduction in the amount of tobacco used: irritability, frustration or anger; anxiety; difficulty concentrating; increased appetite; restlessness; depressed mood; and/or insomnia).
  - Tobacco (or a closely related substance, such as nicotine) is taken to relieve and avoid withdrawal symptoms.
Cigarette Smoking

15-20% of women have been reported to smoke throughout pregnancy, despite intentions to refrain from smoking (Bruin et al, 2010).

75% of pregnant women who smoke report the desire to quit smoking, but only 20-30% successfully abstain from smoking (Bruin et al, 2010).

Cigarette smoking during pregnancy is associated with multiple adverse outcomes, including spontaneous abortion, placenta previa, placental abruption, preterm birth, stillbirth, fetal growth restriction, low birth weight, and sudden infant death syndrome (SIDS) (Thompson et al, 2009; Bruin et al, 2010).

Secondhand smoke exposure of the infant after delivery increases risk of respiratory tract infections, ear infections, and SIDS.

Cigarette smoking has been shown to decrease serum prolactin levels and milk yield (Bruin et al, 2010).

Management of Smoking Cessation in Pregnancy

Clinicians should inquire about tobacco use and smoke exposure during every prenatal visit.

Cessation of tobacco use, prevention of exposure to secondhand smoke, and prevention of smoking relapse are recommended.

The U.S. Preventive Services Task Force recommends clinicians provide pregnancy-tailored counseling for those who smoke and offer effective tobacco dependence interventions to pregnant smokers at the first prenatal visit and throughout the course of pregnancy (USPSTF, 2015).

Pregnant women who smoke should be offered behavioral support.

In heavy smokers, limited studies have found that the combination of cognitive-behavioral therapy (CBT) and nicotine replacement therapy (NRT) is effective for smoking cessation; however, these studies were reported to have bias that influenced the results (Pollack et al, 2007; USPSTF, 2015).

The U.S. Preventive Services Task Force reports that use of nicotine replacement products or other pharmaceuticals for smoking cessation during pregnancy and lactation have not been sufficiently evaluated to determine the safety or efficacy of use (USPSTF, 2015).

Alternative FDA-approved treatments for smoking cessation such as varenicline and bupropion have more limited data regarding use in pregnancy and breastfeeding (Cressman, et al, 2012) and are not recommended.
Medications Used to Treat Smoking Cessation

**Nicotine Replacement Therapy (NRT)**
- Nicotine crosses the placenta, concentrates in fetal blood and amniotic fluid, and is detectable in breast milk during lactation, resulting in fetal and neonatal exposure to nicotine.
- One study of fifteen lactating women who smoked an average of 17 cigarettes per day found that during smoking, the breastmilk nicotine concentration was 200 micrograms/L.
- For nicotine replacement therapy, the 21 mg transdermal nicotine patch produced breastmilk nicotine concentrations similar to those found in women who smoked 17 cigarettes per day (Ilett et al, 2003).
- Steady-state breastmilk nicotine concentrations for nicotine patches were proportionate to doses delivered by the transdermal nicotine patch as follows:
  - 21 mg transdermal nicotine patch: 175 mcg/L breastmilk nicotine concentration
  - 14 mg transdermal nicotine patch: 140 mcg/L breastmilk nicotine concentration
  - 7 mg transdermal nicotine patch: 70 mcg/L breastmilk nicotine concentration

**Bupropion**
- Limited data exist on the use of bupropion in pregnant and breastfeeding mothers.
- Bupropion use during pregnancy has not been reported to be associated with increased risk of major congenital malformations (Chun-Fai Chan, et al, 2005; Yonkers et al, 2014).
- There is no evidence that bupropion is associated with a higher risk of spontaneous abortion compared to other antidepressants or among pregnant women taking bupropion for smoking cessation (Cressman et al, 2012).
- However, there have been case reports of breastfed infants having possible seizures in partially breastfed infants. Infants exposed to SSRIs and bupropion through breastmilk should be monitored for vomiting, diarrhea, jitteriness or sedation, and serum levels should be obtained to rule out toxicity if suspected (LactMed, 2017).

**Varenicline**
- There are limited data on the fetal effects of varenicline use during pregnancy, and no data on effects of infant exposure to varenicline during breastfeeding (Coleman, 2016; LactMed 2017).
Management of Smoking Cessation During Pregnancy

<table>
<thead>
<tr>
<th>Level 0 - Screening, comprehensive assessment and prenatal care by multidisciplinary team, and brief intervention. See Principles of Practice.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level 1 - Evidence-based psychosocial intervention with a qualified therapist.</strong> Evidence-based interventions include a combination of behavioral therapeutic approaches, telephone support, and self-help material.</td>
</tr>
<tr>
<td>Note: One method has not been proven more effective than another method; most interventions involve a combination of psychosocial treatments.</td>
</tr>
<tr>
<td>- Evidence suggests that adding a psychosocial mood management intervention to standard smoking cessation programs can increase long-term cessation rates in smokers with current and past depression compared with standard intervention alone.</td>
</tr>
<tr>
<td>- Recommend abstinence from cigarette smoking, tobacco, and nicotine use.</td>
</tr>
<tr>
<td>See Table 2 on page 10 through 13 for evidence-based psychosocial interventions for substance use disorders.</td>
</tr>
<tr>
<td><strong>Five A’s of Smoking Cessation (AHRQ, 2012):</strong></td>
</tr>
<tr>
<td>1. <strong>Ask</strong> the individual about smoking status at the first pre-natal visit and subsequent visits. The woman should choose the statement that best describes smoking status:</td>
</tr>
<tr>
<td>A. I have never smoked LESS THAN 100 cigarettes in my lifetime.</td>
</tr>
<tr>
<td>B. I stopped smoking BEFORE I found out I was pregnant, and I am not smoking now.</td>
</tr>
<tr>
<td>C. I stopped smoking AFTER I found out I was pregnant, and I am not smoking now.</td>
</tr>
<tr>
<td>D. I smoke some now, but I have cut down on the number of cigarettes I smoke SINCE I found out I was pregnant.</td>
</tr>
<tr>
<td>E. I smoke regularly now, about the same as BEFORE I found out I was pregnant</td>
</tr>
<tr>
<td>- If the answer given is (b) or (c), reinforce the decision to quit, congratulate on success in quitting, and encourage remaining smoke-free.</td>
</tr>
<tr>
<td>- If the answer given is (d) or (e), document smoking status and proceed to the steps below.</td>
</tr>
<tr>
<td>2. <strong>Advise</strong> the individual who smokes to cease smoking by providing evidence about the risks of continued use to the individual and fetus or infant.</td>
</tr>
<tr>
<td>3. <strong>Assess</strong> the individual’s willingness to attempt to quit smoking. Motivational techniques should be utilized.</td>
</tr>
<tr>
<td>4. <strong>Assist</strong> the individual interested in quitting by providing pregnancy-specific self-help smoking cessation materials. Encourage importance of a smoke-free space at home and seeking out a “quitting buddy” (e.g., former smoker or non-smoker). Encourage talking about the quitting process. Refer resources such as smoker’s quit line, 1-800-QUIT NOW for ongoing counseling and support.</td>
</tr>
<tr>
<td>5. <strong>Arrange</strong> follow-up visits to track the individual’s attempt to quit smoking. For current and former smokers, monitor and record smoking status throughout pregnancy. Congratulate and support success, reinforce steps taken towards quitting, and advise those still considering a cessation attempt at follow-up visits.</td>
</tr>
</tbody>
</table>
### Management of Smoking Cessation During Pregnancy (continued)

<table>
<thead>
<tr>
<th>Level</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| 2     | **No recommendations.**  
No recommendations for Level 2 based on evidence and clinical consensus. |
| 3     | **No recommendations.**  
No recommendations for Level 3 based on the evidence and clinical consensus. |
| 4     | **Consider nicotine replacement therapy if benefits outweigh risks.**  
There is insufficient evidence for the effects of pharmacological interventions (e.g., nicotine replacement therapy, bupropion) on the fetus or infant to recommend use of these methods for smoking cessation in pregnant or lactating women based on evidence alone.  
Based on clinical consensus, cigarette smoking exposes the fetus to more potentially harmful chemicals than nicotine alone; therefore, if abstinence is not possible, consider nicotine replacement therapy. |
| 5     | **Bupropion monotherapy if unable to tolerate nicotine replacement therapy.**  
There are limited data on bupropion use during pregnancy, including effects on the fetus/infant. |

**Not Recommended:**
- Varenicline

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**Florida Pediatric Psychiatry Hotline available to give guidance:**

1-866-487-9507
Other Stimulant Use and Pregnancy

Table 15. 

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description and Signs/Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulant Intoxication</td>
<td>Feeling of exhilaration, increased alertness, restlessness, increased energy, aggression, rambling speech, dilated pupils, delusions/hallucinations, irritability, nausea/vomiting, weight loss, changes in heart rate and blood pressure, insomnia, paranoia, impaired judgment, and/or depression as the drug wears off.</td>
</tr>
<tr>
<td>Stimulant Withdrawal</td>
<td>Fatigue, depression, sleep disturbances.</td>
</tr>
</tbody>
</table>

**CAFFEINE**

- Studies on the effects of caffeine on pregnancy and birth outcomes are mixed. Some studies have reported that high caffeine intake (>300 mg/day) during pregnancy is associated with lower birth weight and smaller head circumference of the infant (Watkinson and Fried, 1985).
- There is insufficient evidence to draw conclusions on the effectiveness of caffeine avoidance on birthweight and pregnancy outcomes. (Jahanfar and Jaafar, 2015; Brent, et al 2011).

**COCAIN**

- Cocaine use during pregnancy is associated with maternal migraines and seizures, premature rupture of membranes, preterm labor, placental abruption, hypertensive crises and spontaneous miscarriage (Forray, 2016).
- Neonates can experience cocaine intoxication and withdrawal. Signs and symptoms of intoxication may occur at much lower concentrations in tolerant newborns than in tolerant adults.
- There is no clear medication therapy for cocaine withdrawal or maintenance of abstinence from cocaine use. Evidence-based treatments for cocaine use in pregnancy include cognitive behavioral therapy (CBT), motivational interviewing (MI), and contingency management (CM). Monitor for suicidality when individuals are going through withdrawal and after withdrawal (Forray, 2016).
- There is no consensus regarding effects of prenatal cocaine exposure on long-term growth or achievement. Long-term effects on behavior and subtle effects on language have been documented with prenatal cocaine exposure (Behnke, 2013).
Other Stimulant Use and Pregnancy (continued)

**Amphetamines**

*Drugs of Abuse*

- **Methamphetamine**
  - *Methamphetamine use is not recommended during pregnancy.*
  - Methamphetamine use during pregnancy has similar effects as cocaine use.
  - Methamphetamine use has been associated with higher risk of preterm delivery, low Apgar scores, placental abruption, cardiac and structural neurological abnormalities, and neonatal mortality (Shah et al, 2012; Good et al, 2010).
  - Methamphetamine and cocaine have similar neurotoxic effects; however, the neurotoxic effects of methamphetamine may be more severe than those of cocaine (McCann and Ricaurte, 2004; Bennet et al, 1993).
  - There is also evidence that suggests increased risk of SIDS with in-utero methamphetamine exposure, even in babies who are not premature.

*Stimulants Used in Treatment of Attention-Deficit Hyperactivity Disorder*

- **Dextroamphetamine**
  - A large cohort study of 50,282 women found that therapeutic use of amphetamine in pregnancy showed no increased risk of congenital malformations (Milkovich and van der Berg, 1977; Golub et al, 2005).
  - However, amphetamine abuse is associated with effects similar to cocaine, including low birth weight, premature births, and neonatal mortality, thought to be related to fetal vasoconstriction from in-utero exposure (Plessinger and Woods, 1993).
  - Newborns exposed to amphetamines in-utero may also have structural neurological abnormalities, and can have jitteriness and trouble sleeping or eating after birth (Golub et al, 2005).
  - Intrauterine growth retardation, small-for-gestational age babies, and gestational hypertension have been reported with prescribed doses (Golub et al, 2005). Amphetamine use is not recommended during pregnancy.

- **Methylphenidate**
  - Studies on methylphenidate are limited.
  - One study found that methylphenidate abuse has been associated with premature birth, intrauterine growth retardation, and neonatal withdrawal syndrome (Forray, 2016).
**Stimulant Use (Other than Nicotine) and Breastfeeding**

- **Caffeine**
  - Caffeine appears in breastmilk rapidly after ingestion by the mother, with peak caffeine levels reported approximately 1 hour after a dose (LactMed, 2017).
  - Mothers with caffeine intakes equivalent to 10 or more cups of coffee per day have reported cases of infants with symptoms of fussiness, jitteriness, and poor sleep patterns. Studies in mothers drinking 5 cups of coffee daily have shown no stimulatory effects on infants 3 weeks or older (LactMed, 2017).
  - While some experts feel that caffeine ingestion up to 300 mg/day may be safe, preterm and young newborns metabolize caffeine very slowly, causing serum levels of caffeine and other metabolites to be similar to maternal levels (LactMed, 2017).
  - A lower daily intake of caffeine is preferable in mothers of preterm infants. The effects of other caffeinated beverages (e.g. cola, energy drinks) may have similar dose-related effects on breastfed infants (LactMed, 2017).
  - Coffee intake more than 450 mL/day has also been associated with lower breastmilk iron concentrations and may lead to mild iron deficiency anemia in some infants (LactMed, 2017).

- **Cocaine**
  - High concentrations of cocaine and its metabolites are found in breastmilk in studies of post-partum women who abused cocaine (LactMed, 2017).
  - Newborn infants are extremely sensitive to cocaine because they are unable to metabolize cocaine to the inactive compound (LactMed, 2017).
  - Serious adverse reactions have been reported in newborn infants exposed to cocaine through breastmilk (LactMed, 2017).
  - Women who have used cocaine should be advised not to breastfeed unless they have a negative maternal urine toxicology screen at delivery, have been abstinent for at least 90 days, are in a substance abuse treatment program and plan to continue the program post-partum, have approval of their substance abuse counselor, are engaged and compliant in prenatal care, and have no other contraindications to breastfeeding (LactMed, 2017).
AMPHETAMINES

Drugs of abuse

- Methamphetamine
  - Breastfeeding is not recommended in mothers who are actively abusing methamphetamine.
  - Random collections of breastmilk have found that methamphetamine and amphetamine are detectable in breastmilk and in the infant’s serum after lactating mothers abused methamphetamine (LactMed, 2017).

Stimulants Used in Treatment of Attention-Deficit Hyperactivity Disorder

- Dextroamphetamine
  - Dextroamphetamine is secreted in breastmilk.
  - The effect of dextroamphetamine in the milk on neurological development of the infant is not well studied.
  - Some evidence suggests that doses prescribed for medical indications may not have adverse effects on the nursing infant (LactMed, 2017).

- Methylphenidate
  - Methylphenidate levels reported in breastmilk range from 15.4 mcg/L in women receiving oral doses of 40 mg twice per day to 19 mcg/L in women receiving oral doses of 52 mg per day. The calculated infant dose was between 2.3 and 2.9 mcg/kg/day.
  - Limited evidence indicates that in prescribed doses for medical indications, methylphenidate levels in milk are low and may not have adverse effects on nursing infants.
  - The effects of neurological development from methylphenidate exposure through breastmilk are not well studied (LactMed, 2017).
Cannabis (Marijuana) Use and Pregnancy

BACKGROUND

According to the World Health Organization (WHO), cannabis is the most common illicit substance worldwide. Cannabis is the third most frequently used substance during pregnancy (WHO, 2017). Seventy-eight (78%) of women with cannabis use achieved abstinence during pregnancy (Forray, 2016).

Table 16.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description and Signs/Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis Intoxication</td>
<td>Euphoria, heightened perception (visual, auditory, taste), increased blood pressure and heart rate, red eyes, difficulty concentrating, decreased coordination, increased appetite, slow reaction time, paranoid thinking.</td>
</tr>
<tr>
<td>Cannabis Withdrawal</td>
<td>Insomnia/sleep disturbance, anxiety, depression, irritability, appetite loss, nausea, headache, chills, restlessness.</td>
</tr>
</tbody>
</table>

EFFECTS OF FETAL EXPOSURE TO CANNABIS DURING PREGNANCY

Cannabis use during pregnancy can lead to preterm labor, low birth-weight, small-for-gestational age babies, and admission to the neonatal intensive care unit. Adverse consequences of cannabis exposure during fetal and child development include decreased attention, decreased executive function, and poor academic achievement. Animal studies show that in-utero exposure to exogenous cannabinoids may cause impaired cognition and increased sensitivity to drugs of abuse. Studies in humans are limited (Ross et al, 2015). Use of marijuana (cannabis) and cannabis-containing products is not recommended during pregnancy.

CANNABIS USE AND BREASTFEEDING

Active compounds of marijuana (e.g. tetrahydrocannabinol) are excreted in breastmilk in small quantities. Marijuana may have effects on infant nervous system development. Mothers who use marijuana should be encouraged to reduce or abstain from marijuana use and minimize infant exposure to marijuana smoke (LactMed, 2017).
## Hallucinogens and Inhalants Use in Pregnancy

### Table 17. Other Substances of Abuse and Effects of Prenatal Exposure

<table>
<thead>
<tr>
<th>Substance</th>
<th>Signs/Symptoms of Intoxication</th>
<th>Signs/Symptoms of Withdrawal</th>
<th>Effects of Exposure During Pregnancy</th>
</tr>
</thead>
</table>
| **Hallucinogens** (e.g., LSD, PCP) | LSD – hallucinations, synesthesias, impulsivity, rapid heart rate and blood pressure, tremors, flashbacks.  
PCP – feeling of being separated from body and surroundings, hallucinations, problems with coordination, aggression, lack of pain sensation, increased blood pressure and heart rate, problem with memory, involuntary eye movements, seizures/coma. | Fatigue, irritability, reduced ability to experience pleasure. | LSD exposure in utero has been linked to limb defects, megacolon, sacral myelomeningocele, heart defects (e.g. Tetrology of Fallot, AV malformations), and hydrocephalus in infants born to mothers who used LSD during pregnancy.  
PCP exposure in utero has been linked to premature birth, respiratory distress, slowed mental and motor development, and abnormal attachment behavior. |
| **Inhalants** (e.g., benzene, petroleum ether, xylene, toluene) | Brief euphoria, decreased inhibition, dizziness, nausea/vomiting, involuntary eye movements, irregular heartbeat, tremors, rash around nose and mouth. | Nausea, excessive sweating, muscle cramps, agitation, tremors, convulsions, hallucinations. | Premature birth, miscarriage, chromosome damage, and delayed growth of skull after birth. |
## Summary Table: Substance Use—Signs/Symptoms of Intoxication and Withdrawal and Effects of Prenatal Exposure

### Table 18.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Signs/Symptoms of Intoxication</th>
<th>Signs/Symptoms of Withdrawal</th>
<th>Effects of Exposure During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Disinhibition of normal social functioning, euphoria (initially), dysphoria (as BAC increases), ataxia, poor judgment, memory loss, slurred speech, vomiting, confusion/disorientation, progressive lethargy, coma, respiratory depression, and death.</td>
<td>Fatigue, headache, insomnia, irritability or excitability, appetite loss, nausea and/or vomiting, palpitations, mood fluctuations, tremors, sweats, and delirium tremens.</td>
<td>Increased risk of miscarriage, preterm delivery, babies that are small-for-gestational age, low birthweight, stillbirth and infant mortality, Fetal Alcohol Spectrum Disorders.</td>
</tr>
<tr>
<td>Opioids</td>
<td>Euphoria commonly followed by apathy, dysphoria, psychomotor agitation or retardation and impaired judgement during or shortly after opioid use. Pupillary constriction and one or more of the following: drowsiness/coma, slurred speech and impairment in attention or memory occur.</td>
<td>Dysphoric mood, nausea/vomiting, muscle aches, lacrimation or rhinorrhea, pupillary dilation, piloerection or sweating, diarrhea, yawning, fever, or insomnia.</td>
<td>Fetal effects: low birthweight, respiratory issues, third trimester bleeding, toxemia and mortality. Opioid exposure during pregnancy has also been associated with obstetric complications such as preeclampsia, miscarriage, premature delivery, fetal growth restriction, and fetal death. Postnatal growth deficiency, microcephaly, neurobehavioral issues and sudden infant death syndrome (SIDS) have also been associated with in utero opioid use.</td>
</tr>
</tbody>
</table>
### Table 18. (continued)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Signs/Symptoms of Intoxication</th>
<th>Signs/Symptoms of Withdrawal</th>
<th>Effects of Exposure During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis-containing substances (e.g., marijuana, hashish)</td>
<td>Euphoria, heightened perception (visual, auditory, taste), increased blood pressure and heart rate, red eyes, difficulty concentrating, decreased coordination, increased appetite, slow reaction time, paranoid thinking.</td>
<td>Anxiety, depression, irritability, appetite loss, nausea, headache, chills, restlessness.</td>
<td>Animal studies show that in-utero exposure to exogenous cannabinoids may cause impaired cognition and increased sensitivity to drugs of abuse.</td>
</tr>
<tr>
<td>Sedative-hypnotics or anxiolytics (e.g. alprazolam, lorazepam, eszopiclone, zaleplon, zolpidem)</td>
<td>Slurred speech, incoordination, unsteady gait, nystagmus, impairment in cognition (e.g., attention, memory, stupor or coma).</td>
<td>Autonomic hyperactivity (e.g., sweating or pulse greater than 10 bpm), hand tremor, insomnia, nausea, vomiting; transient visual, tactile, or auditory hallucinations or illusions; psychomotor agitation, anxiety, grand mal seizures.</td>
<td>Neonatal withdrawal, neonatal flaccidity, respiratory depression. Benzodiazepines: Increased risk of facial clefts and possible increased risk of cardiac malformations with diazepam. Possible increased risks of facial and cardiac malformations with chlordiazepoxide.</td>
</tr>
<tr>
<td>Stimulants (e.g., cocaine, methamphetamine)</td>
<td>Feeling of exhilaration, increased alertness, restlessness, increased energy, aggression, rambling speech, dilated pupils, delusions/hallucinations, irritability, nausea/vomiting, weight loss, changes in heart rate and blood pressure, insomnia, paranoia, impaired judgment.</td>
<td>Fatigue, depression, sleep disturbances.</td>
<td>Cocaine use during pregnancy is associated with maternal migraines and seizures, premature rupture of membranes, preterm labor, placental abruption, hypertensive crises, and spontaneous miscarriage. Neurotoxic effects of methamphetamine use during pregnancy may be more severe than the effects of cocaine.</td>
</tr>
</tbody>
</table>
Table 18. (continued)

<table>
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<tr>
<th>Substance</th>
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                              |                                                                                               |                                               | PCP exposure in utero has been linked to premature birth, respiratory distress, slowed mental and motor development, and abnormal attachment behavior. |
| Inhalants (e.g., benzene, petroleum ether, xylene, toluene) | Brief euphoria, decreased inhibition, dizziness, nausea/vomiting, involuntary eye movements, irregular heartbeat, tremors, rash around nose and mouth. | Nausea, excessive sweating, muscle cramps, agitation, tremors, convulsions, hallucinations. | Premature birth, miscarriage, chromosome damage, and delayed growth of skull after birth. |
**Dual Diagnosis**

**Note:** See the Florida Medicaid Psychotherapeutic Medication Recommendations for Adults for treatment of behavioral health conditions in adults and the Florida Best Practice Recommendations for Psychotherapeutic Medication Use in Children and Adolescents for treatment of behavioral health conditions in children/adolescents for management of psychiatric co-morbidities (e.g., depression, anxiety).

**DEFINITION: TERMINOLOGY**

Dual diagnosis refers to individuals who experience mental illness and substance use problems simultaneously. Dual diagnosis symptoms range from mild depression to symptoms of bipolar disorder becoming more severe due to substance use during periods of mania. According to the National Institute of Mental Health, one-third of all people with mental illness and one-half of all people with severe mental illness experience substance use problems (NAMI, 2013).

**CONSEQUENCES OF PRENATAL DEPRESSION AND ANXIETY**

- Gestational hypertension and pre-eclampsia
- Preterm Birth
- Low Birth Weight
- Operative Delivery and NICU Admission
- Adverse Neurodevelopmental Effects

**DUAL DIAGNOSIS: TREATMENT CONSIDERATIONS**

Treatment of individuals with dual diagnoses involves integrated care for both the specific behavioral health conditions and substance use disorders. Treatment options depend on the severity of illness and include inpatient detoxification, inpatient rehabilitation, evidence-based therapy for both the behavioral health condition and substance use disorder, medication management for the behavioral health condition and/or substance use disorder as indicated, and self-help groups. Refer to the Florida Best Practice Psychotherapeutic Medication Guidelines for Adults for evidence-based treatment of behavioral health conditions in adults.

- Maternal Effects of Antidepressant Use During Pregnancy
  - **Tricyclic antidepressants:** Data are limited on the use of tricyclic antidepressants during pregnancy.
  - **SSRIs:** Pre-term birth (Wisner et al, 2009)
- Treatment Effects on Fetus and Neonates
  - **Tricyclic antidepressants**
    - **Fetal Effects:** The potential teratogenic effects of tricyclic antidepressants remain unclear. Clomipramine may be associated with increased risk of cardiac defects (Bourke et al, 2014).
    - **Neonatal Effects:** Tricyclic antidepressants have been associated with neonatal withdrawal symptoms with third-trimester exposure (Bourke et al, 2014).
  - **SSRIs**

[medicaidmentalhealth.org](http://medicaidmentalhealth.org)
Dual Diagnosis (continued)

✧ **Fetal Effects:** In-utero exposure to SSRIs in pregnancy has been linked to increased risk of developing Autism Spectrum Disorder (Boukhris et al, 2016; Freire et al, 2016). In terms of specific SSRIs, except paroxetine, which has most consistently been associated with increased risk of heart defects, data are mixed.

- Statistically significant associations between SSRI use and anencephaly, craniosynostosis, and omphalocele have been reported (Alwan et al, 2007). Some studies have shown an association between sertraline, fluoxetine, and citalopram and congenital defects, while others have not.
  - Sertraline has been associated with increased risk of omphalocele and septal defects (Kornum 2010; Byatt et al, 2013).
  - Fluoxetine has been associated with hypertrophic stenosis, congenital heart defects, and other abnormalities.
  - Citalopram has been associated with omphalocele, congenital heart defects, and neural tube defects (Byatt et al, 2013).
  - Paroxetine has been associated with increased risk of heart defects (Reis and Kallen 2010; Berard et al, 2017).

✧ **Neonatal Effects:** respiratory distress, low APGAR scores, persistent pulmonary hypertension in the newborn, jaundice, hypoglycemia, convulsions, heart rate variability, REM changes, jitteriness, serotonergic symptoms, low birth weight (Olivier et al, 2013).

- **Fluoxetine:** Poor adaptation
- **Paroxetine:** Serotonergic symptoms

✦ **Mood Stabilizers**

✧ **Lithium:** First-trimester exposure to lithium is associated with highest risk of Ebstein’s anomaly (van der Lugt, et al 2012).

✧ **Divalproex/Valproic acid:** Associated with neural tube defects, craniofacial defects, cardiovascular malformations, hypospadias, and limb malformations (Hill et al, 2010).

▲ Treatment Effects during Breastfeeding

✦ **SSRIs:** Mothers taking an SSRI during pregnancy and postpartum may have more difficulty breastfeeding and may need additional breastfeeding support. Breastfed infants exposed to an SSRI during the third trimester of pregnancy have a lower risk of poor neonatal adaptation than formula-fed infants. Occasional mild side effects such as insomnia, restlessness, and increased crying have been reported in breastfed infants of mothers on SSRIs (LactMed, 2017).

✦ **Mood Stabilizers:**

✧ **Lithium:** Cases of lithium intoxication and increases in TSH levels have been reported in neonates exposed to lithium through breastfeeding.

✧ **Divalproex/Valproic acid:** Theoretical increased risk of valproic acid-induced hepatotoxicity. One possible case of thrombocytopenia reported from valproic acid exposure through breastmilk (LactMed, 2017).
Reproductive Health Planning: Options for Pregnancy Prevention

**ORAL CONTRACEPTIVES**

Oral contraceptive (OC) pills (i.e., birth control pills) are the most commonly used method of birth control among women ages 15-44 years at 28% (Jones et al, 2012). Yet, OCs (combined and progestin-only pills) are considerably less effective than long-acting reversible contraceptive methods such as implants, levonorgestrel intrauterine systems (IUS) or intrauterine devices (IUDs). OCs have a 9% failure rate compared to less than one percent (1%) for implants and IUDs (CDC, 2017).

**ALTERNATIVES TO ORAL CONTRACEPTIVES**

Hormonal alternatives to oral contraceptives include the transdermal patch and the vaginal ring.

Table 19.

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose</th>
<th>Notes</th>
<th>Failure Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaginal Ring</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethinyl estradiol and etonorgestrel (NuvaRing®)</td>
<td>0.12 mg/day</td>
<td>Insert vaginally and leave in for 3 weeks and removed for one week.</td>
<td>9%</td>
</tr>
<tr>
<td><strong>Adolescents and Adults</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethinyl estradiol and norelgestromin (active form of norestimate)</td>
<td>Ethinyl estradiol: 35 mcg/day</td>
<td>Apply weekly for three weeks, then week 4 is patch free.</td>
<td>9%</td>
</tr>
<tr>
<td>[Ortho-Evra®]</td>
<td>Norelgestromin: 200 mcg/day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Long-acting reversible contraceptives (LARCs)

Long-acting reversible contraceptives (LARCs) are recommended to reduce rates of unintended pregnancies due to their high effectiveness rates. The American Congress of Obstetricians and Gynecologists (ACOG) considers implants, levonorgestrel intrauterine systems (IUS) or intrauterine devices (IUDs), and copper IUDs, long-acting reversible contraceptives (LARCs). The National Institute for Health and Care Excellence (NICE) guidelines also include progestogen-only injections as LARCs. Implants and IUDs have effectiveness rates similar to tubal ligation at less than one pregnancy per 100 women per year (ACOG, WHO).

ACOG guidelines indicate that LARCs “should be offered as first-line contraceptive methods and encouraged as options for most women.” Furthermore ACOG Committee Opinion #670 “encourages prenatal counseling of the most effective options for postpartum contraception: IUDs and the implant.” Women should be counseled about convenience and effectiveness of immediate postpartum LARC as well as benefits of reducing unintended pregnancy and lengthening inter-pregnancy intervals (ACOG, 2016).

Table 20.

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose</th>
<th>Notes</th>
<th>Failure Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etonorgestrel (Implanon® or Nexplanon ®)</td>
<td>Release rate varies over time for up to 3 years</td>
<td>Implanted subdermally just beneath skin at the inner side of non-dominant arm</td>
<td>0.05%</td>
</tr>
<tr>
<td>Injections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medroxyprogesterone acetate (Depo-Provera CI®)</td>
<td>150 mg intramuscular (IM) injection</td>
<td>Intramuscular (IM) injection in the gluteal or deltoid muscle every 3 months (13 weeks)</td>
<td>6%</td>
</tr>
<tr>
<td>Medroxyprogesterone acetate (Depo-subQ Provera 104®)</td>
<td>104 mg Subcutaneous (SC) injections</td>
<td>Subcutaneous (SC) injections into anterior thigh or abdomen, once every 3 months (12-14 weeks)</td>
<td>6%</td>
</tr>
<tr>
<td>Intrauterine devices (IUDs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copper IUD (ParaGard T380A®)</td>
<td>Non-hormonal</td>
<td>May remain in place for 10 years</td>
<td>0.8%</td>
</tr>
<tr>
<td>Levonorgestrel (Liletta®)</td>
<td>18.6-16.3 mcg at 1 year 14.3 mcg/day at 2 years 12.6 mcg/day at 3 years</td>
<td>Must be removed by end of third year</td>
<td>0.55%</td>
</tr>
<tr>
<td>Levonorgestrel (Mirena®)</td>
<td>20 mcg/day for up to 5 years</td>
<td></td>
<td>0.2%</td>
</tr>
<tr>
<td>Levonorgestrel (Skyla®)</td>
<td>14 mcg/day for up to 3 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel (Kyleena®)</td>
<td>Average dose of 9 mcg/day for up to 5 years</td>
<td>Must be removed by end of fifth year</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
Resources

**Substance Use and Mental Health**

- Centers for Disease Control and Prevention. Guideline for Prescribing Opioids for Chronic Pain. [https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm](https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm)
- Substance Abuse and Mental Health Services Administration. Substance Use Disorders. [https://www.samhsa.gov/disorders/substance-use](https://www.samhsa.gov/disorders/substance-use)

**Long-Acting Reversible Contraceptives**


**Medication Effects and Breastfeeding**

### List of Abbreviations

**AA:** Alcoholics Anonymous  
**ACOG:** American Congress of Obstetricians and Gynecologists  
**AHCA:** Agency for Healthcare Administration  
**AHRQ:** Agency for Healthcare Research and Quality  
**APA:** American Psychiatric Association  
**APGAR:** Appearance, Pulse Rate, Reflex irritability, Activity, Respiratory effort (scoring system for newborn health)  
**ARBD:** Alcohol-Related Birth Defects  
**ARND:** Alcohol-Related Neurodevelopmental Disorder  
**AUDIT:** Alcohol Use Disorders Identification Test  
**BAC:** Blood Alcohol Concentration  
**BCT:** Behavioral Couples Therapy  
**BNI:** Brief Negotiated Interview (brief interview screening method)  
**bpm:** beats per minute  
**CAGE:** Cut down, Annoyed, Guilty Feelings, Eye-Opener (alcohol screening questionnaire)  
**CBC:** Complete Blood Count  
**CBT:** Cognitive Behavioral Therapy  
**CDC:** Centers for Disease Control and Prevention  
**CET:** Cue Exposure Therapy  
**CIWA-Ar:** Clinical Institute Withdrawal Assessment for Alcohol Scale-Revised  
**CM:** Contingency Management  
**CMHCs:** Community Mental Health Centers  
**CMP:** Comprehensive Metabolic Panel  
**COWS:** Clinical Opiate Withdrawal Scale  
**CRAFFT:** Car, Relax, Alone, Forget, Friends, Trouble (alcohol screening questionnaire)  
**CST:** Coping Skills Training  
**CT:** Computed Tomography  
**DAST-10:** Drug Abuse Screening Test  
**DSM-5:** Diagnostic and Statistical Manual, 5th edition  
**DTs:** Delirium Tremens  
**DUI:** Driving Under the Influence (of Alcohol)  
**DWI:** Driving While Impaired  
**ED:** Emergency Department  
**FAS:** Fetal Alcohol Syndrome
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FASD</td>
<td>Fetal Alcohol Spectrum Disorders</td>
</tr>
<tr>
<td>FDA</td>
<td>U.S. Food and Drug Administration</td>
</tr>
<tr>
<td>FLO</td>
<td>Feedback, listening, information, options/goal-setting (brief intervention model for substance use)</td>
</tr>
<tr>
<td>FRAMES</td>
<td>feedback, responsibility, advice to change, menu of alternative goals/strategies, empathetic counseling, self-efficacy (brief intervention screening model for substance use)</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>IQ</td>
<td>Intelligence Quotient</td>
</tr>
<tr>
<td>IUD</td>
<td>Intrauterine Device</td>
</tr>
<tr>
<td>IUS</td>
<td>Intrauterine Systems</td>
</tr>
<tr>
<td>LARC</td>
<td>Long-Acting Reversible Contraceptive</td>
</tr>
<tr>
<td>LSD</td>
<td>Lysergic Acid Diethylamide</td>
</tr>
<tr>
<td>MAT</td>
<td>Medication-Assisted Therapy</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>mcg/day</td>
<td>micrograms per day</td>
</tr>
<tr>
<td>mcg/kg/day</td>
<td>micrograms per kilogram per day</td>
</tr>
<tr>
<td>mcg/L</td>
<td>micrograms per liter</td>
</tr>
<tr>
<td>MET</td>
<td>Motivational Enhancement Therapy</td>
</tr>
<tr>
<td>MI</td>
<td>Motivational Interviewing</td>
</tr>
<tr>
<td>mg</td>
<td>milligrams</td>
</tr>
<tr>
<td>mg/day</td>
<td>milligrams per day</td>
</tr>
<tr>
<td>mL</td>
<td>milliliters</td>
</tr>
<tr>
<td>mL/day</td>
<td>milliliters per day</td>
</tr>
<tr>
<td>NAMI</td>
<td>National Alliance on Mental Illness</td>
</tr>
<tr>
<td>NAS</td>
<td>Neonatal Abstinence Syndrome</td>
</tr>
<tr>
<td>NIAAA</td>
<td>National Institute on Alcohol Abuse and Alcoholism</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>NIDA</td>
<td>National Institute on Drug Abuse</td>
</tr>
<tr>
<td>NIMH</td>
<td>National Institute of Mental Health</td>
</tr>
<tr>
<td>NRT</td>
<td>Nicotine Replacement Therapy</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Non-Steroidal Anti-Inflammatory Drugs</td>
</tr>
<tr>
<td>OB</td>
<td>Obstetrics</td>
</tr>
<tr>
<td>OB-GYN</td>
<td>Obstetrician-Gynecologist</td>
</tr>
</tbody>
</table>
OCs: Oral Contraceptives
OOWS: Objective Opioid Withdrawal Scale
PCP: Phencyclidne
REM: Rapid Eye Movement
RPT: Relapse Prevention Therapy
SAMHSA: Substance Abuse and Mental Health Services Administration
SAWS: Short Alcohol Withdrawal Scale
SC: Subcutaneous
SD: Standard Deviation
SIDS: Sudden Infant Death Syndrome
SMI: Serious Mental Illness
SNRIs: Serotonin/Norepinephrine Reuptake Inhibitor
SOWS: Subjective Opioid Withdrawal Scale
SSRI: Selective Serotonin Reuptake Inhibitor
T-ACE: Tolerance, Annoyance, Cut Down, Eye-Opener (alcohol screening questionnaire)
TCAs: Tricyclic Antidepressants
TSH: Thyroid Stimulating Hormone
TWEAK: Tolerance, Worried, Eye opener, Amnesia, K/Cut down (alcohol screening questionnaire)
UDS: Urine Drug Screen
USPSTF: U.S. Preventive Services Task Force
VACTERL syndrome: A disorder that affects many body systems. VACTERL stands for vertebral defects, anal atresia, cardiac defects, trachea-esophageal fistula, renal anomalies, and limb abnormalities.
WHO: World Health Organization
### Appendix A: SAMHSA Brief Intervention Models

**Table 21.**

<table>
<thead>
<tr>
<th>SAMHSA Brief Intervention Models</th>
<th>Description and Link</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brief Negotiated Interview and Active Referral to Treatment: Provider Training Algorithm</strong></td>
<td>Flowchart created by Boston University School of Public Health; includes brief screening questions to ask during brief intervention. <a href="http://www.integration.samhsa.gov/clinical-practice/sbirt/Brief-negotiated_interview_and_active_referral_to_treatment.pdf">http://www.integration.samhsa.gov/clinical-practice/sbirt/Brief-negotiated_interview_and_active_referral_to_treatment.pdf</a></td>
</tr>
<tr>
<td><strong>Brief Negotiated Interview (BNI) Steps</strong></td>
<td>List of potential questions and responses providers may use during brief intervention. <a href="http://www.integration.samhsa.gov/clinical-practice/sbirt/Brief_Negotiated_Interview.pdf">http://www.integration.samhsa.gov/clinical-practice/sbirt/Brief_Negotiated_Interview.pdf</a></td>
</tr>
<tr>
<td><strong>FLO Model</strong></td>
<td>The FLO model involves providing feedback, listening and eliciting information, and exploring options/goal-setting to change substance use behaviors. <a href="http://hospitalsbirt.webs.com/FLO%20by%20Dunn%20and%20Field.pdf">http://hospitalsbirt.webs.com/FLO%20by%20Dunn%20and%20Field.pdf</a></td>
</tr>
</tbody>
</table>
| **FRAMES Model\*** | The FRAMES Model involves six components:
- **F** – Feedback of personal risk (e.g., drinking that contributes to medical comorbidities such as hypertension)
- **R** – Responsibility of the individual
- **A** – Advice to change
- **M** – Menu of alternative goals/strategies to reduce drinking/substance use
- **E** – Empathetic counseling

\*Not available in the public domain.

Appendix B: Components of Comprehensive Assessment and Brief Intervention

A Comprehensive Assessment Includes:

- A full range of psychiatric symptoms and disorders as well as impairment from these symptoms and disorders. Refer to the Florida Best Practice Psychotherapeutic Medication Guidelines for Adults.
- Risk assessment for substance use, misuse, and overdose.
- Suicide risk assessment.
- A full medical history.
- A relevant medical work up, physical examination and nutritional status evaluation.
- Family history, which includes past and current history of psychiatric illnesses, substance use and treatment history of parents, siblings and other relatives.
- Assessment of family structure and functioning.
- Assessment of environmental risk factors and stressors including history of abuse (physical, sexual) or neglect, traumatic life events, domestic violence, economic instability, etc.
- Use of screening tools to assess for and monitor co-morbid psychiatric symptoms with higher risk for substance use (e.g., depression).
- Use of collateral sources of information as appropriate (e.g., family members).
- Evaluation of the health of the fetus or infant.

Physical Examination

- Physical exam should include identifying physical signs of intoxication or withdrawal.

Note: Pregnant women with substance use disorders and severe mental illness may have more limited access to care. Pregnant women with substance use disorders may be more likely to seek care late in pregnancy, miss appointments, experience poor weight gain, or exhibit signs of withdrawal or intoxication.

Laboratory Tests

- Routine prenatal laboratory tests should be performed.
- Urine drug tests may be used to detect or confirm suspected substance use. These tests should be done with patient’s consent and in compliance with state laws.
- Counsel and test for HIV, hepatitis B and C, and liver function as indicated based on clinical history and physical examination (e.g., in cases of intravenous illicit opioid use).
Appendix B: Components of Comprehensive Assessment and Brief Intervention (continued)

Comprehensive Prenatal Care Includes:

- Assembling a multidisciplinary team of healthcare and social service providers.
- Scheduling frequent prenatal visits to monitor fetal and maternal health status and providing education.
- Evaluation of fetal health status by a trained professional throughout gestation.
- Referral for early ultrasound to confirm gestational age and establish an accurate baseline for tracking fetal growth/development.
- Monitoring for pregnancy complications (e.g. growth restriction, maternal withdrawal, third trimester bleeding) and referral for prenatal follow-up with OB-GYN.
- Communicating between providers (e.g. informing the pediatrician of the possibility of neonatal withdrawal).

Brief Intervention Includes:

- Population-specific, evidence-based motivational techniques to assess readiness to abstain from substance use and encouragement of positive lifestyle changes. The goal of brief intervention is to help individuals abstain from use of substances that are potentially harmful to the fetus.
- Education about the effects of substance use or misuse on the individual and, if pregnant or breastfeeding, on the fetus or infant.
- Education about the risks and benefits of continuing or discontinuing psychotherapeutic medications and/or medications for treatment of substance use (e.g., methadone or buprenorphine medication-assisted therapy for opioid use disorders) on the mother and fetus or infant.
- Addressing anxiety related to substance use disclosure and potential legal issues.

Additional Considerations in Treatment Planning:

- Abnormal laboratory results
- Absence of support network
- Acute illness
- Poorly controlled medical comorbidities (e.g., diabetes mellitus, chronic obstructive pulmonary disease)
- Serious mental illness (e.g., suicidal ideation, psychosis)
- Alcohol use: severe alcohol withdrawal symptoms, high risk of delirium tremens, history of alcohol withdrawal seizure
- Urine drug screen positive for multiple substances
Appendix C: Alcohol Use Screening Algorithm

**NIAAA 1-ITEM ALCOHOL PRE-SCREENER**

“How many times in the past year have you had 4 or more drinks in a day?”

**NIDA 1-ITEM DRUG USE PRE-SCREENER**

“How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?”

**The Health Belief Model**

**Figure 3.**

- Perceived Seriousness
- Perceived Susceptibility
- Perceived Threats
- Perceived Benefits versus Perceived Barriers
- Self-Efficacy
- Cues to Action

**Likelihood of Engaging in Health-Promoting Behavior**

Appendix E: 
Alcohol Use Disorders 
Severity of Alcohol Use and Hierarchy of Intervention

SEVERITY OF ALCOHOL USE AND HIERARCHY OF INTERVENTION

The chart below illustrates the severity of alcohol use disorders and intensity of treatment in the general population.

Figure 4.
References

References for Introduction:


DeCesaris. Prenatal Care for Women with Serious Mental Illness. Journal of Student Nursing Research [Internet] 2013 Jul [cited 2017 Apr 19]; 6(1). Available at: http://repository.upenn.edu/cgi/viewcontent.cgi?article=1018&context=josnr


References for General Principles of Practice:


References (continued)


References for Evidence-Based Psychosocial Interventions for Substance Use Disorders:


References for Breastfeeding and Substance Use: General considerations


References for Alcohol Use and Pregnancy:


References (continued)


References (continued)


References for Sedative-Hypnotic Use and Pregnancy:

Czeizel AE, Rockenbauer M, Sørensen HT and Olsen J. A population-based case-control study of oral chlordiazepoxide use during pregnancy and risk of congenital abnormalities.
References (continued)


References for Sedative/Hypnotic Use Disorders and Pregnancy:


References for Opioid Use Disorders and Pregnancy:


References for Cigarette Smoking, Nicotine, and Pregnancy:


References (continued)


References for Other Stimulant Use and Pregnancy:


Behnke M, Smith VC, the Committee on Substance Abuse, and the Committee on Fetus and Newborn. Prenatal substance abuse: short- and long-term effects on the exposed fetus [Internet]. Pediatrics. 2013 [cited 17 May 2017]; 131: e1009-1024.

Bennett BA, Hyde CE and Clodfelter JE. Differing neurotoxic potencies of methamphetamine, mazindol, and cocaine in mesencephalic cultures. J Neurochem. 1993 Apr; 60(4); 1444-52.


References (continued)


References for Cannabis Use and Pregnancy:


References for Dual Diagnosis and Pregnancy:


References for Reproductive Health Planning: Options for Pregnancy Prevention


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