CLINICAL GUIDELINES PROGRAM
NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV • HCV • STIs • SUBSTANCE USE • LGBTQ+ HEALTH

Substance Use Disorder Treatment in Pregnant Adults

Updates, Authorship, and Related Resources

Date of current publication	July 16, 2021
Intended users	Clinicians in New York State with patients who have substance use disorder(s) during pregnancy
Lead author	Kelly S. Ramsey, MD, MPH, MA, FACP
Writing group	Sharon Stancliff, MD; Lyn C. Stevens, MS, NP, ACRN; Christopher J. Hoffmann, MD, MPH; Charles J. Gonzalez, MD
Author and writing group conflict of interest disclosures	There are no author or writing group conflict of interest disclosures.
Date of original publication	July 16, 2021
Committee	Substance Use Guidelines Committee
Developer and funder	New York State Department of Health AIDS Institute (NYSDOH AI)
Development process	See Supplement: Guideline Development and Recommendation Ratings
Related NYSDOH AI resources	**Guidelines** • Substance Use Harm Reduction in Medical Care • Substance Use Screening, Risk Assessment, and Use Disorder Diagnosis in Adults • Treatment of Alcohol Use Disorder • Treatment of Opioid Use Disorder **Podcast** • Viremic—Cases in HIV

Substance Use Disorder Treatment in Pregnant Adults

Date of current publication: July 16, 2021
Lead author: Kelly S. Ramsey, MD, MPH, MA, FACP
Writing group: Sharon Stancliff, MD; Lyn C. Stevens, MS, NP, ACRN; Christopher J. Hoffmann, MD, MPH; Charles J. Gonzalez, MD
Committee: Substance Use Guidelines Committee
Date of original publication: July 16, 2021

Contents

Purpose of This Guideline

Goals: This guideline on the treatment of substance use disorders (SUDs) in pregnant adults (≥18 years old) was developed by the New York State Department of Health (NYSDOH) AIDS Institute (AI) to establish a New York State standard of care. The goal of this guideline is to ensure that healthcare providers in New York State are aware of and able to provide appropriate options for SUD treatment during pregnancy and to:

- Inform clinicians of available treatment options for SUDs to expand access to SUD treatment for pregnant individuals.
- Provide evidence-based recommendations to guide the management of substance use and SUDs during pregnancy.
- Promote a harm reduction approach to SUD treatment in pregnancy by providing practical strategies for reducing the negative consequences of drug and alcohol use during pregnancy.
- Increase awareness among healthcare providers about the stigma associated with drug and alcohol use during pregnancy.

→ KEY POINTS

- Healthcare providers who have a conscious or unconscious bias against pregnant patients who use drugs or alcohol may be reluctant to provide care or may make erroneous judgments about a patient's fitness as a parent [Terplan, et al. 2015].
- Discrimination and prejudice impede engagement in care, including prenatal care, and can impair parental and neonatal health outcomes [Rutman, et al. 2020; Jarlenski, et al. 2019; Stone 2015; Roberts and Nuru-Jeter 2010].

Use of this guideline: This guideline is intended for clinicians with patients who have SUDs during pregnancy. SUD treatment during pregnancy can be managed in various inpatient and outpatient settings. Communication and coordination among healthcare providers are essential.

Many aspects of SUD treatment are the same for pregnant and nonpregnant patients. The recommendations in this guideline focus on aspects of SUD treatment that *differ* for pregnant individuals; where appropriate, clinicians are referred to the following NYSDOH AI guidelines for more information:

- Treatment of Opioid Use Disorder
- Treatment of Alcohol Use Disorder
- Substance Use Harm Reduction in Medical Care

The recommendations presented here address the treatment of SUD in pregnant patients; they do not address the management of pregnancy itself.

Prevalence and Risks of Substance Use Disorder During Pregnancy

Prevalence

In 2018, the Centers for Disease Control and Prevention reported that in the United States, the number of pregnant individuals with opioid use disorder (OUD) at the time of labor and delivery more than quadrupled from 1999 to 2014 [Haight, et al. 2018]. In New York State, the rate of newborns with neonatal withdrawal syndrome (NOWS) per 1,000 delivery hospitalizations/newborn discharges increased from 2.6 in 2008 to 5.8 in 2014 [NYSDOH 2023].

There are few data on the prevalence of other substance use disorders (SUDs) in pregnant individuals. A population-based study of deliveries in Massachusetts between 2003 and 2007 found that 5% of mothers had an SUD, but only 66% were taking treatment [Kotelchuck, et al. 2017]. Among a total of 76,799 deliveries between 2003 and 2013 in Korea, 1211 (1.6%) women had an alcohol use disorder preceding delivery (AUD) [Oh, et al. 2020].

Estimates of substance *use* among pregnant individuals based on national surveys in the United States include:

- In 2018, approximately 4.7% of pregnant individuals reported cannabis use, 9.9% reported alcohol use, 0.9% reported opioid use, and 11.6% reported tobacco use in the last 30 days [SAMHSA 2019].
- **Alcohol:** In 2018, 19.6% of respondents in their first trimester and 4.7% in their second or third trimesters reported alcohol use in the last 30 days [England, et al. 2020]. Overall, 38.2% of pregnant respondents who reported alcohol use in the previous 30 days also reported using 1 or more other substances in the same period, most commonly tobacco and cannabis [England, et al. 2020].
- **Tobacco:** The overall prevalence of tobacco use during pregnancy in the United States continues to decline, but less significant declines have been reported among people of lower education levels and socioeconomic status [Drake, et al. 2018].
- **Cannabis:** The estimated prevalence of cannabis use in the last 30 days increased from 3.4% in 2002 to 2003 to 4.7% in 2018; over the same period, the prevalence of daily or near-daily cannabis use in the last 30 days increased from 0.9% to 1.5% [SAMHSA 2019; Volkow, et al. 2017].

However, these data are self-reported and, because of the stigma associated with substance use during pregnancy, may underestimate the extent of use.

Risks

Prenatal tobacco use and prenatal alcohol use have well-established obstetric, neonatal, and adverse developmental effects, and OUD often results in NOWS [Guille and Aujla 2019]. The data on most other substances suggest potential adverse effects, including low birthweight and premature birth, but the results are variable. For example, a population-based study of deliveries in Massachusetts between 2003 and 2007 found that women who received SUD treatment had lower odds of

premature birth (AOR 0.61, 95% CI 0.55-0.68), low birthweight (AOR 0.54, 95% CI 0.49-0.61), and neonatal mortality (AOR=0.49, 95% CI: 0.31–0.74) than those who did not receive treatment [Kotelchuck, et al. 2017].

In clinical studies, including those discussed below, it is difficult to quantify the degree to which the biological effects of the substance contribute to poor outcomes, compared with other health, socioeconomic, and environmental factors, such as polysubstance use, cigarette smoking, and lack of adequate prenatal care. Comprehensive prenatal care and appropriate SUD treatment are vital to promoting the health and well-being of the dyad.

Opioids: Opioid use during pregnancy has been associated with an increased risk of preterm birth and stillbirth [Kaltenbach, et al. 2018; Jones and Fielder 2015]. However, individuals receiving OUD treatment during pregnancy, compared to no treatment, had lower odds of preterm birth (0.51 [0.43–0.61]) and low birthweight (0.46 [0.39–0.55]) [Kotelchuck, et al. 2017].

Systematic reviews and meta-analyses have demonstrated that prenatal opioid exposure, compared with no exposure, is negatively associated with neurocognitive and physical development in children ≥6 months old [Yeoh, et al. 2019; Baldacchino, et al. 2014]. However, many of the studies included in the meta-analyses did not have control groups matched for familial, socioeconomic, and environmental risks, which may have contributed to observed cognitive differences. Another meta-analysis found no significant differences in developmental outcomes in children with prenatal exposure to buprenorphine or methadone compared with children who had no exposure to those substances when all studied had comparable levels of prenatal exposure to tobacco smoke [Nelson, et al. 2020].

Alcohol: Approximately 1 in 3 infants born to individuals with AUD display symptoms of fetal alcohol spectrum disorder (FASD). Subtle manifestations of FASD include slight learning disabilities or slight physical abnormalities; severe manifestations include central nervous system dysfunction, low IQ, microcephaly, delayed growth, and facial abnormalities [Miller 2018]. A multisite study using active case ascertainment methods estimated an FASD prevalence rate of 1% to 5% among first graders exposed to alcohol in utero [Muggli, et al. 2017]. In a study that compared children aged 9 and 10 years with and without prenatal alcohol exposure, exposure was associated with increased psychopathology, attention deficits, and impulsiveness [Lees, et al. 2020].

Alcohol use during pregnancy may increase the risk of miscarriage, stillbirth, and preterm delivery, and the risks may be more pronounced with heavy alcohol use [Bailey and Sokol 2011]. However, the role of sociodemographic and lifestyle factors that co-occur with alcohol use during pregnancy and the synergistic effects of these factors plus alcohol use is unclear. Most available studies evaluate the impact of alcohol use, not alcohol use disorder (AUD), before or during pregnancy. In a large cohort study from Korea, the diagnosis of AUD preceding birth was associated with an increased risk of intrauterine growth restriction but not associated with other birth complications [Oh, et al. 2020]. The increased risk was more marked in individuals diagnosed with AUD in the 12 months preceding birth.

Tobacco: Tobacco use during pregnancy has been linked to low birth weight, preterm birth, placental abruption, miscarriage, stillbirth, poor fetal neurodevelopment, sudden unexpected infant death, and various congenital disabilities [Anderson, et al. 2019; Akerman, et al. 2015; Cressman, et al. 2012; Forinash, et al. 2010].

Cannabis: A systematic review and meta-analysis found that individuals who used cannabis during pregnancy had an increase in the odds of anemia (pooled OR) =1.36: 95% CI 1.10 to 1.69) compared with women with no cannabis use [Gunn, et al. 2016]. In addition, the meta-analysis found that infants exposed to cannabis in utero had a decrease in birth weight (pOR=1.77: 95% CI 1.04 to 3.01) and an increased need for placement in the neonatal intensive care unit (pOR=2.02: 1.27 to 3.21) compared with infants whose mothers did not use cannabis [Gunn, et al. 2016]. In a large population-based, retrospective cohort study, the CUD rate among pregnant individuals increased from 2.8 to 6.9 per 1,000 deliveries from 2001 to 2012 [Shi, et al. 2021]. Prenatal CUD was associated with an increased likelihood that infants would be small-for-gestational-age (OR = 1.13, 95% CI = 1.08, 1.18), born preterm (OR = 1.06, 95% CI = 1.01, 1.12), of low birth weight (OR = 1.13, 95% CI = 1.07, 1.20), or would die within 1 year of birth (OR = 1.35, 95% CI = 1.12, 1.62). Infants born to a parent with CUD who also used tobacco had greater odds of preterm birth, low birth weight, hospitalization, and death associated with prenatal CUD than infants born to a parent who did not use tobacco [Shi, et al. 2021].

Cocaine and methamphetamine: Meta-analyses indicated that cocaine and specifically crack use during pregnancy may be associated with significantly higher odds of preterm delivery, low birth weight, and small-for-gestational-age infants [Dos Santos, et al. 2018; Gouin, et al. 2011]. However, the authors note several limitations in the studies, including the difficulty of accurately measuring illicit substance use patterns among women throughout pregnancy and a pattern of polysubstance use in this population, and they emphasize the impact of adverse personal and social circumstances on study outcomes [Gouin, et al. 2011].

The Maternal Lifestyle Study (MLS), a prospective, longitudinal study of infants with prenatal exposure to cocaine and other substances, found that after controlling for birth weight and indices of the caregiving environment, prenatal cocaine exposure was not associated with mental, psychomotor, or behavioral functioning through 3 years of age [Messinger, et al. 2004]. A similar longitudinal, controlled cohort study, the Infant Development, Environment, and Lifestyle (IDEAL) study, evaluated the effects of prenatal methamphetamine exposure on neonatal outcomes at birth and over time. Overall, investigators found no differences in maternal complications or newborn health outcomes [Smith, et al. 2015; Shah, et al. 2012]. Neonates exposed to methamphetamine in utero had smaller head circumferences and were shorter than neonates who were not exposed. Differences in height between the groups persisted through 3 years of age [Shah, et al. 2012; Zabaneh, et al. 2012]. An analysis through 7.5 years of age found no significant behavioral differences between infants/children with prenatal methamphetamine exposure and those with no exposure groups [Chu, et al. 2020].

Even if substance use treatment is declined, reaching and engaging pregnant individuals who use substances may improve prenatal care and support harm reduction. In a retrospective cohort study, pregnant individuals who used drugs who obtained prenatal care delivered infants of greater weight and with larger head circumferences than did those who obtained no care ($P < .05$) [Berenson, et al. 1996]. In another retrospective cohort study that stratified results by the intensity of prenatal care received and current injection drug use, status among pregnant individuals, greater engagement in prenatal care (i.e., care utilization) improved outcomes [El-Mohandes, et al. 2003]. In addition, the risk for prematurity, low birth weight, and small-for-gestational-age infants decreased regardless of IDU status.

Efforts at the healthcare delivery level to increase engagement in care can involve collocating and coordinating prenatal, perinatal, substance use, mental health, and trauma and violence treatment, including social services. Integrating the different aspects of care helps pregnant individuals get to appointments, address multiple needs, and participate in clinic programming [Rutman, et al. 2020].

Goals of Substance Use Disorder Treatment During Pregnancy

For recommendations on substance use screening during pregnancy, see the NYSDOH AI guideline Substance Use Screening, Risk Assessment, and Use Disorder Diagnosis in Adults.

Pregnancy is not a contraindication for substance use disorder (SUD) treatment. Treatment can be managed in various settings by perinatal, primary care, or SUD specialty providers. SUD treatment and other aspects of care for pregnant patients should be coordinated among healthcare providers.

SUD treatment goals during pregnancy can include:

- Abstaining from or reducing substance use
- Preventing adverse effects of substance use or withdrawal for the pregnant individual and fetus
- Staying in care, which can also facilitate prevention, diagnosis, and treatment of other conditions
- Reducing high-risk behaviors, such as injection drug use and use or reuse of unsterile equipment and sharing injection equipment, and reducing related complications, such as infection and overdose
- Improving the quality of life and other social conditions, such as employment, stable housing, and risk of incarceration

Barriers to care: Engagement in substance use care is associated with better maternal and neonatal outcomes [Minozzi, et al. 2020; Chamberlain, et al. 2017; Binder and Vavrinková 2008; O'Connor and Whaley 2007]. However, pregnant individuals who use substances can face substantial obstacles to healthcare access, ranging from lack of transportation to fear of legal consequences, which may delay care until late in the pregnancy or the point of delivery [Stone 2015]. Pregnant Black women are more likely to be tested for drug use during pregnancy and referred to child protective services than their non-Black counterparts despite equivalent rates of positive drug tests between the 2 groups [Kunins, et al. 2007]. The influence of implicit care provider bias and institutional racism in the healthcare system on these different testing and reporting rates cannot be ignored. Most states have laws requiring the reporting of prenatal drug exposure [Guttmacher Institute 2022]. Fear of being reported, legal action, and child services involvement may lead to the avoidance of prenatal or substance use treatment and possible negative health consequences for the parent and infant [Angelotta, et al. 2016; House, et al. 2016; Stone 2015].

Opioid Use Disorder Treatment During Pregnancy

Note: Many aspects of opioid use disorder (OUD) treatment in pregnant individuals are similar to treatment in nonpregnant individuals, including the preferred medications. The recommendations below focus on *differences* in treatment during pregnancy; consult the NYSDOH AI guidelines Treatment of Opioid Use Disorder and Substance Use Harm Reduction in Medical Care for additional recommendations.

☑ RECOMMENDATIONS

Opioid Use Disorder Treatment

- Clinicians should advise their patients to avoid abrupt discontinuation of opioids, including BUP or methadone, during pregnancy because of the risks posed by withdrawal or resumption of unhealthy use (i.e., heroin) following abstinence. (B2)
- When offering pregnant patients BUP treatment or referral to an OTP for methadone treatment, clinicians should discuss the maternal and fetal risks and benefits of both medications (see Table 1: Considerations in Choosing Methadone or Buprenorphine for OUD Treatment During Pregnancy); the treatment choice should be based on patient preference whenever possible. (A3)
- Clinicians should educate patients who take opioids, BUP, or methadone during pregnancy about the risk of NOWS, an expected and treatable outcome (see guideline section Neonatal Opioid Withdrawal Syndrome). (A3)
- Clinicians should inform patients that breastfeeding while taking BUP or methadone is safe and may reduce the risk of NOWS. (A2)
- Clinicians should not recommend naltrexone initiation, which requires withdrawal from opioids, for a pregnant patient who is actively using opioids. (A2)
  - If a pregnant patient is abstinent from opioids and requests treatment with naltrexone, clinicians should discuss naltrexone as an alternative treatment and inform the patient of the associated risks and benefits. (A3)
  - Clinicians should inform patients who become pregnant while taking naltrexone of the risks and benefits and preferred pharmacologic treatment options (see Table 2: Benefits and Risks of Continuing or Stopping Naltrexone During Pregnancy). (B3)
- Before initiating BUP in a pregnant patient with OUD, clinicians should confirm that the patient is experiencing at least mild opioid withdrawal symptoms (B3) and should consult with an experienced substance use treatment provider regarding the risk of precipitated withdrawal. (A3)
- Clinicians should advise patients who initiate BUP or methadone during pregnancy, and those who become pregnant while taking BUP or methadone, to continue treatment throughout pregnancy, labor, delivery, postpartum, and breastfeeding. (A2)
- At each visit, clinicians should monitor pregnant patients taking BUP for opioid cravings and withdrawal symptoms and, if present, increase the dose as appropriate for the individual and reassess at the next visit; any dose increase should be maintained until treatment goals can be evaluated postpartum. (A3)
  - If taking a dose of 32 mg BUP mg daily does not allow the patient to meet treatment goals, clinicians should recommend methadone treatment. (A3)
- If a pregnant patient is considering a change from methadone to BUP, the clinician should consult an experienced substance use treatment provider because of the risk of precipitated withdrawal. (A3)

Abbreviations: BUP, buprenorphine; NOWS, neonatal opioid withdrawal syndrome; OTP, opioid treatment program.

Avoid opioid withdrawal: Abrupt discontinuation of opioids, including BUP or methadone, should be avoided during pregnancy to prevent or minimize withdrawal symptoms. Consultation with an experienced substance use treatment provider may be appropriate. Inconsistent opioid levels during pregnancy may precipitate withdrawal in the fetus, which can harm placental function and can increase the risks of NOWS, stunted growth, preterm labor, fetal convulsions, and fetal death [Hudak and Tan 2012; Kaltenbach, et al. 1998].

Maternal and fetal risks and benefits of opioid use and treatment: Treatment with BUP or methadone is the standard of care for OUD in pregnant patients (see SAMHSA Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants). Treatment with BUP or methadone reduced use of opioids and decreased risk of preterm

delivery, low infant birth weight, and transmission of HIV to the neonate [Minozzi, et al. 2020; ACOG(a) 2017; Saia, et al. 2016; Wiegand, et al. 2015; Gawronski, et al. 2014; Mozurkewich and Rayburn 2014; Lund, et al. 2013; Wong, et al. 2011; Jones, et al. 2010; Binder and Vavrinková 2008]. Table 1, below, summarizes the risks and benefits of BUP and methadone.

Although infants exposed to BUP or methadone can experience NOWS, the severity of symptoms is reduced when the mother is taking medication for OUD treatment [Brogly, et al. 2014; Fajemirokun-Odudeyi, et al. 2006]. The risk of NOWS does not differ based on treatment with BUP or methadone, but studies indicate that infants exposed to BUP/NLX in utero are less likely to require treatment for NOWS than those exposed to other opioid agonist medications, including BUP, methadone, or long-acting opioids [Link, et al. 2020]. In a study comparing BUP and methadone treatment during pregnancy, neonates exposed to BUP had significantly less severe NOWS, a shorter duration of treatment for NOWs, and shorter hospital stay than those exposed to methadone [Jones, et al. 2010].

A long-term study of infants exposed to BUP or methadone in utero reported healthy growth and cognitive and psychological development at 36 months of age for both groups [Kaltenbach, et al. 2018]. In addition, a recent meta-analysis found no significant differences in cognitive development scores in children up to 5 years old with and without prenatal exposure to methadone or BUP [Nelson, et al. 2020].

Buprenorphine monoformulation or buprenorphine/naloxone: A recent systematic review of 5 studies with 6 study groups found no significant differences in adverse maternal and neonatal outcomes when comparing BUP/naloxone (NLX) or methadone treatment in pregnancy. Outcomes included admission to the neonatal intensive care unit, full-term delivery, vaginal delivery, neonatal length of stay, gestational age at delivery, neonatal length, birthweight, and neonatal head circumference [Link, et al. 2020; Mullins, et al. 2020; Nechanská, et al. 2018; Jumah, et al. 2016; Wiegand, et al. 2015; Gawronski, et al. 2014]. Pregnant patients who are initiating or continuing BUP maintenance can choose either the monoformulation or BUP/NLX.

Table 1: Considerations in Choosing Methadone or Buprenorphine for OUD Treatment During Pregnancy [a]

Factor	Buprenorphine	Methadone
Setting	Available through office-based prescription or a specialty OTP	• Available only through a specialty OTP • Pregnant individuals receive priority access
Initiation requirement	• Mild opioid withdrawal required before treatment can be initiated [b] • Cautious, slow, and low-dose induction advised [c]	Withdrawal not required
Safety and effectiveness	• Safe throughout pregnancy, labor, delivery, and postpartum • Dose can be increased to control cravings and prevent withdrawal • Dose increase may be required later in pregnancy to maintain the appropriate effect	
Treatment duration	Continue treatment throughout pregnancy, labor, delivery, and postpartum	
Can the regimen be changed?	Switch to methadone is possible if needed to control cravings and avoid opioid withdrawal	Switch to BUP is not advised because of the potential for precipitated opioid withdrawal symptoms
Effect on opioid use	Equally effective in reducing opioid use during pregnancy [Minozzi, et al. 2020]	
Effect on infant	• Duration, severity, and dose of medication required for NOWS may be reduced • No known effects on growth or cognitive or psychological development	No known effects on growth or cognitive or psychological development
Pain management	Nonopioid and opioid analgesic agents are used *in addition to* the maintenance OUD treatment dose of methadone or BUP [ASAM 2019]. The addition of a short-acting full-agonist opioid can be considered for managing moderate to severe acute pain. When adding a full-agonist opioid analgesic, patients will likely need a higher dose than opioid-naive patients to achieve adequate analgesia.	
Breastfeeding	Breastfeeding, breastmilk, and skin-to-skin contact all reduce the severity and duration of NOWS	

Table 1: Considerations in Choosing Methadone or Buprenorphine for OUD Treatment During Pregnancy [a]		
Factor	**Buprenorphine**	**Methadone**

Abbreviations: BUP, buprenorphine; NOWS, neonatal opioid withdrawal syndrome; OTP, opioid treatment program; OUD, opioid use disorder.

Notes:

a. For adverse events associated with each medication, see package inserts for SUBUTEX (buprenorphine sublingual tablets) and DISKETS Dispersible Tablets CII (methadone hydrochloride tablets for oral suspension, USP).
b. See the Clinical Opiate Withdrawal Scale and Subjective Opiate Withdrawal Scale.
c. Slow, low-dose induction: Initiate treatment with 2 mg of BUP, followed 30 to 60 minutes later by an additional 2 mg. The pattern of increasing BUP in 2 mg increments and waiting 30 to 60 minutes before the next increase continues until the dose is sufficient to control opioid cravings and prevent withdrawal.

Naltrexone: The NYSDOH AI guideline Treatment of Opioid Use Disorder > Treatment Considerations recommends naltrexone as an alternative to be offered if patients cannot take BUP or methadone or prefer naltrexone.

If a pregnant individual is currently using opioids, initiation of naltrexone is not recommended because withdrawal from opioids is required [Towers, et al. 2020; ACOG(a) 2017; Jones, et al. 2013; FDA 2010; Hulse, et al. 2004]. If a patient taking naltrexone becomes pregnant, clinicians should inform the patient of the risks and benefits of naltrexone and the preferred pharmacologic treatment options to support informed and shared decision-making about treatment (see Table 2, below). If the patient opts to discontinue naltrexone and initiate methadone or BUP, clinicians should educate the patient about the risk of NOWS.

Table 2: Benefits and Risks of Continuing or Discontinuing Naltrexone During Pregnancy [a]	
Continuing Naltrexone	**Discontinuing Naltrexone**
• **Benefits:** Ongoing blockade of the mu-opioid receptor decreases opioid cravings; no risk of neonatal opioid withdrawal syndrome (NOWS) in the neonate • **Risks:** Insufficient data regarding teratogenicity or effects on milk production or infants exposed through breastfeeding	• **Benefit:** No fetal in utero exposure • **Risks:** Reduced opioid tolerance that could result in overdose if opioid use is resumed, risk of NOWS increased if the patient uses opioids

Note:

a. See package insert for Vivitrol (naltrexone for extended-release injectable suspension).

Initiating buprenorphine: In pregnant patients, BUP should be initiated when a patient is experiencing mild opioid withdrawal symptoms (see the Clinical Opiate Withdrawal Scale and Subjective Opiate Withdrawal Scale) [Wesson and Ling 2003; Handelsman, et al. 1987]. For nonpregnant patients, clinicians are advised to initiate treatment when the patient is experiencing moderate withdrawal symptoms. However, if a pregnant individual is experiencing physiological withdrawal, it affects the fetus, too, so medication is initiated earlier in withdrawal to avoid the increased risk to the fetus.

One emerging strategy for BUP/NLX induction is "microdosing," which does not require opioid withdrawal [Randhawa, et al. 2020; Klaire, et al. 2019; Hämmig, et al. 2016]. A small initial dose (e.g., 0.5 mg/0.125 mg) is followed by small incremental increases over 7 to 10 days; patients can continue to use other opioids until the therapeutic level of BUP/NLX is reached. Case reports on nonpregnant adults indicate that BUP/NLX microdosing is well tolerated and may reduce opioid cravings and withdrawal symptoms during induction [Klaire, et al. 2019; Hämmig, et al. 2016]. Microdosing is an emerging strategy for BUP/NLX induction, and studies are needed to guide clinical care. To date, BUP/NLX microdosing has not been studied in pregnant individuals. Because of the lack of data, this committee does not take a position on microdosing during BUP/NLX induction in pregnant patients.

Although there is little published evidence, clinical experience supports a cautious approach to BUP induction in pregnant individuals, with slow titration to the optimal dose for a pregnant patient. For example, clinicians can advise patients to take an initial dose of BUP 2 mg, followed 30 to 60 minutes later by an additional 2 mg [Jones, et al. 2008]. If the patient experiences any worsening of opioid withdrawal symptoms within 30 to 60 minutes after a dose of BUP, the interval between doses can be decreased. The pattern of increasing BUP in 2 mg increments and waiting 30 to 60 minutes before the next increase continues until the dose is sufficient to control opioid cravings and prevent withdrawal.

Continuing opioid use disorder treatment through pregnancy, labor, delivery, and postpartum: Patients with OUD who initiate BUP or methadone during pregnancy or who become pregnant while taking either medication should continue treatment with the same medication throughout the intra- and postpartum periods [Meyer, et al. 2015; Lund, et al. 2013; Jones, et al. 2010].

If treatment goals are not being met with BUP treatment during the pregnancy, clinicians should refer the patient to an OTP for methadone treatment if available [ACOG(a) 2017]. However, during pregnancy, a switch from methadone to BUP is not recommended because the transition could cause precipitated opioid withdrawal symptoms and may require inpatient care and monitoring to decrease the risk of miscarriage or premature delivery. If a patient requests a change from methadone to BUP, clinicians are advised to consult with an expert in OUD treatment during pregnancy.

Monitor for dose increase later in pregnancy: An increased dose of BUP or methadone may be required late in the second and third trimesters because of increased blood volume and metabolism later in pregnancy [Bastian, et al. 2017; Albright, et al. 2011; Cleary, et al. 2010]. Patients may opt to split their BUP dose during the day if it suits their comfort level. Clinicians should assess withdrawal symptoms and opioid cravings at every visit. If a pregnant patient is experiencing any opioid withdrawal symptoms or opioid cravings, the dose of medication should be increased, typically in increments of 5 mg to 10 mg per day for methadone (every 3 to 5 days as needed) and 2 mg to 4 mg per day for BUP. The medication dose should be reassessed at each visit. Patient education is essential to ensure that the patient understands that increasing the dose of either BUP or methadone will not increase the risk of NOWS [Wong, et al. 2018; Cleary, et al. 2010; Jones, et al. 2010].

→ KEY POINTS

- Opioid overdose during pregnancy is an increasing cause of and contributor to maternal mortality [Mangla, et al. 2019; NYSDOH 2019].
- Naloxone is the standard of care for overdose prevention in pregnant individuals.

If a pregnant patient taking methadone has withdrawal symptoms or cravings that are not relieved by a dose increase, the OTP should perform testing for the patient's serum peak and trough levels of methadone. If the peak-to-trough level ratio is higher than 3:1, the methadone dosage should be divided and administered twice daily, ideally every 12 hours.

Pain management: At a minimum, the maintenance OUD treatment dose of methadone or BUP is maintained [ASAM 2019]. Nonopioid medications are the first-line option. The addition of a short-acting full-agonist opioid can be considered to manage moderate to severe acute pain. When adding a full-agonist opioid analgesic, patients will likely need a higher dose than opioid-naive patients to achieve adequate analgesia [ASAM 2019].

Breastfeeding: Breastfeeding is safe when a patient takes methadone, BUP, or naltrexone [LactMed(a) 2025a; LactMed(a) 2025b; LactMed(d) 2025]. In addition, breastfeeding has been shown to decrease the risk of NOWS and, when NOWS does occur, decrease the need for pharmacologic treatment [Reece-Stremtan and Marinelli 2015; Welle-Strand, et al. 2013; McQueen, et al. 2011; Jansson, et al. 2008]. This benefit is likely due to the skin-to-skin contact inherent in breastfeeding rather than the minuscule amount of BUP or methadone in breast milk. The only contraindication to breastfeeding is HIV infection. Hepatitis C virus infection is *not* a contraindication to breastfeeding as long as the skin of the nipple is intact.

Postpartum considerations: Following birth, a patient who is taking medications to treat OUD will require continued treatment and support. The postpartum period can be stressful for new parents, particularly if they lack social support and have comorbidities, such as mental health diagnoses or chronic medical conditions; during this period, individuals who use opioids are at increased risk for recurrence of use and unintentional overdoses [Schiff, et al. 2018]. One study found that individuals who gave birth to infants with NOWS had a significantly higher incidence of major depression, postpartum depression, and anxiety in the 12 months postpartum than matched controls [Corr, et al. 2020]. A population-based study in Massachusetts found that overdose events decreased with progression through the pregnancy and were lowest in the third trimester (3/100,000 person-days); the highest risk of overdose occurred 7 to 12 months after delivery (12.3/100,000 person-days) [Schiff, et al. 2018].

In the postpartum period, the mother should continue taking BUP or methadone for as long as a benefit is derived. If the patient's dose of BUP or methadone was increased during pregnancy, clinicians should not decrease the dose to the prepregnancy level immediately postpartum; dose decreases should be individualized.

Neonatal Opioid Withdrawal Syndrome

☑ RECOMMENDATIONS

Neonatal Opioid Withdrawal Syndrome

- Clinicians should provide patient education about NOWS that addresses the risk of NOWS, harm reduction strategies, typical symptoms and duration, and pharmacologic and nonpharmacologic treatment options. (A3)
- When an infant is at risk of NOWS, the clinician should recommend postpartum contact, including breastfeeding, rooming-in, and skin-to-skin contact. (A2)

Abbreviation: NOWS, neonatal opioid withdrawal syndrome.

Clinicians should inform pregnant patients who are taking opioids, buprenorphine (BUP), or methadone, that NOWS is an expected and treatable neonatal outcome. Patient education about NOWS may reduce stress after delivery.

Risk of neonatal opioid withdrawal syndrom0: A fetus that is exposed to opioids, methadone, or BUP during pregnancy is at risk of developing NOWS [ACOG(a) 2017; Kraft, et al. 2016; McQueen and Murphy-Oikonen 2016; Saia, et al. 2016; Gawronski, et al. 2014; Hall, et al. 2014; Kocherlakota 2014; Wong, et al. 2011; Jones, et al. 2010; Bakstad, et al. 2009].

Harm reduction: Strategies to reduce the severity of NOWS include treatment with BUP or methadone and preventing opioid withdrawal in pregnant patients who use opioids [Brogly, et al. 2014; Fajemirokun-Odudeyi, et al. 2006]. There is no association between BUP or methadone dose and the likelihood of NOWS; therefore, dose reductions to avoid NOWS are not advised [Kaltenbach, et al. 1998]. Reducing the dose of BUP or methadone may increase illicit drug use and increase the risk to the fetus.

Symptoms: Signs of opioid withdrawal generally occur within the first 48 hours of life for neonates exposed to BUP in utero and within 5 days for those exposed to methadone. Symptoms include tremors, hypertonicity, irritability, vomiting, and respiratory distress, and the number, severity, and duration of symptoms vary in individual neonates [Zelson, et al. 1973]. Multiple factors affect the expression of symptoms: neonatal gestational age, sex, and genetics; maternal substance use factors, exposure to medications (selective serotonin reuptake inhibitors, benzodiazepines, gabapentinoids), smoking, and metabolism [Kraft, et al. 2016]. Diagnosis of NOWS is based on maternal history and neonatal clinical features, with or without biological testing [Anbalagan, et al. 2024].

Tools such as the Finnegan Neonatal Abstinence Scoring System [Finnegan and Kaltenbach 1997] and the *MOTHERS score* [Jones, et al. 2010] are used to assess central nervous system, metabolic, vasomotor, respiratory, and gastrointestinal symptoms. The score is used to guide treatment decisions, including the initiation of pharmacologic treatment. A diagnosis of NOWS can require individually tailored supportive care strategies because presenting symptoms can vary [Wiles, et al. 2014; Velez and Jansson 2008].

Treatment: The treatment goals are to minimize the severity and duration of withdrawal symptoms in the infant and reduce the length of hospital stay and the need for adjunctive therapies. Current practice encourages nonpharmacologic management of NOWS and infant-family contact [Ryan, et al. 2019; Grossman, et al. 2018].

Because many NOWS symptoms are associated with infant overstimulation, nonpharmacologic care focuses on controlling environmental factors to maximize infant comfort. Methods include swaddling, quiet and dimly lit rooms, skin-to-skin contact, breastfeeding, and infant positioning [Ryan, et al. 2019]. Several studies have found that rooming-in, or keeping an infant with the parent instead of a neonatal intensive care unit, is associated with decreased need for NOWS pharmacologic treatment and reduced length of hospital stay [Lembeck, et al. 2019; Holmes, et al. 2016; Saiki, et al. 2010; Abrahams, et al. 2007]. In the “eating/sleeping/consoling” (ESC) approach, if infants can be consoled in less than 10 minutes, eat an ounce or more of formula or breastfeed well, and sleep for an hour or longer at a time with nonpharmacologic strategies, no medication is indicated for the treatment of NOWS [Grossman, et al. 2018].

Mild cases of NOWS (Finnegan Score <8) can often be managed with nonpharmacologic treatment; more severe cases may require adjunctive medication [Ryan, et al. 2019]. Medication, generally morphine and, less commonly, methadone, is the first-line pharmacologic treatment for NOWS [Kocherlakota 2014; Hudak and Tan 2012; Jansson and Velez 2012; Osborn(a), et al. 2010; Osborn(b), et al. 2010].

Buprenorphine is safe for the treatment of NOWS, and sublingual dosing has been demonstrated to be feasible in the neonatal population [Kraft, et al. 2008]. BUP has been shown to have an efficacy advantage over standard opioid therapy for NOWS in controlled clinical trials and treatment settings [Kraft 2018]; however, its use is not yet widespread.

There is significant variability in treatment approaches to NOWS, and an optimal protocol has not been established [Kraft, et al. 2016; Tolia, et al. 2015; Patrick, et al. 2014; O'Grady, et al. 2009; Sarkar and Donn 2006]. Despite significant effort in the medical community to find the most effective medication and dosing regimen for treatment of NOWS, the use of a standardized institutional protocol based on best practices is more effective than a specific medication (morphine or methadone) in reducing the total length of hospital stay and duration of pharmacologic treatment [Kraft, et al. 2016]. The most effective treatment approaches employ a systematic, multidisciplinary, and multimodal approach.

Alcohol Use and Alcohol Use Disorder Treatment During Pregnancy

Note: This section of the guideline addresses alcohol use in general, rather than alcohol use disorder (AUD), because the risk of harm to the fetus is greater with nondependent alcohol use than with nondependent use of other substances. Some aspects of treatment for pregnant individuals with AUD are similar to those for nonpregnant individuals.

The recommendations below focus on *differences* in treatment during pregnancy; consult the NYSDOH AI guidelines Treatment of Alcohol Use Disorder and Substance Use Harm Reduction in Medical Care for additional recommendations.

☑ RECOMMENDATIONS

Alcohol Use Disorder Treatment

- Clinicians should recommend inpatient alcohol withdrawal management for pregnant patients with or at risk for moderate, severe, or complicated alcohol withdrawal (CIWA-Ar scores ≥10), and consult with an OB/GYN. (A3)
- Clinicians should use caution when prescribing a benzodiazepine medication for pregnant patients. (B3)
- Clinicians should advise pregnant patients who use alcohol to abstain from or minimize use during pregnancy and minimize use during breastfeeding to prevent harm to the developing fetus or infant. (A2)
- Clinicians should provide harm reduction counseling to help minimize the effects of alcohol on the patient and the fetus. (A3)
- If a pregnant individual cannot decrease or cease alcohol use, the clinician should discuss pharmacotherapy for AUD as a harm reduction approach and engage the patient in shared decision-making regarding its use. (B3)
- If a patient becomes pregnant while taking pharmacologic medication for AUD or requests medication during pregnancy, clinicians should inform them of the risks and benefits of preferred agents during pregnancy and breastfeeding. (A3)
- Clinicians should identify and inform patients with AUD and risky alcohol use about available support or behavioral treatment options and provide these options or refer as indicated. (A3)

Abbreviations: CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised; OB/GYN, obstetrician/gynecologist.

Alcohol withdrawal: Pregnancy is considered a relative indication for inpatient management of alcohol withdrawal and may be indicated for any pregnant patient who requires symptom management. For pregnant patients with a score of 10 or higher on the CIWA-Ar scale or at risk for moderate, severe, or complicated alcohol withdrawal, a referral for inpatient withdrawal management is recommended [ASAM 2020; VA/DoD 2015]. Clinicians should consult with an OB/GYN during withdrawal management [ASAM 2020].

Symptoms of alcohol withdrawal syndrome include autonomic hyperactivity (sweating, fast pulse); increased hand tremors; insomnia; nausea; vomiting; transient hallucinations or perceptual disturbances of the auditory, visual, or tactile type; psychomotor agitation; anxiety; and generalized seizures [Kattimani and Bharadwaj 2013]. Physiologic and psychological stress during pregnancy can adversely affect the pregnant individual and the fetus and result in preterm birth and low birth weight [DeVido, et al. 2015; Enlow, et al. 2009; Hobel, et al. 2008].

Benzodiazepines are commonly used in treating alcohol withdrawal in nonpregnant adults, but data on the safety of benzodiazepines during pregnancy are unclear [DeVido, et al. 2015]. Fetal exposure to benzodiazepines in the first trimester has not been associated with an increased risk of congenital disabilities in limited studies [Bellantuono, et al. 2013]. The World Health Organization and the American Society of Addiction Medicine recommend short-term, limited use of benzodiazepines in pregnant patients who develop alcohol withdrawal and note that the risk of fetal adverse events has to be balanced with the potential harm of complications of severe alcohol withdrawal [ASAM 2020; WHO 2014].

Encourage abstinence or minimal alcohol use: Clinicians should encourage pregnant individuals who use alcohol or have AUD to abstain from or minimize use during pregnancy to decrease the risk of fetal alcohol spectrum disorder (FASD) [Reece-Stremtan and Marinelli 2015; WHO 2014]. Expert consultation or inpatient management of alcohol withdrawal may be needed with patients who are physically dependent on alcohol (see discussion of alcohol withdrawal, above). During pregnancy, heavy alcohol use may lead to various congenital disabilities and alterations in neonatal growth and development [Lees, et al. 2020; Miller 2018]. FASD, which is characterized by congenital abnormalities associated with exposure to alcohol in utero, may cause mild or subtle problems, such as a slight learning disability or physical abnormality, or it may cause more severe problems, such as central nervous system dysfunction, low IQ, microcephaly, delayed growth, and facial abnormalities [Miller 2018].

There is no known safe amount of alcohol use during pregnancy, and there is clear evidence that binge drinking and heavy drinking during pregnancy are associated with adverse fetal effects [Carson, et al. 2017; Flak, et al. 2014; O'Leary and Bower 2012]. Because of the linear dose-response of alcohol on the fetus and the potentially serious and irreversible consequences in the fetus and neonate of in utero exposure, abstaining from or minimizing use is recommended [Chang 2024; May, et al. 2016].

Behavioral treatment: Clinicians should provide or refer pregnant patients who use alcohol for counseling or other psychosocial treatment. A meta-analysis of alcohol screening and brief intervention studies in pregnant patients found that abstinence during pregnancy was consistently higher in the intervention groups (counseling on alcohol use) than the control groups (odds ratio, 2.26; 95% CI, 1.43 to 3.56; 5 studies [n = 796]) after 6 to 12 months [O'Connor, et al. 2018]. Among trials reporting abstinence before delivery, abstinence ranged from 72% to 90% among intervention participants and 55% to 74% among control participants [O'Connor, et al. 2018].

Referral options may include intensive outpatient substance use treatment, mental health treatment, peer support groups (e.g., 12-step, SMART Recovery), electronic apps (e.g., SMART Recovery, In the Rooms), public health, and other community-based recovery coaching, and other available psychosocial interventions. Cognitive-behavioral therapy, motivational interviewing, and contingency management may also help a pregnant patient minimize substance use [WHO 2014]. There is wide variability in the efficacy of these interventions, and recommendations and referrals should be tailored to the individual patient's needs and preferences.

Harm reduction counseling: Pregnant patients who cannot abstain from alcohol use may be able to decrease use or address other treatment goals. Harm reduction approaches during pregnancy have been shown to decrease alcohol use, reduce healthcare costs, improve engagement and retention in prenatal services and substance use treatment, and improve health outcomes for parents and their children [Racine, et al. 2009; Poole and Greaves 2007]. Clinicians should discuss and encourage harm reduction strategies.

Focusing health messages on abstinence and improving fetal health, although pertinent given the low threshold at which fetal harm can occur, can fail to consider a patient's social context and address the root causes of alcohol use during pregnancy [O'Leary and Bower 2012]. Studies have shown that trauma, interpersonal violence, and structural inequities may impact alcohol use in pregnancy [Varcoe, et al. 2014; Poole and Greaves 2007]. Patient counseling recommending abstinence can be presented in a rational, nonjudgmental manner, with the treatment goal being to reduce harm to the pregnant individual and the fetus [O'Leary and Bower 2012].

An abstinence-based approach can also perpetuate the social stigmatization of those who use alcohol and inadvertently discourage engagement in care, which contributes to long-term harm to both parents and children. Individuals who use alcohol during pregnancy may avoid accessing prenatal and other medical and social care for fear of judgment or punitive measures, such as child welfare authorities removing their child [Varcoe, et al. 2014; Poole and Greaves 2007].

Pharmacologic treatment: Acamprosate and naltrexone are the preferred agents for pharmacologic treatment of AUD in nonpregnant individuals. However, few data are available from well-controlled studies of acamprosate or naltrexone in pregnant individuals, and the potential carcinogenic, mutagenic, or fertility effects in humans are unknown. In a small study among pregnant individuals treated with naltrexone, outcomes for neonates exposed to naltrexone in utero did not appear to differ from other neonates [Hulse, et al. 2004]. Gabapentin may be considered, but caution should be taken with its use during the third trimester [Patorno, et al. 2020]. Treatment with disulfiram is not advised during pregnancy.

If a patient becomes pregnant while taking medication for AUD, continuing treatment during pregnancy requires informed decision-making after weighing the risks to the fetus and the benefits to the pregnant patient [Kelty, et al. 2019]. With effective pharmacologic treatment, a pregnant patient may be able to reduce or abstain from alcohol use, which may improve maternal health and will minimize fetal exposure to alcohol and the risk of associated harms, such as FASD [Reece-Stremtan and Marinelli 2015; WHO 2014].

Breastfeeding: The effects of alcohol use during lactation are complex, and there is conflicting evidence on the effects of infant exposure to alcohol in breast milk [May, et al. 2016; Haastrup, et al. 2014]. Alcohol is excreted into breast milk in concentrations similar to those in parental blood, which means that the amount of alcohol ingested by an infant through breast milk is a fraction of the amount consumed by the parent. Alcohol can disrupt breastfeeding by decreasing milk production and let down [LactMed 2025]. However, the effect of occasional alcohol consumption on milk production appears small, temporary, and clinically irrelevant [Haastrup, et al. 2014].

The American Society of Addiction Medicine recommends that patients who use alcohol and are breastfeeding wait for 2 hours per drink after drinking [Miller 2018]. For example, after 2 drinks, the individual should wait for at least 4 hours before breastfeeding. Breast milk can also be pumped and discarded after alcohol consumption. However, there is little clinical evidence to suggest that breastfed children are adversely affected by occasional alcohol use [Haastrup, et al. 2014]. Over-the-counter test strips are available to measure alcohol in breastmilk, but there are no clinical studies currently available on the use of the test strips.

Breastfeeding while taking acamprosate is not recommended. It is unknown if breastfed infants are exposed to acamprosate through breast milk [FDA 2004]. Naltrexone use is not contraindicated during breastfeeding; limited data indicate that naltrexone is minimally excreted into breast milk [LactMed(a) 2025b].

Tobacco Use Disorder Treatment During Pregnancy

☑ RECOMMENDATIONS

Tobacco Use Disorder Treatment

- For pregnant patients with tobacco use disorder, clinicians should:
  - Advise patients to abstain from or minimize use during pregnancy to prevent harm to themselves and the fetus. (A2)
  - Offer NRT with or without bupropion after discussing the risks and benefits. (A2)
  - Perform or refer for psychosocial counseling and support. (A1)

Abbreviation: NRT, nicotine replacement therapy.

Clinicians should advise pregnant patients who use tobacco to abstain from or minimize use during pregnancy. Tobacco and nicotine use during pregnancy has been linked to low birth weight, preterm birth, placental abruption, miscarriage, stillbirth, sudden infant death syndrome, poor fetal neurodevelopment, and a variety of congenital disabilities [Akerman, et al. 2015; Cressman, et al. 2012; Forinash, et al. 2010].

Pharmacologic Treatment

Nicotine replacement therapy: Clinicians should provide information about available pharmacologic treatment and offer NRT (patch, gum, lozenge, nasal spray, or inhaler), bupropion, or a combination of these medications. The choice is guided by patient preference. Of note, due to sex-based differences in the cytochrome P450 system and the number of beta-2 nicotinic acetylcholine receptors and hormonal and mood modulation effects of nicotine, NRT may be less effective in women than men [Terplan, et al. 2020]. Data regarding the efficacy of NRT is limited [Terplan, et al. 2020]. To potentially minimize NRT exposure to the fetus and a breastfeeding infant, patients may choose to take an immediate-release form of NRT, such as gum or an inhaler, instead of a slow-release form, such as the patch [Dempsey, et al. 2002]. The patch releases medication continuously, but the user controls dosing with lozenges, chewing gum, and inhalers. If the patient is wearing a nicotine patch, removing it at night may minimize fetal exposure to nicotine.

NRT medications are taken according to instructions for nonpregnant patients (see agent prescribing information). However, it is important to inform patients that the rate of nicotine metabolism increases in pregnant individuals, which could impair the effectiveness of NRT [Dempsey, et al. 2002]. A dose increase in NRT may be warranted.

There are conflicting data on NRT use during pregnancy, with limited evidence of efficacy in smoking cessation or reduction but mixed evidence regarding harm [Claire, et al. 2020; Terplan, et al. 2020; Coleman, et al. 2012]. In a systematic review and meta-analysis, NRT was associated with a 40% increase in smoking cessation rate measured in late pregnancy [Coleman, et al. 2012]. However, evidence suggests that if potentially biased, non-placebo-controlled, randomized trials are excluded from the meta-analysis, NRT was no more effective than placebo [Claire, et al. 2020]. Furthermore, there is little evidence that NRT during pregnancy has positive or negative effects on birth outcomes. One study that followed infants after birth found an association between maternal NRT and healthy developmental outcomes [Cooper, et al. 2014].

Bupropion and varenicline: Bupropion, an antidepressant with dopaminergic and noradrenergic activity, can be prescribed concurrently with NRT for pregnant individuals [Cressman, et al. 2012]. In a pooled analysis from 2 bupropion studies, there was no clear effect on smoking cessation during later pregnancy (relative risk, 0.74), but the lack of effect may have been due to small sample sizes [Claire, et al. 2020]. There are limited and conflicting data on the fetal effects due to bupropion use. The estimated prevalence rate of congenital heart defects among infants with *in utero* exposure to bupropion is higher than in the general population but remains relatively low (2.1/1000 births) [Byatt, et al. 2013; Alwan, et al. 2010; Reller, et al. 2008; Chun-Fai-Chan, et al. 2005].

There is insufficient evidence to support a recommendation for varenicline, a partial agonist of α4β2 nicotinic receptors, during pregnancy and postpartum. In a population-based cohort study among individuals in the first trimester of pregnancy, researchers found a significant reduction in the risk of any adverse perinatal event and no increased risk of major congenital anomalies in infants exposed to varenicline compared with those exposed to NRT [Tran, et al. 2020].

Breastfeeding: Animal data suggest that exposure to nicotine may interfere with lung development or may be associated with sudden infant death syndrome, but the risks are not well established for exposure to nicotine in human infants. As a result, some experts recommend that while a patient is breastfeeding, an alternative to NRT may be preferred for tobacco cessation treatment [LactMed(b) 2023]. One option is bupropion. At doses of up to 300 mg daily, this medication produces low levels in breastmilk that are not expected to cause adverse effects in infants. Though data in breastfed infants are scant, bupropion treatment in a nursing parent is not a contraindication to breastfeeding [LactMed(b) 2025].

The National Institutes of Health LactMed database notes that no information is available on the use of varenicline during breastfeeding, and an alternate medication is preferred, especially while nursing a newborn or preterm infant [LactMed(e) 2024]. If an individual chooses to breastfeed while taking varenicline, the infant should be monitored for seizures and excessive vomiting [LactMed(e) 2024; McAllister-Williams, et al. 2017].

Behavioral Treatment

For pregnant patients who use tobacco, clinicians should perform or refer for counseling or other psychosocial and behavioral treatment. A 2017 meta-analysis found a 17% reduction in low birth weight, a significantly higher mean birth weight and a 22% reduction in neonatal intensive care admissions among infants born to individuals who participated in psychosocial interventions for tobacco use [Chamberlain, et al. 2017]. Counseling, feedback, and incentive-based programs were reported to increase the proportion of individuals who stopped smoking in late pregnancy [Chamberlain, et al. 2017].

It is important to discuss all available resources for supporting tobacco cessation with patients, including electronic resources. Providing continual support and addressing psychosocial stressors in the postpartum period are needed to ensure continued cessation success [ACOG 2020].

◊ RESOURCES

- Centers for Disease Control and Prevention: You Can Help Your Patients Quit Tobacco Use
- American Association for Respiratory Care: Smoking Cessation for Pregnant Women
- Association of State and Territorial Health Officials: Smoking Cessation Strategies for Women Before, During, and After Pregnancy
- Agency for Healthcare Research and Quality: Tobacco Use Counseling
- U.S. Preventive Services Task Force: Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women: Recommendation Statement
- American College of Obstetricians and Gynecologists: Committee Opinion on Tobacco and Nicotine Cessation in Pregnancy, Number 807, May 2020

Treatment of Other Substance Use Disorders During Pregnancy

☑ RECOMMENDATIONS

Treatment of Other Substance Use Disorders

- Clinicians should advise pregnant patients who use any substances to abstain from or minimize use during pregnancy to prevent adverse maternal and neonatal effects. (A3)
- Clinicians should identify and inform patients about all available treatment options and resources for support and provide appropriate interventions or referrals as needed. (A3)

Few data are available on the risks of active cannabis use while breastfeeding, and no clear guidance is available on the length of time to wait after cannabis use before breastfeeding; when counseling patients, it is important to discuss potential risks and benefits, reasons for cannabis use, and possible alternatives to use [LactMed(c) 2025; Metz and Borgelt 2018; ACOG(b) 2017]. Breastfeeding is not advised for individuals actively using cocaine or methamphetamine.

There are no U.S. Food and Drug Administration (FDA)-approved medications to treat stimulant use disorders (e.g., cocaine, amphetamine, and methamphetamine). A recent clinical trial found a potential benefit associated with bupropion and naltrexone in treating methamphetamine use disorder [Trivedi, et al. 2021]. No pregnant patients were included in the study.

Referral options include inpatient withdrawal management, an intensive outpatient substance use disorder (SUD) treatment program, treatment for a mental health condition and SUD (for patients with dual diagnosis), support groups (e.g., 12-step, SMART Recovery), apps (e.g., SMART Recovery, In the Rooms), public health nursing, community-based care management, peer support, recovery coaching, and any other psychosocial supports. Behavioral interventions, such as cognitive-behavioral therapy, motivational interviewing, and contingency management, may also play a role in assisting a pregnant patient to minimize substance use [WHO 2014].

All Recommendations

☑ ALL RECOMMENDATIONS: SUBSTANCE USE DISORDER TREATMENT IN PREGNANT ADULTS

Opioid Use Disorder Treatment

- Clinicians should advise their patients to avoid abrupt discontinuation of opioids, including BUP or methadone, during pregnancy because of the risks posed by withdrawal or resumption of unhealthy use (i.e., heroin) following abstinence. (B2)
- When offering pregnant patients BUP treatment or referral to an OTP for methadone treatment, clinicians should discuss the maternal and fetal risks and benefits of both medications (see Table 1: Considerations in Choosing Methadone or Buprenorphine for OUD Treatment During Pregnancy); the treatment choice should be based on patient preference whenever possible. (A3)
- Clinicians should educate patients who take opioids, BUP, or methadone during pregnancy about the risk of NOWS, an expected and treatable outcome (see guideline section Neonatal Opioid Withdrawal Syndrome). (A3)
- Clinicians should inform patients that breastfeeding while taking BUP or methadone is safe and may reduce the risk of NOWS. (A2)
- Clinicians should not recommend naltrexone initiation, which requires withdrawal from opioids, for a pregnant patient who is actively using opioids. (A2)
  - If a pregnant patient is abstinent from opioids and requests treatment with naltrexone, clinicians should discuss naltrexone as an alternative treatment and inform the patient of the associated risks and benefits. (A3)
  - Clinicians should inform patients who become pregnant while taking naltrexone of the risks and benefits and preferred pharmacologic treatment options (see Table 2: Benefits and Risks of Continuing or Stopping Naltrexone During Pregnancy). (B3)
- Before initiating BUP in a pregnant patient with OUD, clinicians should confirm that the patient is experiencing at least mild opioid withdrawal symptoms (B3) and should consult with an experienced substance use treatment provider regarding the risk of precipitated withdrawal. (A3)
- Clinicians should advise patients who initiate BUP or methadone during pregnancy, and those who become pregnant while taking BUP or methadone, to continue treatment throughout pregnancy, labor, delivery, postpartum, and breastfeeding. (A2)
- At each visit, clinicians should monitor pregnant patients taking BUP for opioid cravings and withdrawal symptoms and, if present, increase the dose as appropriate for the individual and reassess at the next visit; any dose increase should be maintained until treatment goals can be evaluated postpartum. (A3)
  - If taking a dose of 32 mg BUP mg daily does not allow the patient to meet treatment goals, clinicians should recommend methadone treatment. (A3)
- If a pregnant patient is considering a change from methadone to BUP, the clinician should consult an experienced substance use treatment provider because of the risk of precipitated withdrawal. (A3)

Neonatal Opioid Withdrawal Syndrome

- Clinicians should provide patient education about NOWS that addresses the risk of NOWS, harm reduction strategies, typical symptoms and duration, and pharmacologic and nonpharmacologic treatment options. (A3)
- When an infant is at risk of NOWS, the clinician should recommend postpartum contact, including breastfeeding, rooming-in, and skin-to-skin contact. (A2)

Alcohol Use Disorder Treatment

- Clinicians should recommend inpatient alcohol withdrawal management for pregnant patients with or at risk for moderate, severe, or complicated alcohol withdrawal (CIWA-Ar scores ≥10), and consult with an OB/GYN. (A3)
- Clinicians should use caution when prescribing a benzodiazepine medication for pregnant patients. (B3)
- Clinicians should advise pregnant patients who use alcohol to abstain from or minimize use during pregnancy and minimize use during breastfeeding to prevent harm to the developing fetus or infant. (A2)
- Clinicians should provide harm reduction counseling to help minimize the effects of alcohol on the patient and the fetus. (A3)

☑ ALL RECOMMENDATIONS: SUBSTANCE USE DISORDER TREATMENT IN PREGNANT ADULTS

- If a pregnant individual cannot decrease or cease alcohol use, the clinician should discuss pharmacotherapy for AUD as a harm reduction approach and engage the patient in shared decision-making regarding its use. (B3)
- If a patient becomes pregnant while taking pharmacologic medication for AUD or requests medication during pregnancy, clinicians should inform them of the risks and benefits of preferred agents during pregnancy and breastfeeding. (A3)
- Clinicians should identify and inform patients with AUD and risky alcohol use about available support or behavioral treatment options and provide these options or refer as indicated. (A3)

Tobacco Use Disorder Treatment

- For pregnant patients with tobacco use disorder, clinicians should:
  - Advise patients to abstain from or minimize use during pregnancy to prevent harm to themselves and the fetus. (A2)
  - Offer NRT with or without bupropion after discussing the risks and benefits. (A2)
  - Perform or refer for psychosocial counseling and support. (A1)

Treatment of Other Substance Use Disorders

- Clinicians should advise pregnant patients who use any substances to abstain from or minimize use during pregnancy to prevent adverse maternal and neonatal effects. (A3)
- Clinicians should identify and inform patients about all available treatment options and resources for support and provide appropriate interventions or referrals as needed. (A3)

Abbreviations: AUD, alcohol use disorder; BUP, buprenorphine; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised; NOWS, neonatal opioid withdrawal syndrome; NRT, nicotine replacement therapy; OB/GYN, obstetrician/gynecologist; OTP, opioid treatment program; OUD, opioid use disorder.

References

Abrahams RR, Kelly SA, Payne S, et al. Rooming-in compared with standard care for newborns of mothers using methadone or heroin. *Can Fam Physician* 2007;53(10):1722–30. [PMID: 17934036] https://pubmed.ncbi.nlm.nih.gov/17934036

ACOG. Tobacco and nicotine cessation during pregnancy: ACOG committee opinion, number 807. *Obstet Gynecol* 2020;135(5):e221–29. [PMID: 32332417] https://pubmed.ncbi.nlm.nih.gov/32332417

ACOG(a). Committee opinion no. 711: opioid use and opioid use disorder in pregnancy. *Obstet Gynecol* 2017;130(2):e81–94. [PMID: 28742676] https://pubmed.ncbi.nlm.nih.gov/28742676

ACOG(b). Committee opinion no. 722: marijuana use during pregnancy and lactation. *Obstet Gynecol* 2017;130(4):e205–9. [PMID: 28937574] https://pubmed.ncbi.nlm.nih.gov/28937574

Akerman SC, Brunette MF, Green AI, et al. Treating tobacco use disorder in pregnant women in medication-assisted treatment for an opioid use disorder: a systematic review. *J Subst Abuse Treat* 2015;52:40–47. [PMID: 25592332] https://pubmed.ncbi.nlm.nih.gov/25592332

Albright B, de la Torre L, Skipper B, et al. Changes in methadone maintenance therapy during and after pregnancy. *J Subst Abuse Treat* 2011;41(4):347–53. [PMID: 21741197] https://pubmed.ncbi.nlm.nih.gov/21741197

Alwan S, Reefhuis J, Botto LD, et al. Maternal use of bupropion and risk for congenital heart defects. *Am J Obstet Gynecol* 2010;203(1):52.e1–6. [PMID: 20417496] https://pubmed.ncbi.nlm.nih.gov/20417496

Anbalagan S, Falkowitz DM, Mendez MD. StatPearls: neonatal abstinence syndrome. 2024 Apr 1. https://www.ncbi.nlm.nih.gov/books/NBK551498/ [accessed 2025 Sep 23]

Anderson TM, Lavista Ferres JM, Ren SY, et al. Maternal smoking before and during pregnancy and the risk of sudden unexpected infant death. *Pediatrics* 2019;143(4). [PMID: 30858347] https://pubmed.ncbi.nlm.nih.gov/30858347

Angelotta C, Weiss CJ, Angelotta JW, et al. A moral or medical problem? The relationship between legal penalties and treatment practices for opioid use disorders in pregnant women. *Womens Health Issues* 2016;26(6):595–601. [PMID: 27773527] https://pubmed.ncbi.nlm.nih.gov/27773527

ASAM. National practice guideline for the treatment of opioid use disorder: 2020 focused update. 2019 Dec 18. https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline [accessed 2025 Sep 23]

ASAM. Clinical practice guideline on alcohol withdrawal management. 2020 Jan 23. https://www.asam.org/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf [accessed 2025 Sep 23]

Bailey BA, Sokol RJ. Prenatal alcohol exposure and miscarriage, stillbirth, preterm delivery, and sudden infant death syndrome. *Alcohol Res Health* 2011;34(1):86–91. [PMID: 23580045] https://pubmed.ncbi.nlm.nih.gov/23580045

Bakstad B, Sarfi M, Welle-Strand GK, et al. Opioid maintenance treatment during pregnancy: occurrence and severity of neonatal abstinence syndrome. A national prospective study. *Eur Addict Res* 2009;15(3):128–34. [PMID: 19332991] https://pubmed.ncbi.nlm.nih.gov/19332991

Baldacchino A, Arbuckle K, Petrie DJ, et al. Neurobehavioral consequences of chronic intrauterine opioid exposure in infants and preschool children: a systematic review and meta-analysis. *BMC Psychiatry* 2014;14:104. [PMID: 24708875] https://pubmed.ncbi.nlm.nih.gov/24708875

Bastian JR, Chen H, Zhang H, et al. Dose-adjusted plasma concentrations of sublingual buprenorphine are lower during than after pregnancy. *Am J Obstet Gynecol* 2017;216(1):64.e1–7. [PMID: 27687214] https://pubmed.ncbi.nlm.nih.gov/27687214

Bellantuono C, Tofani S, Di Sciascio G, et al. Benzodiazepine exposure in pregnancy and risk of major malformations: a critical overview. *Gen Hosp Psychiatry* 2013;35(1):3–8. [PMID: 23044244] https://pubmed.ncbi.nlm.nih.gov/23044244

Berenson AB, Wilkinson GS, Lopez LA. Effects of prenatal care on neonates born to drug-using women. *Subst Use Misuse* 1996;31(8):1063–76. [PMID: 8806168] https://pubmed.ncbi.nlm.nih.gov/8806168

Binder T, Vavrinková B. Prospective randomised comparative study of the effect of buprenorphine, methadone and heroin on the course of pregnancy, birthweight of newborns, early postpartum adaptation and course of the neonatal abstinence syndrome (NAS) in women followed up in the outpatient department. *Neuro Endocrinol Lett* 2008;29(1):80–86. [PMID: 18283247] https://pubmed.ncbi.nlm.nih.gov/18283247

Brogly SB, Saia KA, Walley AY, et al. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. *Am J Epidemiol* 2014;180(7):673–86. [PMID: 25150272] https://pubmed.ncbi.nlm.nih.gov/25150272

Byatt N, Deligiannidis KM, Freeman MP. Antidepressant use in pregnancy: a critical review focused on risks and controversies. *Acta Psychiatr Scand* 2013;127(2):94–114. [PMID: 23240634] https://pubmed.ncbi.nlm.nih.gov/23240634

Carson G, Cox LV, Crane J, et al. No. 245-alcohol use and pregnancy consensus clinical guidelines. *J Obstet Gynaecol Can* 2017;39(9):e220–54. [PMID: 28859770] https://pubmed.ncbi.nlm.nih.gov/28859770

Chamberlain C, O'Mara-Eves A, Porter J, et al. Psychosocial interventions for supporting women to stop smoking in pregnancy. *Cochrane Database Syst Rev* 2017;2(2):CD001055. [PMID: 28196405] https://pubmed.ncbi.nlm.nih.gov/28196405

Chang G. Alcohol intake and pregnancy. 2024 Nov 20. https://www.uptodate.com/contents/alcohol-intake-and-pregnancy [accessed 2025 Sep 23]

Chu EK, Smith LM, Derauf C, et al. Behavior problems during early childhood in children with prenatal methamphetamine exposure. *Pediatrics* 2020;146(6). [PMID: 33172920] https://pubmed.ncbi.nlm.nih.gov/33172920

Chun-Fai-Chan B, Koren G, Fayez I, et al. Pregnancy outcome of women exposed to bupropion during pregnancy: a prospective comparative study. *Am J Obstet Gynecol* 2005;192(3):932–36. [PMID: 15746694] https://pubmed.ncbi.nlm.nih.gov/15746694

Claire R, Chamberlain C, Davey MA, et al. Pharmacological interventions for promoting smoking cessation during pregnancy. *Cochrane Database Syst Rev* 2020;3(3):CD010078. [PMID: 32129504] https://pubmed.ncbi.nlm.nih.gov/32129504

Cleary BJ, Donnelly J, Strawbridge J, et al. Methadone dose and neonatal abstinence syndrome-systematic review and meta-analysis. *Addiction* 2010;105(12):2071–84. [PMID: 20840198] https://pubmed.ncbi.nlm.nih.gov/20840198

Coleman T, Chamberlain C, Davey MA, et al. Pharmacological interventions for promoting smoking cessation during pregnancy. *Cochrane Database Syst Rev* 2012;(9):CD010078. [PMID: 22972148] https://pubmed.ncbi.nlm.nih.gov/22972148

Cooper S, Taggar J, Lewis S, et al. Effect of nicotine patches in pregnancy on infant and maternal outcomes at 2 years: follow-up from the randomised, double-blind, placebo-controlled SNAP trial. *Lancet Respir Med* 2014;2(9):728–37. [PMID: 25127405] https://pubmed.ncbi.nlm.nih.gov/25127405

Corr TE, Schaefer EW, Hollenbeak CS, et al. One-year postpartum mental health outcomes of mothers of infants with neonatal abstinence syndrome. *Matern Child Health J* 2020;24(3):283–90. [PMID: 31925632] https://pubmed.ncbi.nlm.nih.gov/31925632

Cressman AM, Pupco A, Kim E, et al. Smoking cessation therapy during pregnancy. *Can Fam Physician* 2012;58(5):525–27. [PMID: 22586193] https://pubmed.ncbi.nlm.nih.gov/22586193

Dempsey D, Jacob P, 3rd, Benowitz NL. Accelerated metabolism of nicotine and cotinine in pregnant smokers. *J Pharmacol Exp Ther* 2002;301(2):594–98. [PMID: 11961061] https://pubmed.ncbi.nlm.nih.gov/11961061

DeVido J, Bogunovic O, Weiss RD. Alcohol use disorders in pregnancy. *Harv Rev Psychiatry* 2015;23(2):112–21. [PMID: 25747924] https://pubmed.ncbi.nlm.nih.gov/25747924

Dos Santos JF, de Melo Bastos Cavalcante C, Barbosa FT, et al. Maternal, fetal and neonatal consequences associated with the use of crack cocaine during the gestational period: a systematic review and meta-analysis. *Arch Gynecol Obstet* 2018;298(3):487–503. [PMID: 29951712] https://pubmed.ncbi.nlm.nih.gov/29951712

Drake P, Driscoll AK, Mathews TJ. Cigarette smoking during pregnancy: United States, 2016. *NCHS Data Brief* 2018;(305):1–8. [PMID: 29528282] https://pubmed.ncbi.nlm.nih.gov/29528282

El-Mohandes A, Herman AA, Nabil El-Khorazaty M, et al. Prenatal care reduces the impact of illicit drug use on perinatal outcomes. *J Perinatol* 2003;23(5):354–60. [PMID: 12847528] https://pubmed.ncbi.nlm.nih.gov/12847528

England LJ, Bennett C, Denny CH, et al. Alcohol use and co-use of other substances among pregnant females aged 12-44 years - United States, 2015-2018. *MMWR Morb Mortal Wkly Rep* 2020;69(31):1009–14. [PMID: 32759915] https://pubmed.ncbi.nlm.nih.gov/32759915

Enlow MB, Kullowatz A, Staudenmayer J, et al. Associations of maternal lifetime trauma and perinatal traumatic stress symptoms with infant cardiorespiratory reactivity to psychological challenge. *Psychosom Med* 2009;71(6):607–14. [PMID: 19553287] https://pubmed.ncbi.nlm.nih.gov/19553287

Fajemirokun-Odudeyi O, Sinha C, Tutty S, et al. Pregnancy outcome in women who use opiates. *Eur J Obstet Gynecol Reprod Biol* 2006;126(2):170–75. [PMID: 16202501] https://pubmed.ncbi.nlm.nih.gov/16202501

FDA. Campral (acamprosate calcium) delayed-release tablets. 2004 Jul 29. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2004/21-431_Campral.cfm [accessed 2025 Sep 23]

FDA. Vivitrol (naltrexone for extended-release injectable suspension). 2010 Oct. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021897s015lbl.pdf [accessed 2025 Sep 23]

Finnegan LP, Kaltenbach K. Primary pediatric care: assessment and management of neonatal abstinence syndrome. 1997. https://www.google.com/books/edition/_/AnFkQgAACAAJ

Flak AL, Su S, Bertrand J, et al. The association of mild, moderate, and binge prenatal alcohol exposure and child neuropsychological outcomes: a meta-analysis. *Alcohol Clin Exp Res* 2014;38(1):214–26. [PMID: 23905882] https://pubmed.ncbi.nlm.nih.gov/23905882

Forinash AB, Pitlick JM, Clark K, et al. Nicotine replacement therapy effect on pregnancy outcomes. *Ann Pharmacother* 2010;44(11):1817–21. [PMID: 20978216] https://pubmed.ncbi.nlm.nih.gov/20978216

Gawronski KM, Prasad MR, Backes CR, et al. Neonatal outcomes following in utero exposure to buprenorphine/naloxone or methadone. *SAGE Open Med* 2014;2:2050312114530282. [PMID: 26770721] https://pubmed.ncbi.nlm.nih.gov/26770721

Gouin K, Murphy K, Shah PS. Effects of cocaine use during pregnancy on low birthweight and preterm birth: systematic review and metaanalyses. *Am J Obstet Gynecol* 2011;204(4):340.e1–12. [PMID: 21257143] https://pubmed.ncbi.nlm.nih.gov/21257143

Grossman MR, Lipshaw MJ, Osborn RR, et al. A novel approach to assessing infants with neonatal abstinence syndrome. *Hosp Pediatr* 2018;8(1):1–6. [PMID: 29263121] https://pubmed.ncbi.nlm.nih.gov/29263121

Guille C, Aujla R. Developmental consequences of prenatal substance use in children and adolescents. *J Child Adolesc Psychopharmacol* 2019;29(7):479–86. [PMID: 31038354] https://pubmed.ncbi.nlm.nih.gov/31038354

Gunn JK, Rosales CB, Center KE, et al. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. *BMJ Open* 2016;6(4):e009986. [PMID: 27048634] https://pubmed.ncbi.nlm.nih.gov/27048634

Guttmacher Institute. Substance use during pregnancy. 2022 Aug 1. https://www.guttmacher.org/state-policy/explore/substance-use-during-pregnancy [accessed 2021 Jun 23]

Haastrup MB, Pottegård A, Damkier P. Alcohol and breastfeeding. *Basic Clin Pharmacol Toxicol* 2014;114(2):168–73. [PMID: 24118767] https://pubmed.ncbi.nlm.nih.gov/24118767

Haight SC, Ko JY, Tong VT, et al. Opioid use disorder documented at delivery hospitalization - United States, 1999-2014. *MMWR Morb Mortal Wkly Rep* 2018;67(31):845–49. [PMID: 30091969] https://pubmed.ncbi.nlm.nih.gov/30091969

Hall ES, Wexelblatt SL, Crowley M, et al. A multicenter cohort study of treatments and hospital outcomes in neonatal abstinence syndrome. *Pediatrics* 2014;134(2):e527–34. [PMID: 25070317] https://pubmed.ncbi.nlm.nih.gov/25070317

Hämmig R, Kemter A, Strasser J, et al. Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. *Subst Abuse Rehabil* 2016;7:99–105. [PMID: 27499655] https://pubmed.ncbi.nlm.nih.gov/27499655

Handelsman L, Cochrane KJ, Aronson MJ, et al. Two new rating scales for opiate withdrawal. *Am J Drug Alcohol Abuse* 1987;13(3):293–308. [PMID: 3687892] https://pubmed.ncbi.nlm.nih.gov/3687892

Hobel CJ, Goldstein A, Barrett ES. Psychosocial stress and pregnancy outcome. *Clin Obstet Gynecol* 2008;51(2):333–48. [PMID: 18463464] https://pubmed.ncbi.nlm.nih.gov/18463464

Holmes AV, Atwood EC, Whalen B, et al. Rooming-in to treat neonatal abstinence syndrome: improved family-centered care at lower cost. *Pediatrics* 2016;137(6). [PMID: 27194629] https://pubmed.ncbi.nlm.nih.gov/27194629

House SJ, Coker JL, Stowe ZN. Perinatal substance abuse: at the clinical crossroads of policy and practice. *Am J Psychiatry* 2016;173(11):1077–80. [PMID: 27798997] https://pubmed.ncbi.nlm.nih.gov/27798997

Hudak ML, Tan RC. Neonatal drug withdrawal. *Pediatrics* 2012;129(2):e540–60. [PMID: 22291123] https://pubmed.ncbi.nlm.nih.gov/22291123

Hulse GK, O'Neil G, Arnold-Reed DE. Methadone maintenance vs. implantable naltrexone treatment in the pregnant heroin user. *Int J Gynaecol Obstet* 2004;85(2):170–71. [PMID: 15099783] https://pubmed.ncbi.nlm.nih.gov/15099783

Jansson LM, Choo R, Velez ML, et al. Methadone maintenance and breastfeeding in the neonatal period. *Pediatrics* 2008;121(1):106–14. [PMID: 18166563] https://pubmed.ncbi.nlm.nih.gov/18166563

Jansson LM, Velez M. Neonatal abstinence syndrome. *Curr Opin Pediatr* 2012;24(2):252–58. [PMID: 22227786] https://pubmed.ncbi.nlm.nih.gov/22227786

Jarlenski M, Minney S, Hogan C, et al. Obstetric and pediatric provider perspectives on mandatory reporting of prenatal substance use. *J Addict Med* 2019;13(4):258–63. [PMID: 30550393] https://pubmed.ncbi.nlm.nih.gov/30550393

Jones HE, Chisolm MS, Jansson LM, et al. Naltrexone in the treatment of opioid-dependent pregnant women: the case for a considered and measured approach to research. *Addiction* 2013;108(2):233–47. [PMID: 22471668] https://pubmed.ncbi.nlm.nih.gov/22471668

Jones HE, Fielder A. Neonatal abstinence syndrome: historical perspective, current focus, future directions. *Prev Med* 2015;80:12–17. [PMID: 26232620] https://pubmed.ncbi.nlm.nih.gov/26232620

Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med* 2010;363(24):2320–31. [PMID: 21142534] https://pubmed.ncbi.nlm.nih.gov/21142534

Jones HE, Martin PR, Heil SH, et al. Treatment of opioid-dependent pregnant women: clinical and research issues. *J Subst Abuse Treat* 2008;35(3):245–59. [PMID: 18248941] https://pubmed.ncbi.nlm.nih.gov/18248941

Jumah NA, Edwards C, Balfour-Boehm J, et al. Observational study of the safety of buprenorphine+naloxone in pregnancy in a rural and remote population. *BMJ Open* 2016;6(10):e011774. [PMID: 27799240] https://pubmed.ncbi.nlm.nih.gov/27799240

Kaltenbach K, Berghella V, Finnegan L. Opioid dependence during pregnancy. Effects and management. *Obstet Gynecol Clin North Am* 1998;25(1):139–51. [PMID: 9547764] https://pubmed.ncbi.nlm.nih.gov/9547764

Kaltenbach K, O'Grady KE, Heil SH, et al. Prenatal exposure to methadone or buprenorphine: early childhood developmental outcomes. *Drug Alcohol Depend* 2018;185:40–49. [PMID: 29413437] https://pubmed.ncbi.nlm.nih.gov/29413437

Kattimani S, Bharadwaj B. Clinical management of alcohol withdrawal: a systematic review. *Ind Psychiatry J* 2013;22(2):100–108. [PMID: 25013309] https://pubmed.ncbi.nlm.nih.gov/25013309

Kelty E, Tran D, Lavin T, et al. Prevalence and safety of acamprosate use in pregnant alcohol-dependent women in New South Wales, Australia. *Addiction* 2019;114(2):206–15. [PMID: 30152012] https://pubmed.ncbi.nlm.nih.gov/30152012

Klaire S, Zivanovic R, Barbic SP, et al. Rapid micro-induction of buprenorphine/naloxone for opioid use disorder in an inpatient setting: a case series. *Am J Addict* 2019;28(4):262–65. [PMID: 30901127] https://pubmed.ncbi.nlm.nih.gov/30901127

Kocherlakota P. Neonatal abstinence syndrome. *Pediatrics* 2014;134(2):e547–61. [PMID: 25070299] https://pubmed.ncbi.nlm.nih.gov/25070299

Kotelchuck M, Cheng ER, Belanoff C, et al. The prevalence and impact of substance use disorder and treatment on maternal obstetric experiences and birth outcomes among singleton deliveries in Massachusetts. *Matern Child Health J* 2017;21(4):893–902. [PMID: 27832443] https://pubmed.ncbi.nlm.nih.gov/27832443

Kraft WK. Buprenorphine in neonatal abstinence syndrome. *Clin Pharmacol Ther* 2018;103(1):112–19. [PMID: 29105752] https://pubmed.ncbi.nlm.nih.gov/29105752

Kraft WK, Gibson E, Dysart K, et al. Sublingual buprenorphine for treatment of neonatal abstinence syndrome: a randomized trial. *Pediatrics* 2008;122(3):e601–7. [PMID: 18694901] https://pubmed.ncbi.nlm.nih.gov/18694901

Kraft WK, Stover MW, Davis JM. Neonatal abstinence syndrome: pharmacologic strategies for the mother and infant. *Semin Perinatol* 2016;40(3):203–12. [PMID: 26791055] https://pubmed.ncbi.nlm.nih.gov/26791055

Kunins HV, Bellin E, Chazotte C, et al. The effect of race on provider decisions to test for illicit drug use in the peripartum setting. *J Womens Health (Larchmt)* 2007;16(2):245–55. [PMID: 17388741] https://pubmed.ncbi.nlm.nih.gov/17388741

LactMed. Drugs and lactation database: alcohol. 2025 Jun 15. https://www.ncbi.nlm.nih.gov/books/NBK501469/ [accessed 2025 Sep 23]

LactMed(a). Drugs and lactation database: buprenorphine. 2025a Aug 15. https://www.ncbi.nlm.nih.gov/books/NBK501202/ [accessed 2025 Sep 19]

LactMed(a). Drugs and lactation database: naltrexone. 2025b Jun 15. https://www.ncbi.nlm.nih.gov/books/NBK501239/ [accessed 2025 Sep 19]

LactMed(b). Drugs and lactation database: nicotine. 2023 Nov 15. https://www.ncbi.nlm.nih.gov/books/NBK501586/ [accessed 2025 Sep 23]

LactMed(b). Drugs and lactation database: bupropion. 2025 Aug 15. https://www.ncbi.nlm.nih.gov/books/NBK501184/ [accessed 2025 Sep 23]

LactMed(c). Drugs and lactation database: cannabis. 2025 Jul 15. https://www.ncbi.nlm.nih.gov/books/NBK501587/ [accessed 2025 Sep 23]

LactMed(d). Drugs and lactation database: methadone. 2025 Aug 15. https://www.ncbi.nlm.nih.gov/books/NBK501233/ [accessed 2025 Sep 19]

LactMed(e). Drugs and lactation database: varenicline. 2024 Jun 15. https://www.ncbi.nlm.nih.gov/books/NBK501688/ [accessed 2025 Sep 23]

Lees B, Mewton L, Jacobus J, et al. Association of prenatal alcohol exposure with psychological, behavioral, and neurodevelopmental outcomes in children from the Adolescent Brain Cognitive Development Study. *Am J Psychiatry* 2020;177(11):1060–72. [PMID: 32972200] https://pubmed.ncbi.nlm.nih.gov/32972200

Lembeck AL, Tuttle D, Locke R, et al. Outcome differences in neonates exposed in-utero to opioids managed in the NICU versus pediatric floor. *J Addict Med* 2019;13(1):75–78. [PMID: 30252690] https://pubmed.ncbi.nlm.nih.gov/30252690

Link HM, Jones H, Miller L, et al. Buprenorphine-naloxone use in pregnancy: a systematic review and metaanalysis. *Am J Obstet Gynecol MFM* 2020;2(3):100179. [PMID: 33345863] https://pubmed.ncbi.nlm.nih.gov/33345863

Lund IO, Fischer G, Welle-Strand GK, et al. A comparison of buprenorphine + naloxone to buprenorphine and methadone in the treatment of opioid dependence during pregnancy: maternal and neonatal outcomes. *Subst Abuse* 2013;7:61–74. [PMID: 23531704] https://pubmed.ncbi.nlm.nih.gov/23531704

Mangla K, Hoffman MC, Trumpff C, et al. Maternal self-harm deaths: an unrecognized and preventable outcome. *Am J Obstet Gynecol* 2019;221(4):295–303. [PMID: 30849358] https://pubmed.ncbi.nlm.nih.gov/30849358

May PA, Hasken JM, Blankenship J, et al. Breastfeeding and maternal alcohol use: prevalence and effects on child outcomes and fetal alcohol spectrum disorders. *Reprod Toxicol* 2016;63:13–21. [PMID: 27174445] https://pubmed.ncbi.nlm.nih.gov/27174445

McAllister-Williams RH, Baldwin DS, Cantwell R, et al. British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017. *J Psychopharmacol* 2017;31(5):519–52. [PMID: 28440103] https://pubmed.ncbi.nlm.nih.gov/28440103

McQueen K, Murphy-Oikonen J. Neonatal abstinence syndrome. *N Engl J Med* 2016;375(25):2468–79. [PMID: 28002715] https://pubmed.ncbi.nlm.nih.gov/28002715

McQueen KA, Murphy-Oikonen J, Gerlach K, et al. The impact of infant feeding method on neonatal abstinence scores of methadone-exposed infants. *Adv Neonatal Care* 2011;11(4):282–90. [PMID: 22123351] https://pubmed.ncbi.nlm.nih.gov/22123351

Messinger DS, Bauer CR, Das A, et al. The maternal lifestyle study: cognitive, motor, and behavioral outcomes of cocaine-exposed and opiate-exposed infants through three years of age. *Pediatrics* 2004;113(6):1677–85. [PMID: 15173491] https://pubmed.ncbi.nlm.nih.gov/15173491

Metz TD, Borgelt LM. Marijuana use in pregnancy and while breastfeeding. *Obstet Gynecol* 2018;132(5):1198–1210. [PMID: 30234728] https://pubmed.ncbi.nlm.nih.gov/30234728

Meyer MC, Johnston AM, Crocker AM, et al. Methadone and buprenorphine for opioid dependence during pregnancy: a retrospective cohort study. *J Addict Med* 2015;9(2):81–86. [PMID: 25622120] https://pubmed.ncbi.nlm.nih.gov/25622120

Miller S. The ASAM principles of addiction medicine. 2018. https://shop.lww.com/The-ASAM-Principles-of-Addiction-Medicine/p/9781496370983

Minozzi S, Amato L, Jahanfar S, et al. Maintenance agonist treatments for opiate-dependent pregnant women. *Cochrane Database Syst Rev* 2020;11(11):CD006318. [PMID: 33165953] https://pubmed.ncbi.nlm.nih.gov/33165953

Mozurkewich EL, Rayburn WF. Buprenorphine and methadone for opioid addiction during pregnancy. *Obstet Gynecol Clin North Am* 2014;41(2):241–53. [PMID: 24845488] https://pubmed.ncbi.nlm.nih.gov/24845488

Muggli E, Matthews H, Penington A, et al. Association between prenatal alcohol exposure and craniofacial shape of children at 12 months of age. *JAMA Pediatr* 2017;171(8):771–80. [PMID: 28586842] https://pubmed.ncbi.nlm.nih.gov/28586842

Mullins N, Galvin SL, Ramage M, et al. Buprenorphine and naloxone versus buprenorphine for opioid use disorder in pregnancy: a cohort study. *J Addict Med* 2020;14(3):185–92. [PMID: 31567599] https://pubmed.ncbi.nlm.nih.gov/31567599

Nechanská B, Mravčík V, Skurtveit S, et al. Neonatal outcomes after fetal exposure to methadone and buprenorphine: national registry studies from the Czech Republic and Norway. *Addiction* 2018;113(7):1286–94. [PMID: 29443414] https://pubmed.ncbi.nlm.nih.gov/29443414

Nelson LF, Yocum VK, Patel KD, et al. Cognitive outcomes of young children after prenatal exposure to medications for opioid use disorder: a systematic review and meta-analysis. *JAMA Netw Open* 2020;3(3):e201195. [PMID: 32186745] https://pubmed.ncbi.nlm.nih.gov/32186745

NYSDOH. Maternal mortality and disparate racial outcomes: recommendations to the governor to reduce maternal mortality and racial disparities. 2019 Mar. https://www.health.ny.gov/community/adults/women/task_force_maternal_mortality/docs/maternal_mortality_report.pdf [accessed 2021 Jun 23]

NYSDOH. New York State Maternal and Child Health (MCH) dashboard - state level. 2023 Feb. https://webbi1.health.ny.gov/SASStoredProcess/guest?_program=/EBI/PHIG/apps/mch_dashboard/mch_dashboard&p=sh [accessed 2021 Jun 23]

O'Connor EA, Perdue LA, Senger CA, et al. Screening and behavioral counseling interventions to reduce unhealthy alcohol use in adolescents and adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2018;320(18):1910–28. [PMID: 30422198] https://pubmed.ncbi.nlm.nih.gov/30422198

O'Connor MJ, Whaley SE. Brief intervention for alcohol use by pregnant women. *Am J Public Health* 2007;97(2):252–58. [PMID: 17194863] https://pubmed.ncbi.nlm.nih.gov/17194863

O'Grady MJ, Hopewell J, White MJ. Management of neonatal abstinence syndrome: a national survey and review of practice. *Arch Dis Child Fetal Neonatal Ed* 2009;94(4):F249–52. [PMID: 19174414] https://pubmed.ncbi.nlm.nih.gov/19174414

O'Leary CM, Bower C. Guidelines for pregnancy: what's an acceptable risk, and how is the evidence (finally) shaping up? *Drug Alcohol Rev* 2012;31(2):170–83. [PMID: 21955332] https://pubmed.ncbi.nlm.nih.gov/21955332

Oh SS, Jee Y, Park EC, et al. Alcohol use disorders and increased risk of adverse birth complications and outcomes: an 11-year nationwide cohort study. *Int J Environ Res Public Health* 2020;17(22). [PMID: 33213014] https://pubmed.ncbi.nlm.nih.gov/33213014

Osborn(a) DA, Jeffery HE, Cole MJ. Opiate treatment for opiate withdrawal in newborn infants. *Cochrane Database Syst Rev* 2010;(10):CD002059. [PMID: 20927730] https://pubmed.ncbi.nlm.nih.gov/20927730

Osborn(b) DA, Jeffery HE, Cole MJ. Sedatives for opiate withdrawal in newborn infants. *Cochrane Database Syst Rev* 2010;(10):CD002053. [PMID: 20927729] https://pubmed.ncbi.nlm.nih.gov/20927729

Patorno E, Hernandez-Diaz S, Huybrechts KF, et al. Gabapentin in pregnancy and the risk of adverse neonatal and maternal outcomes: a population-based cohort study nested in the US Medicaid Analytic eXtract dataset. *PLoS Med* 2020;17(9):e1003322. [PMID: 32870921] https://pubmed.ncbi.nlm.nih.gov/32870921

Patrick SW, Kaplan HC, Passarella M, et al. Variation in treatment of neonatal abstinence syndrome in US children's hospitals, 2004-2011. *J Perinatol* 2014;34(11):867–72. [PMID: 24921412] https://pubmed.ncbi.nlm.nih.gov/24921412

Poole N, Greaves L. Highs and lows: Canadian perspectives of women and substance use. 2007. https://store-camh.myshopify.com/products/pg123

Racine N, Motz M, Leslie M, et al. Breaking the Cycle Pregnancy Outreach Program: reaching out to improve the health and well-being for pregnant substance-involved mothers. *J Motherhood Initiative Res Community Involvement* 2009;11(1). https://jarm.journals.yorku.ca/index.php/jarm/article/view/22525

Randhawa PA, Brar R, Nolan S. Buprenorphine-naloxone "microdosing": an alternative induction approach for the treatment of opioid use disorder in the wake of North America's increasingly potent illicit drug market. *CMAJ* 2020;192(3):E73. [PMID: 31959660] https://pubmed.ncbi.nlm.nih.gov/31959660

Reece-Stremtan S, Marinelli KA. ABM clinical protocol #21: guidelines for breastfeeding and substance use or substance use disorder, revised 2015. *Breastfeed Med* 2015;10(3):135–41. [PMID: 25836677] https://pubmed.ncbi.nlm.nih.gov/25836677

Reller MD, Strickland MJ, Riehle-Colarusso T, et al. Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005. *J Pediatr* 2008;153(6):807–13. [PMID: 18657826] https://pubmed.ncbi.nlm.nih.gov/18657826

Roberts SC, Nuru-Jeter A. Women's perspectives on screening for alcohol and drug use in prenatal care. *Womens Health Issues* 2010;20(3):193–200. [PMID: 20457407] https://pubmed.ncbi.nlm.nih.gov/20457407

Rutman D, Hubberstey C, Poole N, et al. Multi-service prevention programs for pregnant and parenting women with substance use and multiple vulnerabilities: program structure and clients' perspectives on wraparound programming. *BMC Pregnancy Childbirth* 2020;20(1):441. [PMID: 32746789] https://pubmed.ncbi.nlm.nih.gov/32746789

Ryan G, Dooley J, Gerber Finn L, et al. Nonpharmacological management of neonatal abstinence syndrome: a review of the literature. *J Matern Fetal Neonatal Med* 2019;32(10):1735–40. [PMID: 29207895] https://pubmed.ncbi.nlm.nih.gov/29207895

Saia KA, Schiff D, Wachman EM, et al. Caring for pregnant women with opioid use disorder in the USA: expanding and improving treatment. *Curr Obstet Gynecol Rep* 2016;5(3):257–63. [PMID: 27563497] https://pubmed.ncbi.nlm.nih.gov/27563497

Saiki T, Lee S, Hannam S, et al. Neonatal abstinence syndrome--postnatal ward versus neonatal unit management. *Eur J Pediatr* 2010;169(1):95–98. [PMID: 19440732] https://pubmed.ncbi.nlm.nih.gov/19440732

SAMHSA. Key substance use and mental health indicators in the United States: results from the 2018 National Survey on Drug Use and Health. 2019 Aug. https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf [accessed 2021 Jun 23]

Sarkar S, Donn SM. Management of neonatal abstinence syndrome in neonatal intensive care units: a national survey. *J Perinatol* 2006;26(1):15–17. [PMID: 16355103] https://pubmed.ncbi.nlm.nih.gov/16355103

Schiff DM, Nielsen T, Terplan M, et al. Fatal and nonfatal overdose among pregnant and postpartum women in Massachusetts. *Obstet Gynecol* 2018;132(2):466–74. [PMID: 29995730] https://pubmed.ncbi.nlm.nih.gov/29995730

Shah R, Diaz SD, Arria A, et al. Prenatal methamphetamine exposure and short-term maternal and infant medical outcomes. *Am J Perinatol* 2012;29(5):391–400. [PMID: 22399214] https://pubmed.ncbi.nlm.nih.gov/22399214

Shi Y, Zhu B, Liang D. The associations between prenatal cannabis use disorder and neonatal outcomes. *Addiction* 2021;116(11):3069–79. [PMID: 33887075] https://pubmed.ncbi.nlm.nih.gov/33887075

Smith LM, Diaz S, LaGasse LL, et al. Developmental and behavioral consequences of prenatal methamphetamine exposure: a review of the Infant Development, Environment, and Lifestyle (IDEAL) study. *Neurotoxicol Teratol* 2015;51:35–44. [PMID: 26212684] https://pubmed.ncbi.nlm.nih.gov/26212684

Stone R. Pregnant women and substance use: fear, stigma, and barriers to care. *Health Justice* 2015;3:2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5151516/

Terplan M, Kennedy-Hendricks A, Chisolm MS. Prenatal substance use: exploring assumptions of maternal unfitness. *Subst Abuse* 2015;9(Suppl 2):1–4. [PMID: 26448685] https://pubmed.ncbi.nlm.nih.gov/26448685

Terplan M, Martin C, Scialli A. How sex and gender impact clinical practice: an evidence-based guide to patient care: addiction: sex and gender evidence in alcohol, tobacco, and opioids. 2020. https://www.elsevier.com/books/how-sex-and-gender-impact-clinical-practice/jenkins/978-0-12-816569-0

Tolia VN, Patrick SW, Bennett MM, et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. *N Engl J Med* 2015;372(22):2118–26. [PMID: 25913111] https://pubmed.ncbi.nlm.nih.gov/25913111

Towers CV, Katz E, Weitz B, et al. Use of naltrexone in treating opioid use disorder in pregnancy. *Am J Obstet Gynecol* 2020;222(1):83.e1–8. [PMID: 31376396] https://pubmed.ncbi.nlm.nih.gov/31376396

Tran DT, Preen DB, Einarsdottir K, et al. Use of smoking cessation pharmacotherapies during pregnancy is not associated with increased risk of adverse pregnancy outcomes: a population-based cohort study. *BMC Med* 2020;18(1):15. [PMID: 32019533] https://pubmed.ncbi.nlm.nih.gov/32019533

Trivedi MH, Walker R, Ling W, et al. Bupropion and naltrexone in methamphetamine use disorder. *N Engl J Med* 2021;384(2):140–53. [PMID: 33497547] https://pubmed.ncbi.nlm.nih.gov/33497547

VA/DoD. Clinical practice guideline for the management of substance use disorders. 2015 Dec. https://www.healthquality.va.gov/guidelines/MH/sud/VADODSUDCPGRevised22216.pdf [accessed 2024 Sep 30]

Varcoe C, Browne AJ, Michaelson L. Physical examination and health assessment: substance use in the context of health assessment. 2014. https://www.google.com/books/edition/_/Idf_nQEACAAJ

Velez M, Jansson LM. The opioid dependent mother and newborn dyad: non-pharmacologic care. *J Addict Med* 2008;2(3):113–20. [PMID: 19727440] https://pubmed.ncbi.nlm.nih.gov/19727440

Volkow ND, Han B, Compton WM, et al. Marijuana use during stages of pregnancy in the United States. *Ann Intern Med* 2017;166(10):763–64. [PMID: 28418460] https://pubmed.ncbi.nlm.nih.gov/28418460

Welle-Strand GK, Skurtveit S, Jansson LM, et al. Breastfeeding reduces the need for withdrawal treatment in opioid-exposed infants. *Acta Paediatr* 2013;102(11):1060–66. [PMID: 23909865] https://pubmed.ncbi.nlm.nih.gov/23909865

Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs* 2003;35(2):253–59. [PMID: 12924748] https://pubmed.ncbi.nlm.nih.gov/12924748

WHO. Guidelines for the identification and management of substance use and substance use disorders in pregnancy. 2014 https://www.ncbi.nlm.nih.gov/books/NBK200701/ [accessed 2025 Sep 23]

Wiegand SL, Stringer EM, Stuebe AM, et al. Buprenorphine and naloxone compared with methadone treatment in pregnancy. *Obstet Gynecol* 2015;125(2):363–68. [PMID: 25569005] https://pubmed.ncbi.nlm.nih.gov/25569005

Wiles JR, Isemann B, Ward LP, et al. Current management of neonatal abstinence syndrome secondary to intrauterine opioid exposure. *J Pediatr* 2014;165(3):440–46. [PMID: 24948346] https://pubmed.ncbi.nlm.nih.gov/24948346

Wong J, Saver B, Scanlan JM, et al. Does maternal buprenorphine dose affect severity or incidence of neonatal abstinence syndrome? *J Addict Med* 2018;12(6):435–41. [PMID: 29905586] https://pubmed.ncbi.nlm.nih.gov/29905586

Wong S, Ordean A, Kahan M. Substance use in pregnancy. *J Obstet Gynaecol Can* 2011;33(4):367–84. [PMID: 21501542] https://pubmed.ncbi.nlm.nih.gov/21501542

Yeoh SL, Eastwood J, Wright IM, et al. Cognitive and motor outcomes of children with prenatal opioid exposure: a systematic review and meta-analysis. *JAMA Netw Open* 2019;2(7):e197025. [PMID: 31298718] https://pubmed.ncbi.nlm.nih.gov/31298718

Zabaneh R, Smith LM, LaGasse LL, et al. The effects of prenatal methamphetamine exposure on childhood growth patterns from birth to 3 years of age. *Am J Perinatol* 2012;29(3):203–10. [PMID: 21818727] https://pubmed.ncbi.nlm.nih.gov/21818727

Zelson C, Lee SJ, Casalino M. Neonatal narcotic addiction. Comparative effects of maternal intake of heroin and methadone. *N Engl J Med* 1973;289(23):1216–20. [PMID: 4748595] https://pubmed.ncbi.nlm.nih.gov/4748595

Supplement: Guideline Development and Recommendation Ratings

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Developer	New York State Department of Health AIDS Institute (NYSDOH AI) Clinical Guidelines Program
Funding source	NYSDOH AI
Program manager	Clinical Guidelines Program, Johns Hopkins University School of Medicine, Division of Infectious Diseases. See Program Leadership and Staff.
Mission	To produce and disseminate evidence-based, state-of-the-art clinical practice guidelines that establish uniform standards of care for practitioners who provide prevention or treatment of HIV, viral hepatitis, other sexually transmitted infections, and substance use disorders for adults throughout New York State in the wide array of settings in which those services are delivered.
Expert committees	The NYSDOH AI Medical Director invites and appoints committees of clinical and public health experts from throughout New York State to ensure that the guidelines are practical, immediately applicable, and meet the needs of care providers and stakeholders in all major regions of New York State, all relevant clinical practice settings, key New York State agencies, and community service organizations.
Committee structure	• Leadership: AI-appointed chair, vice chair(s), chair emeritus, clinical specialist(s), JHU Guidelines Program Director, AI Medical Director, AI Clinical Consultant, AVAC community advisor • Contributing members • Guideline writing groups: Lead author, coauthors if applicable, and all committee leaders
Disclosure and management of conflicts of interest	• Annual disclosure of financial relationships with commercial entities for the 12 months prior and upcoming is required of all individuals who work with the guidelines program, and includes disclosure for partners or spouses and primary professional affiliation. • The NYSDOH AI assesses all reported financial relationships to determine the potential for undue influence on guideline recommendations and, when indicated, denies participation in the program or formulates a plan to manage potential conflicts. Disclosures are listed for each committee member.
Evidence collection and review	• Literature search and review strategy is defined by the guideline lead author based on the defined scope of a new guideline or update. • A comprehensive literature search and review is conducted for a new guideline or an extensive update using PubMed, other pertinent databases of peer-reviewed literature, and relevant conference abstracts to establish the evidence base for guideline recommendations. • A targeted search and review to identify recently published evidence is conducted for guidelines published within the previous 3 years. • Title, abstract, and article reviews are performed by the lead author. The JHU editorial team collates evidence and creates and maintains an evidence table for each guideline.
Recommendation development	• The lead author drafts recommendations to address the defined scope of the guideline based on available published data. • Writing group members review the draft recommendations and evidence and deliberate to revise, refine, and reach consensus on all recommendations. • When published data are not available, support for a recommendation may be based on the committee's expert opinion. • The writing group assigns a 2-part rating to each recommendation to indicate the strength of the recommendation and quality of the supporting evidence. The group reviews the evidence, deliberates, and may revise recommendations when required to reach consensus.

Table S1: Guideline Development: New York State Department of Health AIDS Institute Clinical Guidelines Program	
Review and approval process	• Following writing group approval, draft guidelines are reviewed by all contributors, program liaisons, and a volunteer reviewer from the AI Community Advisory Committee. • Recommendations must be approved by two-thirds of the full committee. If necessary to achieve consensus, the full committee is invited to deliberate, review the evidence, and revise recommendations. • Final approval by the committee chair and the NYSDOH AI Medical Director is required for publication.
External reviews	• External review of each guideline is invited at the developer's discretion. • External reviewers recognized for their experience and expertise review guidelines for accuracy, balance, clarity, and practicality and provide feedback.
Update process	• JHU editorial staff ensure that each guideline is reviewed and determined to be current upon the 3-year anniversary of publication; guidelines that provide clinical recommendations in rapidly changing areas of practice may be reviewed annually. Published literature is surveilled to identify new evidence that may prompt changes to existing recommendations or development of new recommendations. • If changes in the standard of care, newly published studies, new drug approval, new drug-related warning, or a public health emergency indicate the need for immediate change to published guidelines, committee leadership will make recommendations and immediate updates and will invite full committee review as indicated.

Table S2: Recommendation Ratings and Definitions		
Strength	**Quality of Evidence**	
A: Strong B: Moderate C: Optional	1	Based on published results of at least 1 randomized clinical trial with clinical outcomes or validated laboratory endpoints.
	*	Based on either a self-evident conclusion; conclusive, published, in vitro data; or well-established practice that cannot be tested because ethics would preclude a clinical trial.
	2	Based on published results of at least 1 well-designed, nonrandomized clinical trial or observational cohort study with long-term clinical outcomes.
	2†	Extrapolated from published results of well-designed studies (including nonrandomized clinical trials) conducted in populations other than those specifically addressed by a recommendation. The source(s) of the extrapolated evidence and the rationale for the extrapolation are provided in the guideline text. One example would be results of studies conducted predominantly in a subpopulation (e.g., one gender) that the committee determines to be generalizable to the population under consideration in the guideline.
	3	Based on committee expert opinion, with rationale provided in the guideline text.