Clinical Expert Series

What Obstetrician–Gynecologists Should Know About Substance Use Disorders in the Perinatal Period

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Substance use in pregnancy is common; nearly one of five of pregnant individuals have past-month nicotine, alcohol, or illicit substance use, and more than one in 10 meet criteria for a substance use disorder (SUD). Substance use disorders are among the most stigmatized and poorly understood medical conditions, particularly in the perinatal period. The obstetrician–gynecologist (ob-gyn) is a critical member of the health care and social support team for pregnant and postpartum individuals with SUD. Yet, many do not feel knowledgeable in screening and treating SUD, hampering efforts to identify and treat this population. In this review, we focus on practices that ob-gyns can incorporate into daily care. We start with the unique vulnerabilities of the perinatal period and discuss overdose as a leading cause of maternal death in the United States. We then review the basic tenets of addiction medicine including person-centered language and current medical terminology as well as best practices for substance use screening. We provide a review of maternal, fetal, and child effects of the most common substances including tobacco, alcohol, cannabis, opioids, stimulants, and benzodiazepines and their respective treatment recommendations, so that ob-gyns can incorporate basic addiction management into their daily practice.

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Substance use and substance use disorders (SUD) are among the most common and challenging conditions faced by obstetrician–gynecologists (ob-gyns). In the United States, nearly one of five pregnant individuals have past-month nicotine, alcohol, or illicit substance use,[1] and almost 15% meet criteria for SUD.[2] Overdose is a leading cause of maternal death, yet most ob-gyns receive no or minimal training in evidence-based SUD screening or treatment.[3,4] Obstetrician–gynecologists are uniquely positioned to leverage maternal motivation for change to increase the number of individuals with treated addiction in pregnancy, postpartum and beyond. As with all chronic medical conditions, addiction is a result of complex interactions between genetics, environmental conditions, and individual behavior and requires multidisciplinary management and care continuity from pregnancy through postpartum.

Pregnancy significantly affects the prevalence of substance use.[5,6] Although 63.4% of nonpregnant reproductive-aged individuals report past-month use of nicotine, alcohol, or illicit substances, only 18.4% of pregnant individuals report use (Fig. 1). Use for all substances decreases by trimester.[7] The substantial decrease in use may be partly attributable to hormonal changes affecting the brain's reward-reinforcement pathways, leading to decreased craving.[8–12] Those who continue to use in pregnancy likely have addiction and need treatment.[13] Many pregnant individuals with SUD enter remission as a result of these physiologic

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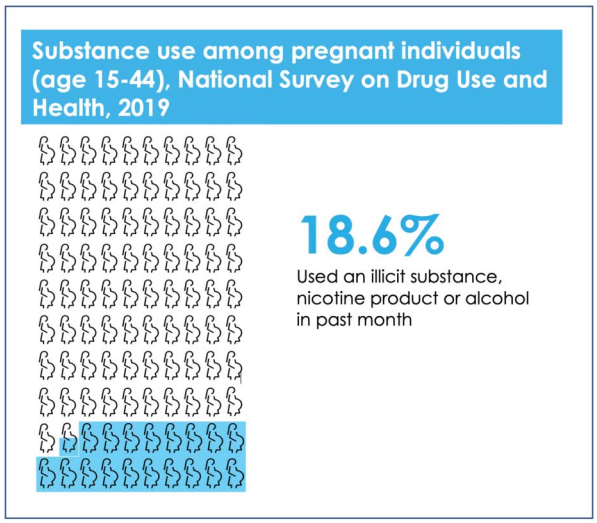

Fig. 1. Proportion of pregnant individuals with past-month substance use, National Survey on Drug Use and Health, 2019.

Smid. Substance Use Disorders Management in Perinatal Period. Obstet Gynecol 2022.

changes, increased maternal motivation, and priority access to treatment programs.

The postpartum period is a particularly vulnerable time with high rates of return to use,[5] and SUD symptom (eg, craving) recurrence.[14–16] Factors contributing to return to use include postpartum physiologic and mental health changes, demands of newborn care, child welfare involvement, and strain on relationships and finances.[17] For those who choose to place a child for adoption, grief over the loss of a child may trigger return to use.[18,19] For postpartum individuals who receive treatment and are in remission, system factors contributing to treatment disengagement and return to use include discrimination, clinician lack of knowledge about importance of treatment continuation, inaccessible SUD treatment for parenting individuals, and insurance change or loss.[20–26] For individuals who chose to terminate pregnancies, many are not offered treatment.[27–29]

For the complex reasons outlined above, overdose is a leading cause of maternal death in the United States.[23,30–36] Mounting evidence suggests that for individuals with SUD, the postpartum period is frequently destabilizing.[31–38] Most deaths occur in the setting of unrecognized or untreated SUD, after 6 weeks postpartum often after a period of remission, and with opioid and polysubstance use.[17,31,34,35,39] Contact with the health care system is common before maternal death, representing missed opportunities for intervention and prevention.[35,40]

These epidemiologic trends highlight two implications for daily practice: 1) ob-gyns should provide anticipatory guidance that untreated SUD is a major risk factor for death in pregnancy and postpartum; 2) ob-gyns should consider scheduling more frequent appointments in pregnancy and the first year postpartum, because they may be the only trusted access point patients have to addiction care.[41,42]

Child Welfare System

Currently, 25 states and the District of Columbia mandate child welfare reporting for drug use in pregnancy, and in three states drug use in pregnancy is grounds for civil commitment.[43] Obstetrician–gynecologists should be aware of state statutes but not perpetuate the erroneous idea that substance use in pregnancy is associated with subsequent child abuse or neglect.[42] The harms of child welfare involvement are well documented for both parent and child[44–46] and perpetuate racial inequities–Black and American Indian children are removed at 2–10 times the rate of White children in the setting of parental substance use.[45,47] Temporary or permanent removal of custody is a risk factor for discontinuation of addiction treatment.[48–50] Destabilization after loss of custody has also been associated with pregnancy-related deaths due to overdose.[36]

The Guttmacher Institute provides a broad overview of state-specific statutes including reporting requirements.[43] Importantly, reporting practices vary locally by county and even hospital. Obstetrician–gynecologists should work with pediatric and social work teams to understand local reporting practices and accurately explain them to patients before delivery.

The role of ob-gyns in the child welfare system process is twofold: 1) to provide support for pregnant and postpartum individuals with child welfare system involvement, and 2) to advocate for public policy reforms that eliminate punitive approaches to substance use in pregnancy and improve access to resources individuals need to meet their parenting and life goals.

Terminology of Substance Use and Addiction

One of the most frequent misconceptions of both pregnant individuals and ob-gyns is that continued substance use in the setting of SUD is a choice, rather than symptom of the medical condition.[51] By using current medical terminology (Table 1) and person-centered language (Table 2), ob-gyns communicate that SUD, like other chronic medical conditions, can be managed and that recovery is possible.[52,53] Many ob-gyns trained when "substance abuse" and "dependence" were the appropriate terms under the *Diagnostic*

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Table 1. Terminology of Substance Use and Addiction

Term	Definition
Substance use	Sporadic use of psychoactive substances
Substance misuse	Excessive use of psychoactive substances, which may lead to physical, social, or emotional harm
Addiction	A treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.[247]
Substance use disorder	DSM-5 uses the same overarching criteria for all substances to diagnosis mild (2–3 symptoms), moderate (4–5), and severe (6 or more) states[248]: • Impaired control o Use in larger amounts or longer periods than intended o Persistent desire or unsuccessful efforts to decrease or stop use o Craving or strong desire to use o Excessive time spent obtaining or using substance or recovering from the effects • Social impairment o Failure to fulfill major role obligations at work, school, or home o Persistent or recurrent social or interpersonal problems exacerbated by use o Reduction or cessation of important social, occupation or recreational activities because of use • Risky use o Use in physically hazardous situations o Continued use despite knowledge of persistent physical or psychologic problems arising from use • Pharmacologic properties o Tolerance as demonstrated by increased amount needed to achieve desires effect; diminished effect with continued use of the same amount o Withdrawal symptoms with cessation or decreased use o Note: Solely pharmacologic symptoms are not sufficient to meet criteria for substance use disorder
Recovery[249]	A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential.

DSM-5, Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition).

and Statistical Manual of Mental Disorders (Fourth Edition) (DSM-IV). In May 2013, the American Psychiatric Association issued the fifth edition of *Diagnostic and Statistical Manual of Mental Disorders*, which integrated the two DSM-IV criteria into SUD, with mild, moderate, and severe subclassifications. We encourage ob-gyns to use appropriate, modern terminology.[51]

Screening and Referral of Pregnant and Postpartum Individuals

The American College of Obstetricians and Gynecologists recommends universal screening before pregnancy and at the first prenatal visit in partnership with the pregnant individual.[42] Although screening may be negative in early pregnancy, substance use patterns may change, particularly postpartum; therefore, ob-gyns should consider screening at least once postpartum. Although pregnant individuals report being asked about substance use during prenatal care,[54,55] universal screening is the exception, rather than the rule.[56,57] Selective screening methods that target "high-risk" individuals based on various criteria (such as late entry into prenatal care), reinforce stereotypes and fail to identify those requiring services.[58]

Several validated tools exist to screen for tobacco, alcohol and other substances including prescription opioid misuse (Table 3).[13,57,59–61] Screening can be verbal, written or electronic depending on patient literacy and clinic resources. To promote clinician-patient partnership and to maximize the therapeutic benefit of screening, we suggest that ob-gyns ask permission first (eg, "Can I ask you some questions about drinking, smoking and other drugs?"). A declined screening must be respected. Pregnant and postpartum individuals have legitimate reasons for initial nondisclosure,[62] including a fear of child welfare notification and prior discrimination.[63,64] Establishing a strong person-centered therapeutic alliance requires trust and time. As with any medical condition, screening is not diagnostic. Substance use does not necessarily equate to SUD. Obstetrician–gynecologists should review SUD criteria (Table 2) to establish a diagnosis.

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Table 2. Stigmatizing and Preferred Language

Stigmatizing Language	Preferred Language
Substance abuse	Substance use or misuse, substance use disorder
Abuser, addict, alcoholic	Person with a substance use disorder
Smoker	Person with cannabis or tobacco or nicotine use disorder
Addicted baby	Neonate with neonatal abstinence syndrome or with in utero exposure to [named substance]
Clean or sober	Abstinent, in remission, toxicology "negative" for [substance]
Dirty	Using [substance], toxicology "positive" for [substance]
Drug of choice, habit	Substance of use
Getting or being high	Intoxicated, under the influence of [substance]
Shooting up	Intravenous drug use, injection drug use
Replacement or substitution treatment for opioid use disorder, opioid replacement, medication-assisted treatment	Medications for opioid use disorder, medications for addiction treatment
Relapse	Return to use, symptom recurrence

SBIRT (Screening, Brief Intervention and Referral to Treatment) is a useful public health approach to the delivery of early intervention and treatment to people with SUD and those at risk of developing these disorders.[57,65] Screening assesses substance use and severity and allows for risk stratification. For those at low risk, ob-gyns should reinforce abstinence and invite pregnant and postpartum individuals to discuss when or if use patterns change. For those at moderate risk, brief intervention (one to five patient-centered sessions lasting less than 15 minutes) focuses on increasing awareness regarding substance use and intrinsic motivation for behavioral change. Brief intervention is associated with a reduction in alcohol use in pregnancy,[66] and a greater reduction is observed when a partner chosen by the patient is included in the intervention.[67] For those at high risk who likely have SUD, direct initiation of treatment or referral to specialty addiction services is warranted. Most pregnant individuals with continued use are motivated to engage in treatment to maximize their health and that of their fetus,[68] particularly when care is nonjudgmental and personalized. Therefore, a referral is best accomplished with a clinician-to-clinician warm handoff. Obstetrician–gynecologists should initiate basic addiction care until specialty care can be arranged. Referrals to specialty care are not always easily accessible; however, online resources are available (Box 1).

Table 3. Screening Tools for Substance Use in Pregnancy

Substance	Tool	Comments
Tobacco, nicotine	5 A's – Tailored Approach[250,251]	Endorsed by both USPSTF and ACOG.[251,252]
Alcohol	Universal nonjudgmental screening question: "How much beer, wine, or other alcoholic beverages do you consume in an average week?" Positive use: Anyone who consumes alcohol should then be further screened with either the 3-question AUDIT-C[253] or T-ACE[254] (both validated in pregnancy).	USPSTF and ACOG recommend screening for unhealthy alcohol use in primary care settings for adults aged 18 years or older, including pregnant individuals, and providing persons engaged in risky drinking with brief behavioral interventions.[82]
Cannabis, opioids, amphetamines, cocaine, benzodiazepines	• 4P's Plus or 5 P's[255] • NIDA Quick Screen followed by ASSIST[256] • SURP-P[257] • CRAFFT (for those aged 26 years and younger)[258] • WIDUS[259]	• Two studies directly compare different screening instruments for substance use (other than tobacco or alcohol) in pregnancy.[260,261] • Accuracy is low for nearly all measures and none is superior. • Ob-gyns should use a validated instrument that is easily integrated into their existing workflow.

USPSTF, U.S. Preventive Services Task Force; ACOG, American College of Obstetricians and Gynecologists; AUDIT-C, Alcohol Use Disorders Identification Test-Concise; NIDA, National Institute on Drug Abuse; ASSIST, Modified Alcohol, Smoking and Substance Involvement Screening Test; SURP-P, Substance Use Risk Profile-Pregnancy; WIDUS, Wayne Indirect Drug Use Screener; ob-gyns, obstetrician–gynecologists.

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Box 1. Resources for Initiation and Referral for Substance Use Disorder Treatment

- SAMHSA Treatment Locator: inpatient, outpatient and residential substance use and mental health resources (https://findtreatment.samhsa.gov/locator).
- National Clinical Consultation Center: free confidential clinician-to-clinician telephone consultation focusing on substance use evaluation and management (Substance Use Warmline (855) 300-3595, https://nccc.ucsf.edu/clinical-resources/substance-use-resources/).
- Academy of Perinatal Harm Reduction: free Pregnancy and Substance Use: A Harm Reduction toolkit and other resources https://www.perinatalharmreduction.org/toolkit-pregnancy-substance-use.
- Perinatal Quality Collaboratives: resources for local referrals (https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pqc-states.html).

Finally, integration of SBIRT does take time and effort. Obstetrician–gynecologists can use billing codes to account for time spent performing structured assessments (https://www.samhsa.gov/sbirt/coding-reimbursement).

Toxicology Testing

Urine toxicology testing is not a substitute for validated screening.[13,42,59] Its use as a primary screening tool in prenatal care is inappropriate[69] and not recommended.[42,70] Urine toxicology tests should be used only when clearly indicated for clinical care and after receiving explicit and documented maternal consent.[59,71,72] For example, ob-gyns can use urine toxicology for harm-reduction counseling by screening for fentanyl with opioid, nonprescribed benzodiazepine, or stimulant use. Of note, opiate immunoassays do not detect synthetic opioids such as fentanyl or oxycodone and generally need to be ordered separately. If urine toxicology is used, ob-gyns must understand test characteristics.[73–75] At minimum, ob-gyns should understand that 1) point-of-care or "presumptive" immunoassay tests are screening tests[76] with high false-positive and false-negative result rates,[77] and 2) confirmatory testing (using gas chromatography–mass spectrometry analysis) is recommended in the event of results not consistent with self-report or treatment plan. Given current laws mandating child welfare notification and their potentially catastrophic consequence to families, thoughtful and judicious use of urine toxicology testing is warranted.[78]

Screening for Comorbidities

One quarter to one third of pregnant individuals with SUD have comorbid mental health conditions, including depression, anxiety, posttraumatic stress disorder, and trauma,[79,80] experience intimate partner violence,[26] and have higher rates of some infectious diseases.[81] Thus, ob-gyns should incorporate universal screening for mental health conditions,[41,82] intimate partner violence,[83] and infectious diseases (human immunodeficiency virus [HIV], hepatitis C, hepatitis B)[84] into practice. Obstetrician–gynecologists should understand infectious disease transmission windows (eg, HIV and hepatitis C test results may be negative for 4–8 weeks postseroconversion) and consider offering preexposure and postexposure prophylaxis for HIV[85] and referral to treatment for hepatitis C postpartum.[86] Re-screening for infectious diseases should be considered after return to use.

Substance Use Disorder Treatment

Once SUD is recognized, treatment should be offered and initiated as soon as possible. As with other chronic medical conditions, SUD outcomes are universally better among treated compared with untreated individuals, and 30–60% of patients will have symptom recurrence.[87] However, unlike other chronic conditions, there are marked gaps in SUD treatment availability. Treatment receipt varies by SUD and is marked by racial inequities in access. Receipt is highest for opioid use disorder (OUD) (34%) and lowest for alcohol use disorder (AUD) (12%).[88] Compared with White pregnant individuals, Black and Latinx individuals have lower odds of receiving treatment for any SUD,[88] and of receiving medication for OUD.[89] When prescribed, Black and Latinx individuals receive lower methadone doses than White individuals.[90] Although pregnant individuals are considered a priority population for treatment, they are no more likely than nonpregnant individuals to actually receive treatment.[88]

Polysubstance use is common among pregnant individuals with SUD,[91,92] and treatment for co-occurring SUD should occur simultaneously. In the following sections, we provide a brief overview of maternal, fetal, and child effects and treatment recommendations for the most common substances. We do not review data on breastfeeding because, per the American Academy of Pediatrics, maternal substance use is "not a categorical contraindication to breastfeeding."[93] However, breastfeeding in the context of continued illicit substance use is not recommended due to a paucity of data on neurodevelopmental outcomes and potential transmission of infectious diseases to the infant.[93]

Tobacco- and Nicotine-Containing Products

Nicotine is the most common modifiable risk factor for adverse perinatal outcomes.[94,95] Overall, 7.2–10%

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of pregnant individuals report smoking tobacco,[96,97] and likely more use nicotine-containing products, because surveillance mechanisms do not ascertain electronic cigarettes, hookah, or cigar use. Nicotine is associated with adverse maternal, fetal, and child outcomes including miscarriage (1% relative risk increase per cigarette smoked per day), ectopic pregnancy,[98] stillbirth, placental abruption,[99] placenta previa,[99] low birth weight,[100] and sudden infant death syndrome.[101–105] Although 50% of individuals will stop smoking in pregnancy, up to 90% will have a return to use within 1 year postpartum.[106]

The mainstay of treatment for nicotine use disorder in pregnancy is behavioral intervention, primarily cognitive behavioral therapy or contingency management. In a Cochrane Review of 72 trials (more than 25,000 pregnant individuals), behavioral interventions significantly reduced smoking in late pregnancy,[107] with an absolute difference of 6 in 100 individuals who stopped smoking. Interventions also reduced low birth weight and preterm delivery. However, in eight trials (more than 1,000 women) behavioral interventions did not reduce return to use postpartum.[107]

Although robust data support behavioral interventions, there is insufficient evidence for nicotine replacement therapy, bupropion hydrochloride sustained release, and varenicline,[108–110] primarily due to exclusion of pregnant individuals from clinical trials. A recent Cochrane Review included 11 trials of 2,412 pregnant individuals who smoked.[111] Nicotine replacement therapy was minimally associated with smoking cessation in late pregnancy but not with improvement in perinatal outcomes. Two small trials of pregnant individuals (n=115) did not demonstrate an association between bupropion use and smoking cessation.[112,113] A subsequent meta-analysis of bupropion use for smoking cessation that included these two trials and cohort studies (n=3,657) suggest safety in pregnancy and breastfeeding.[114] Varenicline, a partial nicotinic receptor agonist selective, reduces tobacco craving, withdrawal symptoms, and the reinforcing effects of smoking relative to placebo, bupropion and nicotine replacement therapy in nonpregnant individuals.[115–118] There are no trials evaluating varenicline in pregnant or postpartum individuals but small case series are reassuring for maternal and infant safety outcomes.[114] Given the magnitude of improvement that nicotine-containing products have on reproductive, pregnancy and child outcomes, ob-gyns should consider offering behavioral interventions in combination with medications in a shared decision-making model to pregnant and postpartum individuals.

Alcohol

In 2019, nearly 5% of pregnant individuals reported binge alcohol use, defined as four or more alcoholic drinks on the same occasion, in the past month.[1] Alcohol is a known teratogen and a leading modifiable cause of intellectual disability and developmental delay in the United States.[119,120] There is no known lower limit of alcohol exposure to avoid fetal alcohol spectrum disorder. Of the 4 million neonates born each year in the United States, 1,000–6,000 have fetal alcohol spectrum disorder,[121] similar to the number of neonates with Down syndrome.[122] Fetal alcohol spectrum disorder is 20 times more common in the United States (1.95/1,000) than in Europe (0.08/1,000)[123] and 10 times more common among individuals in poverty.[123] Obstetrician–gynecologists should be aware of the high rates of alcohol use in pregnancy and provide counseling about potential risks even in the setting of reported nonuse.

Individuals who screen positive for alcohol should be evaluated for AUD. Those with AUD need treatment and to be evaluated for the possibility of withdrawal, a potentially life-threatening condition. The majority of people with AUD experience withdrawal, and 3–5% will have severe withdrawal (delirium tremens) including profound confusion, autonomic hyperactivity, seizures, and cardiovascular collapse.[124] Delirium tremens occurs as early as 48 hours after alcohol cessation and can last up to 7 days. Mortality ranges from 1 to 4%.[124] Withdrawal management rests on 1) assessment using the CIWA-Ar (Clinical Institute for Withdrawal Assessment for Alcohol, Revised) protocol, 2) benzodiazepine treatment, and 3) vitamin supplementation.[125] The American Society of Addiction Medicine recommends initial inpatient management for people at risk of severe withdrawal, including those with history of withdrawal seizures.[126] Pregnancy is considered a medical condition that qualifies for inpatient management, which should be offered to all pregnant individuals with CIWA-Ar scores of 10 or higher. Most importantly, withdrawal management alone is not addiction treatment and is associated with a nearly 5% subsequent yearly mortality rate.[127] Therefore, after withdrawal management, individuals must be linked to continuing care with warm handoff.

The mainstay of AUD treatment is medication with behavioral interventions.[128] Psychosocial interventions alone are associated with high rates of return to use.[129] There are three U.S. Food and Drug Administration–approved medications for AUD treatment: disulfiram (aldehyde dehydrogenase inhibitor), Acamprosate

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(glutamate/GABA neuromodulator), and naltrexone (mu-opioid receptor antagonist). None of these medications have been evaluated through randomized trials in pregnancy.[130] However, alcohol and untreated AUD are likely more harmful than medications for AUD in pregnancy.[131] When contrasted to the known risks of alcohol, consideration of medication for AUD should be standard in clinical care for pregnant and postpartum individuals.

Cannabis

Among pregnant individuals, 5.4% reported past-month cannabis use[1] and it is the most common substance used in the United States that is illegal under federal law.[97] As of 2021, cannabis is legal for medical or recreational use in 36 states.[132] Reasons for cannabis use in pregnancy include perceived safety over pharmaceuticals in the self-treatment of nausea and vomiting of pregnancy,[133] and mental health conditions,[134,135] as well as recreational use.[136–138] Obstetrician–gynecologists should also be aware of a growing number of novel substances containing synthetic cannabinoids. Known as spice or K2, synthetic cannabinoids have more potent effects than natural cannabinoids[139] including respiratory distress, hypertension, acute renal failure, coagulopathy, cognitive impairment, psychosis, suicidal ideation, and death.[140–143] Maternal and perinatal outcomes of synthetic cannabinoids are limited to case reports.[144,145]

The American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, and the U.S. Surgeon General all advise against the recommendation of medical cannabis during prefertilization, pregnancy, and lactation due to unknown and potentially harmful maternal, fetal, and child effects.[146–148]

As with most substances, studies investigating treatment for cannabis use disorder have systematically excluded pregnant and lactating individuals. There are no approved medications for cannabis use disorder[149]; however, *N*-acetylcysteine[150] and gabapentin[151] have shown promise. Clinical trials focused on behavioral interventions including motivational enhancements, cognitive behavioral therapy, and contingency management have found modest benefits.[152]

Opioids

From 1999 to 2014, the rate of deliveries complicated by maternal OUD more than quadrupled (1.5/1,000 deliveries in 1999 to 6.5 in 2014) and in some states, the rate increased nearly 10-fold.[30] Available data regarding fetal effects of opioids are inconsistent and often poor quality. A recent systematic review showed a possible association between oral clefts and ventricular septal defects, although many included studies had unclear exposure and outcome measurements.[153] A review of medications for opioid use disorder (MOUD) did not show increased risk of congenital anomalies for buprenorphine or methadone.[154]

Many ob-gyns and patients are concerned about fetal withdrawal and fetal death from opioid withdrawal. Though two case reports linked fetal stress and death with opioid withdrawal in the 1970s,[155,156] recent studies have failed to show a link between maternal withdrawal and fetal loss.[157,158] Among women receiving methadone or buprenorphine, there is a decrease in fetal heart rate variability and movement at peak dose[159–161]; however, this is not associated with an increase in fetal loss and should not change antepartum or intrapartum monitoring requirements.[162–164]

Obstetrician–gynecologists should have a working knowledge of neonatal abstinence syndrome, which can result from prenatal opioid exposure, including MOUD. Neonatal abstinence syndrome is constellation of symptoms characterized by disturbances in the gastrointestinal, autonomic and central nervous systems including irritability, high pitched cry, poor sleep, and uncoordinated sucking leading to poor feeding. Neonatal abstinence syndrome is an expected, limited, and treatable condition occurring in 30–80% of neonates with prenatal opioid exposure.[165] Management includes both nonpharmacologic approaches (low stimulation environment, kangaroo or skin-to-skin contact, breastfeeding, and paired care or "rooming-in") and pharmacologic interventions including opioids (morphine, buprenorphine or methadone) and adjuvant treatment (phenobarbital, clonidine, ondansetron).[166–169] Multiple studies demonstrate that when controlled for polysubstance use and other confounding factors, MOUD dose (methadone[170–172] or buprenorphine[173,174]) is not correlated with neonatal abstinence syndrome. Therefore, ob-gyns should counsel both patients and treatment practitioners that arbitrarily restricting MOUD to decrease neonatal abstinence syndrome is discouraged.

Medications for opioid use disorder, including methadone, buprenorphine, and naltrexone (Table 4), save lives[175] and are the mainstay OUD treatment.[42,175] Behavioral interventions, such as contingency management,[176] cognitive behavioral therapy,[177] and family therapy,[178] can be helpful, but receipt of MOUD should not be contingent on participation in therapy.[179] Misconceptions about MOUD, such as, "they replace one addiction for another" or that they are supplemental, are common[51] and stigmatize treatment in this population. Optimal

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Table 4. Medications for Opioid Use Disorder

Medication	Mechanism	Initial Dose	Dosing	Special Considerations	Pregnancy Considerations
Methadone	Full mu-agonist and weak NMDA receptor antagonist	5–20 mg/d initially; not more than 40 mg/d; do not increase more than 10% every 3 d due to long half-life	80 and 120 mg/d,[262] (average for OUD treatment, although widely varies)	Must be dispensed by federally licensed outpatient treatment program; do not initiate if no local resource available QT prolongation Significant interactions with medications, including antiretrovirals, ondansetron, macrolide antibiotics, antiarrhythmic (sotalol) and psychotropic medications (olanzapine, haloperidol),	Split dosing in pregnancy associated with decrease in maternal symptoms[159,171,263] and possible decrease in neonatal abstinence syndrome.[264] Restricting dose in an attempt to decrease NAS is discouraged.
Buprenorphine	Partial mu-agonist with a very high affinity for the mu-opioid receptor Partial antagonist effect on the mu receptor; buprenorphine decreases the risk of overdose[265]	2–4-mg sublingual testing dose; after 6–12 h from short-acting and 24–72 h from long-acting opioids; multiple initiation protocols exist; micro-dosing protocols available in setting of fentanyl[266–268]	Sublingual: 2–32 mg/d Extended-release: 300 mg and 100 mg/mo subcutaneous Note: Sublocade, a commercially available extended-release buprenorphine, is not recommended in pregnancy because it contains N-methyl-2-pyrrolidone, an excipient that is associated with miscarriage, reduced fetal weight, and developmental delays in animal models.[269,270]	Requires "X-Waiver" to prescribe. Training requirements for physicians and other qualifying clinicians with fewer than 30 patients were recently removed but must still submit Notice of Intent to SAMHSA. May precipitate withdrawal, and mild–moderate withdrawal symptoms should be present before initiation. Monoproduct was previously recommended in pregnancy. Recent systemic review supports that combination product is safe.[42,271–274]	Symptoms may be improved with 2- or 3- times-daily dosing in pregnancy.
Naltrexone	Nonselective opioid receptor antagonist	25–50 mg orally for 1 wk, then 380 mg injection monthly	Oral: generally 25–50 mg/d Extended-release: 380 mg/3–4 wk intramuscular	Will precipitate withdrawal if administered within 10–14 d of opioid use.	Limited data on maternal, fetal, and child outcomes.[275–283]

NMDA N-methyl-D-aspartate; OUD opioid use disorder; NAS, neonatal abstinence syndrome; SAMHSA Substance Abuse and Mental Health Administration.

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duration of treatment is not established and for some individuals, taking MOUD may be lifelong. Among pregnant individuals, MOUD improve pregnancy and substance use outcomes and decrease overdose risk compared with no treatment.[17] Medication discontinuation postpartum is associated with return to use, overdose, and death.[180,181] Despite public health and professional society recommendations supporting MOUD[42,59,182] pregnant and postpartum individuals with OUD face significant barriers to treatment including stigma, discrimination, lack of knowledgeable clinicians, and misinformation about neonatal abstinence syndrome.[183–187]

Obstetrician–gynecologists should know how to manage acute opioid withdrawal and use this time to offer MOUD. The Clinical Opiate Withdrawal Scale (available at http://www.drugabuse.gov/nidamed-medical-health-professionals) characterizes symptoms and severity of withdrawal. Typically, symptoms from short-acting opioids, including heroin, occur within 8–24 hours, peak at 1–3 days, and take 4–10 days to subside.[188] For long-acting opioids such as methadone or buprenorphine, withdrawal symptoms typically occur 12–48 hours after last use and may last 10–20 days. Opioid withdrawal alone rarely results in severe morbidity or mortality; however, caution should be taken as polysubstance use is common and benzodiazepine and alcohol withdrawal can be fatal.[188]

In the inpatient setting, ob-gyns can initiate either methadone (Appendix 1, available online at http://links.lww.com/AOG/C559) or buprenorphine (Appendix 2, available online at http://links.lww.com/AOG/C559) for the management of opioid withdrawal based on patient preference and the ability to continue the medication on discharge. In the outpatient setting, ob-gyns need a buprenorphine waiver to prescribe.[189] Recent policy changes eliminate the special training previously required and allows eligible practitioners to prescribe to up to 30 patients with an X-waiver.[14] For those who intend to prescribe for more than 30 patients or those seeking training, ob-gyn–focused trainings exist (https://www.asam.org/blog-details/article/2021/08/09/asam-announces-partnership-with-the-acog-to-provide-waiver-qualifying-course-on-treatment-for-opioid-use-disorders).

Obstetrician–gynecologists should be aware of community resources including peer recovery support services[190] and community reinforcement programs ("12-step programs").[191] For individuals with OUD, participation in peer services is associated with greater number of attended OUD medical appointments compared with those not receiving peer services.[192] Recent qualitative data suggest that peer services are acceptable and valued among pregnant and postpartum individuals with OUD.[193] Both peer services[194] and community reinforcement programs[195] are available through telehealth and online.

Naloxone is a short-acting opioid antagonist used for the rapid reversal of opioid overdose and is a life-saving medication. Naloxone treats overdose and not OUD and should be administered immediately when overdose is suspected.[196] Given the increase in both intentional and unintentional fentanyl use, pregnant and postpartum individuals and their support individuals should be counseled about the need to call emergency medical services after overdose, because multiple doses of naloxone may be needed.[197] Naloxone co-prescription and training on overdose recognition is recommended for individuals with OUD and people in their support systems.[198,199]

Detoxification or medically supervised withdrawal is not recommended in pregnancy. A recent systematic review found that detoxification is associated with return to use and no improvement in maternal or neonatal outcomes (including neonatal abstinence syndrome).[200] Detoxification should be attempted only after shared decision making with counseling on the risk of return to use.

Cocaine

The unscientific and racist rhetoric surrounding cocaine use in pregnancy, which associated prenatal cocaine exposure with lifelong emotional, mental, and physical disability, is a cautionary tale for the field of substance use in pregnancy.[201,202] Subsequent research on cocaine and birth and developmental outcomes has failed to confirm previously described adverse child neurodevelopmental outcomes.[203] Systematic review data, with strict attention to comparison group selection, also do not confirm any teratogenic effect of cocaine.[203]

Nonetheless, ob-gyns do need to understand management of maternal cocaine toxicity. Cocaine can cause hypertensive emergencies, which are associated with preterm birth, placental abruption, and preeclampsia-like symptoms.[204–206] The adrenergic effects of acute cocaine ingestion include increased heart rate, blood pressure, and systemic vascular resistance, leading to increased myocardial oxygen demand,[207] which in association with coronary artery vasospasm, can cause myocardial ischemia, infarction, or arrhythmia.[208] Importantly, β-blockade is contraindicated after cocaine use because it can lead to unopposed α-adrenergic stimulation, resulting in end-organ ischemia and coronary vasospasm. Therefore, hydralazine, not labetalol, is the preferred

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medication for treatment of hypertensive emergency in pregnant individuals who use cocaine.

There are no medications approved for the treatment of cocaine use disorder.[209] Antidepressants are most studied – and appear to have no effect on cocaine use or treatment retention. Modest increases in abstinence have been seen with bupropion, topiramate and psychostimulants.[209,210] None of these medications have been studied in pregnancy. Treatment for cocaine addiction in pregnancy remains contingency management and motivational interviewing based – best provided within a comprehensive care setting and grounded in the principles of harm reduction.[211,212] Fetal surveillance, other than serial assessment of fetal growth, is not warranted for cocaine use alone.

Methamphetamine

Methamphetamine is the second most commonly used substance globally.[213] Methamphetamine use in pregnancy has been increasing, especially in the West and rural regions of the United States, where it is present in 1% of births.[214] Due to its vasoconstrictive properties, methamphetamine is thought to increase the risk for preterm birth, low birth weight, and small for gestational age.[215] The IDEAL (Infant Development and Lifestyle) study a prospective, multisite cohort of methamphetamine-exposed and matched unexposed neonates, was designed to prevent repeating the misleading and damaging science of early cocaine research. Neonatal effects of methamphetamine, especially immediately after birth, mirrored those of cocaine: findings are subtle and vary by time of assessment. Within 5 days of birth, prenatal methamphetamine exposure was associated with decreased arousal, increased stress, and poor quality of movement in an apparent dose–response fashion.[216] However, by 1 month of age, there were no differences in NICU Network Neurobehavioral Scale scores between the groups.[217] Though subtle effects on fine-motor skills were observed at 1 year, with the poorest performance observed in children with greater methamphetamine exposure, there were no differences at 3 years of age.[218]

There are no medications approved for the treatment of methamphetamine use disorder. A systematic review of 43 studies evaluating 23 different medications alone or in combination demonstrated, at best, a weak effect on treatment outcomes most consistently with stimulant agonists, naltrexone, and topiramate.[219] None of these medications have been studied for methamphetamine addiction in pregnancy. Similar to cocaine addiction, treatment is primarily contingency management and motivational interviewing – best provided within a comprehensive care setting and grounded in the principles of harm reduction.[211,212] Fetal surveillance, other than serial assessment of fetal growth, in this population is not warranted for methamphetamine use alone.

Benzodiazepines

Benzodiazepines are a class of medications that are prescribed for acute and chronic management of conditions such as seizures, insomnia, and anxiety. Benzodiazepines are prescribed more commonly to women than to men and are among the most frequently prescribed medications in pregnancy.[220] Among privately insured pregnant individuals, 0.8% had a benzodiazepine prescription,[221] but there are limited data on benzodiazepine use disorder. Benzodiazepines are a significant part of the overdose crisis in the United States. Concurrent opioid and benzodiazepine use increases the risk of opioid-related accidental poisoning, especially in the first 90 days of a new prescription.[222] Unlike opioids, there are no national guidelines for benzodiazepine prescribing and few evaluated interventions to reduce benzodiazepine-related problems.[223] Although benzodiazepines have benefit in the management of acute conditions (such as seizure or alcohol withdrawal), benzodiazepines (alone or in combination with selective serotonin reuptake inhibitors) do not improve outcomes in the chronic management of depression or anxiety beyond the first 4 weeks of treatment.[224,225] Tolerance to benzodiazepines develops rapidly and withdrawal can be severe and life-threatening. Therefore, initiation of benzodiazepine prescribing for chronic conditions is generally not recommended. Although use of benzodiazepines with MOUD is associated with overdose and overdose death,[226] MOUD should not be withheld due to current benzodiazepine use.[227]

The fetal effects of in utero exposure to benzodiazepines do not suggest teratogenicity. Though initial reports described facial clefts associated with diazepam, later prospective studies failed to support this finding.[228,229] Neonates with extended in utero exposure to diazepam have exhibited withdrawal symptoms similar to opioids,[230] including hypertonia, irritability, abnormal sleep patterns, inconsolable crying, tremors, bradycardia, cyanosis, poor sucking, apnea, diarrhea, vomiting, and aspiration.[231] Benzodiazepine exposure is associated with longer neonatal abstinence syndrome treatment especially in the context of methadone.[232] A single prospective cohort of 550 children followed up to 4 years of age found no

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negative effects of benzodiazepine exposure on neurocognitive development or intelligence.[233]

For individuals with benzodiazepine use disorder, gradual outpatient tapers are likely more effective than short-term inpatient care.[234] Symptom-based benzodiazepine withdrawal protocols appear superior to standing taper regimens in pregnancy.[235] Cognitive-behavioral therapy can help maintain abstinence.[236] Abrupt cessation can be severe and life-threatening. Benzodiazepine withdrawal is assessed and managed in the same fashion as alcohol withdrawal. However, individuals with an addiction to benzodiazepines require more than withdrawal management. Given the similarities with alcohol addiction, medications for AUD should be considered for chronic disease management. No additional fetal surveillance is required for benzodiazepine use.

Labor and Delivery and Postpartum Management Considerations

Pregnant people with SUD often experience discrimination from clinicians.[237,238] Concern about untreated or undertreated pain is common for people with SUD, especially those with OUD.[59] MOUD do not provide analgesia, and people with addiction may require more pain medication during labor.[239,240] MOUD should be continued at the same dose throughout the birthing hospitalization, and pain management should be multimodal, using nonopioid medications, regional anesthesia, and opioid agonists if needed.[59,241] Undertreated pain is likely a greater risk for return to use or SUD recurrence than judicious use of an opioid agonist for postoperative pain.[242] Preoperative and postoperative MOUD discontinuation is associated with overdose and should be avoided.[243] For people with untreated addiction, the birthing hospitalization is an important opportunity to connect to continuing care, and everyone with SUD, not only those with OUD, should receive naloxone and training in its use before discharge.[72] Peer recovery support[193,244,245] and trauma-informed doula[246] care should also be considered as an effective method of providing compassionate care for this population.

CONCLUSIONS

Obstetrician–gynecologists are often the primary clinician for pregnant individuals with SUD and must be prepared to address substance use in daily practice by universally screening, providing evidence-based counseling, and facilitating SUD treatment. Adverse pregnancy outcomes associated with SUDs reflect a constellation of patient-level and non–patient-related factors. Patient-level factors such as stress and mental health, lack of adequate prenatal care, exposure to infectious diseases, polysubstance use, psychiatric comorbidity, and exposure to poverty and intimate partner violence significantly contribute to the trajectory of addiction. However, non–patient-related factors such as an obstetric workforce untrained in addiction medicine, punitive public policy, the discriminatory child welfare system, stigmatization of SUD, lack of access to evidence-based treatment, and limited research to guide counseling and treatment play an equally important role in maternal, fetal, and newborn outcomes. These factors independently and collaboratively place the pregnant and postpartum individuals and their families at risk of poor outcomes.

A coordinated, multidisciplinary approach that supports pregnant and postpartum individuals in their lives, parenting, and treatment without criminal sanctions has the best chance for helping families.[42] As ob-gyns' basic knowledge about addiction and treatment improves, our ability to provide patient-centered and nonjudgmental care will also improve. Herein lies our best chance to improve the health outcomes of pregnant and postpartum individuals with SUD, their children and their families.

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