Clinical Expert Series

CME

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

Marcela C. Smid, MD, MS, and Mishka Terplan, MD, MPH

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.

(Obstet Gynecol 2022;139:317–37)

DOI: 10.1097/AOG.0000000000004657

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

From the Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, University of Utah Health, Salt Lake City, Utah; and the Friends Research Institute, Baltimore Maryland.

Each author has confirmed compliance with the journal's requirements for authorship.

Corresponding author: Marcela Smid, MD, MS, Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, University of Utah Health Salt Lake City, UT; email: Marcela.Smid@hsc.utah.edu.

Financial Disclosure

Marcela C. Smid serves as a medical consultant for Gilead Science Inc. Mishka Terplan is on the scientific advisory committee for Foundation for Opioid Response Efforts.

ISSN: 0029-7844/22

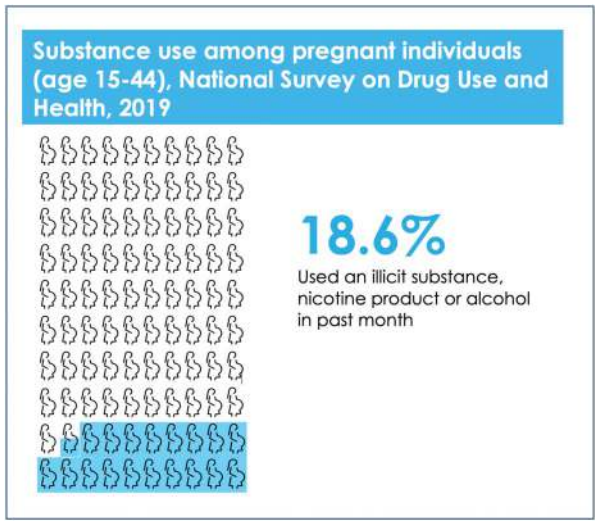

Fig. 1. Proportion of pregnant individuals with past-month substance use, National Survey on Drug Use and Health, 2019.

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*

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.

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.

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%

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

(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

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.

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

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

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.

REFERENCES

1. Substance Abuse and Mental Health Services Administration. 2019 NSDUH detailed tables. Accessed July 18, 2021. https://www.samhsa.gov/data/report/2019-nsduh-detailed-tables.
2. Vesga-López O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS. Psychiatric disorders in pregnant and postpartum women in the United States. Arch Gen Psychiatry 2008;65:805–15. doi: 10.1001/archpsyc.65.7.805
3. Isaacson JH, Fleming M, Kraus M, Kahn R, Mundt M. A national survey of training in substance use disorders in residency programs. J Stud Alcohol 2000;61:912–5. doi: 10.15288/jsa.2000.61.912
4. Garbarino AH, Kohn JR, Coverdale JH, Kilpatrick CC. Current trends in psychiatric education among obstetrics and gynecology residency programs. Acad Psychiatry 2019;43:294–9. doi: 10.1007/s40596-019-01018-w
5. Forray A, Merry B, Lin H, Ruger JP, Yonkers KA. Perinatal substance use: a prospective evaluation of abstinence and relapse. Drug Alcohol Depend 2015;150:147–55. doi: 10.1016/j.drugalcdep.2015.02.027
6. Forray A, Foster D. Substance use in the perinatal period. Curr Psychiatry Rep 2015;17:91. doi: 10.1007/s11920-015-0626-5
7. Terplan M, McNamara EJ, Chisolm MS. Pregnant and nonpregnant women with substance use disorders: the gap between treatment need and receipt. J Addict Dis 2012;31:342–9. doi: 10.1080/10550887.2012.735566
8. Yonkers KA, Forray A, Nich C, Carroll KM, Hine C, Merry BC, et al. Progesterone reduces cocaine use in postpartum women with a cocaine use disorder: a randomized, double-blind study. Lancet Psychiatry 2014;1:360–7. doi: 10.1016/s2215-0366(14)70333-5

9. Forray A, Gilstad-Hayden K, Suppies C, Bogen D, Sofuoglu M, Yonkers KA. Progesterone for smoking relapse prevention following delivery: a pilot, randomized, double-blind study. Psychoneuroendocrinology 2017;86:96–103. doi: 10.1016/j.psyneuen.2017.09.012
10. Lynch WJ, Sofuoglu M. Role of progesterone in nicotine addiction: evidence from initiation to relapse. Exp Clin Psychopharmacol 2010;18:451–61. doi: 10.1037/a0021265
11. Peltier MR, Sofuoglu M. Role of exogenous progesterone in the treatment of men and women with substance use disorders: a narrative review. CNS Drugs 2018;32:421–35. doi: 10.1007/s40263-018-0525-5
12. Allen SS, Allen AM, Lunos S, Tosun N. Progesterone and postpartum smoking relapse: a pilot double-blind placebo-controlled randomized trial. Nicotine Tob Res 2016;18:2145–53. doi: 10.1093/ntr/ntw156
13. American Society of Addiction Medicine. Public policy statement on substance use, misuse, and use disorders during and following pregnancy, with an emphasis on opioids. Accessed December 20, 2021. https://www.asam.org/advocacy/public-policy-statements/details/public-policy-statements/2021/08/09/substance-use-misuse-and-use-disorders-during-and-following-pregnancy-with-an-emphasis-on-opioids
14. Lee CW, Ho IK. Sex differences in opioid analgesia and addiction: interactions among opioid receptors and estrogen receptors. Mol Pain 2013;9:45. doi: 10.1186/1744-8069-9-45
15. Chartoff EH, Mavrikaki M. Sex differences in kappa opioid receptor function and their potential impact on addiction. Front Neurosci 2015;9:466. doi: 10.3389/fnins.2015.00466
16. Chartoff EH, McHugh RK. Translational studies of sex differences in sensitivity to opioid addiction. Neuropsychopharmacology 2016;41:383–4. doi: 10.1038/npp.2015.272
17. Schiff DM, Nielsen T, Terplan M, Hood M, Bernson D, Diop H, et al. Fatal and nonfatal overdose among pregnant and postpartum women in Massachusetts. Obstet Gynecol 2018;132:466–74. doi: 10.1097/aog.0000000000002734
18. Siverns K, Morgan G. "If only I could have said, if only somebody was listening": mothers' experiences of placing their child into care. Adoption Q 2021:1–23. doi: 10.1080/10926755.2021.1908473
19. Aloi JA. Nursing the disenfranchised: women who have relinquished an infant for adoption. J Psychiatr Ment Health Nurs 2009;16:27–31. doi: 10.1111/j.1365-2850.2008.01324.x
20. Mehta PK, Bachhuber MA, Hoffman R, Srinivas SK. Deaths from unintentional injury, homicide, and suicide during or within 1 year of pregnancy in Philadelphia. Am J Public Health 2016;106:2208–10. doi: 10.2105/ajph.2016.303473
21. Spelke B, Ramos S, Yu H, Cohen M, Booker TL. On the future of maternal mortality review in Rhode Island. R I Med J (2013) 2018;101:34–6.
22. Zaharatos J, St Pierre A, Cornell A, Pasalic E, Goodman D. Building U.S. capacity to review and prevent maternal deaths. J Womens Health (Larchmt) 2018;27:1–5. doi: 10.1089/jwh.2017.6800
23. St Pierre A, Zaharatos J, Goodman D, Callaghan WM. Challenges and opportunities in identifying, reviewing, and preventing maternal deaths. Obstet Gynecol 2018;131:138–42. doi: 10.1097/aog.0000000000002417
24. Mattocks KM, Clark R, Weinreb L. Initiation and engagement with methadone treatment among pregnant and postpartum women. Women's Health Issues 2017;27:646–51. doi: 10.1016/j.whi.2017.05.002
25. Kelly PJ, Blacksin B, Mason E. Factors affecting substance abuse treatment completion for women. Issues Ment Health Nurs 2001;22:287–304. doi: 10.1080/01612840152053110
26. Pallatino C, Chang JC, Krans EE. The intersection of intimate partner violence and substance use among women with opioid use disorder. Subst Abus 2021;42:197–204. doi: 10.1080/08897077.2019.1671296
27. Loree AM, Gariepy A, Ruger JP, Yonkers KA. Postpartum contraceptive use and rapid repeat pregnancy among women who use substances. Subst Use Misuse 2018;53:162–9. doi: 10.1080/10826084.2017.1327976
28. Terplan M, Hand DJ, Hutchinson M, Salisbury-Afshar E, Heil SH. Contraceptive use and method choice among women with opioid and other substance use disorders: a systematic review. Prev Med 2015;80:23–31. doi: 10.1016/j.ypmed.2015.04.008
29. MacAfee LK, Dalton V, Terplan M. Pregnancy intention, risk perception, and contraceptive use in pregnant women who use drugs. J Addict Med 2019;13:177–81. doi: 10.1097/adm.0000000000000471
30. Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM. Opioid use disorder documented at delivery hospitalization - United States, 1999-2014. MMWR Morb Mortal Wkly Rep 2018;67:845–9. doi: 10.15585/mmwr.mm6731a1
31. Gemmill A, Kiang MV, Alexander MJ. Trends in pregnancy-associated mortality involving opioids in the United States, 2007-2016. Am J Obstet Gynecol 2019;220:115–6. doi: 10.1016/j.ajog.2018.09.028
32. Baeva S, Archer NP, Ruggiero K, Hall M, Stagg J, Interis EC, et al. Maternal mortality in Texas. Am J Perinatol 2017;34:614–20. doi: 10.1055/s-0036-1595809
33. Davis N, Smoots A, Goodman D. Pregnancy-related deaths: data from 14 U.S. Maternal mortality review committees, 2008-2017. Centers for Disease Control and Prevention, U. S. Department of Health and Human Services; 2019
34. Hall OT, Hall OE, Rood KM, McKiever ME, Teater J, Senay A. Pregnancy-associated mortality due to accidental drug overdose and suicide in Ohio 2009-2018. Obstet Gynecol 2020;136:654–6. doi: 10.1097/aog.0000000000004066
35. Goldman-Mellor S, Margerison CE. Maternal drug-related death and suicide are leading causes of postpartum death in California. Am J Obstet Gynecol 2019;221:489.e1–9. doi: 10.1016/j.ajog.2019.05.045
36. Smid MC, Maeda J, Stone NM, Sylvester H, Baksh L, Debbink MP, et al. Standardized criteria for review of perinatal suicides and accidental drug-related deaths. Obstet Gynecol 2020;136:645–53. doi: 10.1097/aog.0000000000003988
37. At-risk drinking and alcohol dependence: obstetric and gynecologic implications. Committee Opinion No. 496. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:383–8. doi: 10.1097/AOG.0b013e31822c9906
38. Smid MC, Stone NM, Baksh L, Debbink MP, Einerson BD, Varner MW, et al. Pregnancy-associated death in UT: contribution of drug-induced deaths. Obstet Gynecol 2019;133:1131–40. doi: 10.1097/aog.0000000000003279
39. Virginia Department of Health, Office of the Chief Medical Examiner. Pregnancy-associated deaths from drug overdose in Virginia, 1999-2007: a report from the Virginia Maternal Mortality Review Team. Accessed July 15, 2021. http://www.vdh.virginia.gov/content/uploads/sites/18/2016/04/Final-Pregnancy-Associated-Deaths-Due-to-Drug-Overdose.pdf.
40. Nielsen T, Bernson D, Terplan M, Wakeman SE, Yule AM, Mehta PK, et al. Maternal and infant characteristics associated

with maternal opioid overdose in the year following delivery. Addiction 2020;115:291–301. doi: 10.1111/add.14825

41. Optimizing postpartum care. ACOG Committee Opinion No. 736. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e140–50. doi: 10.1097/aog.0000000000002633
42. Opioid use and opioid use disorder in pregnancy. Committee Opinion No. 711. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e81–94. doi: 10.1097/aog.0000000000002235
43. Guttmacher Institute. Substance use during pregnancy: state laws and policies. Accessed July 15, 2021. https://www.guttmacher.org/state-policy/explore/substance-use-during-pregnancy.
44. Redleaf DL. They took the kids last night: how the child protection system puts families at risk. ABC-CLIO; 2018.
45. Ketteringham ES, Cremer S, Becker C. Healthy mothers, healthy babies: a reproductive justice response to the womb-to-foster-care pipeline. CUNY L Rev 2016;20:77.
46. Roberts DE. The racial geography of child welfare: toward a new research paradigm. Child Welfare 2008;87:125–50.
47. Movement for Family Power. Whatever they do, I'm her comfort, I'm her protector: how the foster system has become ground zero for the US drug war. Accessed July 15, 2021. https://www.movementforfamilypower.org/ground-zero.
48. Fischer G, Eder H, Jagsch R, Lennkh C, Habeler A, Aschauer HN, et al. Maintenance therapy with synthetic opioids within a multidisciplinary program – a stabilizing necessity for pregnant opioid dependent women. Arch Women's Ment Health 1998;1:109–16. doi: 10.1007/s007370050014
49. Clark HW. Residential substance abuse treatment for pregnant and postpartum women and their children: treatment and policy implications. Child Welfare 2001;80:179–98.
50. Schauberger CW, Borgert AJ, Bearwald B. Continuation in treatment and maintenance of custody of newborns after delivery in women with opioid use disorder. J Addict Med 2020;14:119–25. doi: 10.1097/adm.0000000000000534
51. National Institute on Drug Abuse. Your words matter: language showing compassion and care for women, infants, families, and communities impacted by substance use disorder. Accessed July 15, 2021. https://www.drugabuse.gov/sites/default/files/nidamed_words_matter_women_infants_families.pdf.
52. Atayde AMP, Hauc SC, Bessette LG, Danckers H, Saitz R. Changing the narrative: a call to end stigmatizing terminology related to substance use disorders. Addict Res Theor 2021;29:359–62. doi: 10.1080/16066359.2021.1875215
53. Saitz R. International statement recommending against the use of terminology that can stigmatize people. J Addict Med 2016;10:1–2. doi: 10.1097/adm.0000000000000178
54. Pazol K, Robbins CL, Black LI, Ahrens KA, Daniels K, Chandra A, et al. Receipt of selected preventive health services for women and men of reproductive age - United States, 2011-2013. MMWR Surveill Summ 2017;66:1–31. doi: 10.15585/mmwr.ss6620a1
55. Krans EE, Davis MM, Schwarz EB. Psychosocial risk, prenatal counseling and maternal behavior: findings from PRAMS, 2004-2008. Am J Obstet Gynecol 2013;208:141.e1–7. doi: 10.1016/j.ajog.2012.11.017
56. Ko JY, Tong VT, Haight SC, Terplan M, Stark L, Snead C, et al. Obstetrician-gynecologists' practices and attitudes on substance use screening during pregnancy. J Perinatol 2019;40:422–32. doi: 10.1038/s41372-019-0542-3
57. Wright TE, Terplan M, Ondersma SJ, Boyce C, Yonkers K, Chang G, et al. The role of screening, brief intervention, and referral to treatment in the perinatal period. Am J Obstet Gynecol 2016;215:539–47. doi: 10.1016/j.ajog.2016.06.038
58. Kerker BD, Horwitz SM, Leventhal JM. Patients' characteristics and providers' attitudes: predictors of screening pregnant women for illicit substance use. Child Abuse Negl 2004;28:209–23. doi: 10.1016/j.chiabu.2003.07.004
59. Ecker J, Abuhamad A, Hill W, Bailit J, Bateman BT, Berghella V, et al. Substance use disorders in pregnancy: clinical, ethical, and research imperatives of the opioid epidemic: a report of a joint workshop of the Society for Maternal-Fetal Medicine, American College of Obstetricians and Gynecologists, and American Society of Addiction Medicine. Am J Obstet Gynecol 2019;221:B5–28. doi: 10.1016/j.ajog.2019.03.022
60. Substance Abuse and Mental Health Administration. Clinical guidance for treating pregnant and parenting women with opioid use disorder and their infants. Accessed January 15, 2021. https://store.samhsa.gov/product/Clinical-Guidance-for-Treating-Pregnant-and-Parenting-Women-With-Opioid-Use-Disorder-and-Their-Infants/SMA18-5054
61. World Health Organization. Guidelines for the identification and management of substance use and substance use disorders in pregnancy. Accessed July 15th, 2021. https://www.who.int/publications/i/item/9789241548731.
62. Paris R, Herriott AL, Maru M, Hacking SE, Sommer AR. Secrecy versus disclosure: women with substance use disorders share experiences in help seeking during pregnancy. Matern Child Health J 2020;24:1396–403. doi: 10.1007/s10995-020-03006-1
63. Stone R. Pregnant women and substance use: fear, stigma, and barriers to care. Health & Justice 2015;3:2. doi: 10.1186/s40352-015-0015-5
64. Falletta L, Hamilton K, Fischbein R, Aultman J, Kinney B, Kenne D. Perceptions of child protective services among pregnant or recently pregnant, opioid-using women in substance abuse treatment. Child Abuse Negl 2018;79:125–35. doi: 10.1016/j.chiabu.2018.01.026
65. Substance Abuse and Mental Health Administration. About SBIRT: screening, brief intervention, and referral to treatment. Accessed September 14, 2021. https://www.samhsa.gov/sbirt/about.
66. Chang G, Wilkins-Haug L, Berman S, Goetz MA. Brief intervention for alcohol use in pregnancy: a randomized trial. Addiction 1999;94:1499–508. doi: 10.1046/j.1360-0443.1999.941014996.x
67. Chang G, McNamara TK, Orav EJ, Koby D, Lavigne A, Ludman B, et al. Brief intervention for prenatal alcohol use: a randomized trial. Obstet Gynecol 2005;105:991–8. doi: 10.1097/01.Aog.0000157109.05453.84
68. Saia K, Jones H, Terplan M. Pregnancy and the opioid epidemic. Curr Treat Options Psychiatry 2017;4:184–95. doi: 10.1007/s40501-017-0116-y
69. Jarvis M, Williams J, Hurford M, Lindsay D, Lincoln P, Giles L, et al. Appropriate use of drug testing in clinical addiction medicine. J Addict Med 2017;11:163–73. doi: 10.1097/adm.0000000000000323
70. Alcohol abuse and other substance use disorders: ethical issues in obstetric and gynecologic practice. Committee Opinion No. 633. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:1529–37. doi: 10.1097/01.AOG.0000466371.86393.9b
71. Polak K, Kelpin S, Terplan M. Screening for substance use in pregnancy and the newborn. Semin Fetal Neonatal Med 2019;24:90–4. doi: 10.1016/j.siny.2019.01.007

72. Krans EE, Campopiano M, Cleveland LM, Goodman D, Kilday D, Kendig S, et al. National partnership for maternal safety: consensus bundle on obstetric care for women with opioid use disorder. Obstet Gynecol 2019;134:365–75. doi: 10.1097/aog.0000000000003381

73. Starrels JL, Fox AD, Kunins HV, Cunningham CO. They don't know what they don't know: internal medicine residents' knowledge and confidence in urine drug test interpretation for patients with chronic pain. J Gen Intern Med 2012;27:1521–7. doi: 10.1007/s11606-012-2165-7

74. Reisfield GM, Bertholf R, Barkin RL, Webb F, Wilson G. Urine drug test interpretation: what do physicians know? J Opioid Manag 2007;3:80–6. doi: 10.5055/jom.2007.0044

75. Reisfield GM, Webb FJ, Bertholf RL, Sloan PA, Wilson GR. Family physicians' proficiency in urine drug test interpretation. J Opioid Manag 2007;3:333–7. doi: 10.5055/jom.2007.0022

76. Luzzi V. Point of care devices for drugs of abuse testing: limitations and pitfalls. Critical issues in alcohol and drugs of abuse testing: Elsevier; 2019. p. 141–8.

77. Herring C, Muzyk AJ, Johnston C. Interferences with urine drug screens. J Pharm Pract 2011;24:102–8. doi: 10.1177/0897190010380463

78. Terplan M, Minkoff H. Neonatal abstinence syndrome and ethical approaches to the identification of pregnant women who use drugs. Obstet Gynecol 2017;129:164–7. doi: 10.1097/aog.0000000000001781

79. Arnaudo CL, Andraka-Christou B, Allgood K. Psychiatric comorbidities in pregnant women with opioid use disorders: prevalence, impact, and implications for treatment. Curr Addict Rep 2017;4:1–13. doi: 10.1007/s40429-017-0132-4

80. Shen Y, Lo-Ciganic WH, Segal R, Goodin AJ. Prevalence of substance use disorder and psychiatric comorbidity burden among pregnant women with opioid use disorder in a large administrative database 2009-2014. J Psychosom Obstet Gynaecol 2020:1–7. doi: 10.1080/0167482x.2020.1727882

81. Ko JY, Haight SC, Schillie SF, Bohm MK, Dietz PM. National trends in hepatitis C infection by opioid use disorder status among pregnant women at delivery hospitalization - United States, 2000-2015. MMWR Morb Mortal Wkly Rep 2019;68:833–8. doi: 10.15585/mmwr.mm6839a1

82. Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, et al. Screening and behavioral counseling interventions to reduce unhealthy alcohol use in adolescents and adults: US preventive services task force recommendation statement. JAMA 2018;320:1899–909. doi: 10.1001/jama.2018.16789

83. Intimate partner violence. Committee Opinion No. 518. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;119:412–7. doi: 10.1097/AOG.0b013e318249ff74

84. American College of Obstetricians and Gynecologists. Routine hepatitis C virus screening in pregnant individuals. Accessed July 17, 2021. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2021/05/routine-hepatitis-c-virus-screening-in-pregnant-individuals.

85. World Health Organization. WHO technical brief: preventing HIV during pregnancy and breastfeeding in the context of PrEP. Accessed July 15, 2021. https://apps.who.int/iris/bitstream/handle/10665/255866/WHO-HIV-2017.09-eng.pdf.

86. Hughes BL, Page CM, Kuller JA. Hepatitis C in pregnancy: screening, treatment, and management. Am J Obstet Gynecol 2017;217:B2–12. doi: 10.1016/j.ajog.2017.07.039

87. McLellan AT, Lewis DC, O'Brien CP, Kleber HD. Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. JAMA 2000;284:1689–95. doi: 10.1001/jama.284.13.1689

88. Martin CE, Scialli A, Terplan M. Unmet substance use disorder treatment need among reproductive age women. Drug and alcohol dependence 2020;206:107679. doi: 10.1016/j.drugalcdep.2019.107679

89. Schiff DM, Nielsen T, Hoeppner BB, Terplan M, Hansen H, Bernson D, et al. Assessment of racial and ethnic disparities in the use of medication to treat opioid use disorder among pregnant women in Massachusetts. JAMA Netw open 2020;3:e205734. doi: 10.1001/jamanetworkopen.2020.5734

90. Rosenthal EW, Short VL, Cruz Y, Barber C, Baxter JK, Abatemarco DJ, et al. Racial inequity in methadone dose at delivery in pregnant women with opioid use disorder. J Subst Abuse Treat 2021;131:108454. doi: 10.1016/j.jsat.2021.108454

91. Jarlenski M, Krans EE, Chen Q, Rothenberger SD, Cartus A, Zivin K, et al. Substance use disorders and risk of severe maternal morbidity in the United States. Drug Alcohol Depend 2020;216:108236. doi: 10.1016/j.drugalcdep.2020.108236

92. Jarlenski M, Krans EE. Co-occurring substance use disorders identified among delivery hospitalizations in the United States. J Addict Med 2020;15:504–7. doi: 10.1097/adm.0000000000000792

93. Breastfeeding and the use of human milk. Pediatrics 2012;129:e827–41. doi: 10.1542/peds.2011-3552

94. Kurti AN, Redner R, Lopez AA, Keith DR, Villanti AC, Stanton CA, et al. Tobacco and nicotine delivery product use in a national sample of pregnant women. Prev Med 2017;104:50–6. doi: 10.1016/j.ypmed.2017.07.030

95. Johnson AL, Collins LK, Villanti AC, Pearson JL, Niaura RS. Patterns of nicotine and tobacco product use in youth and young adults in the United States, 2011-2015. Nicotine Tob Res 2018;20:S48–54. doi: 10.1093/ntr/nty018

96. Drake P, Driscoll AK, Mathews TJ. Cigarette smoking during pregnancy: United States, 2016. NCHS Data Brief 2018:1–8

97. Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2019 national Survey on drug use and health (HHS publication No. PEP20-07-01-001, NSDUH series H-55). Accessed July 15, 2021. https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR090120.htm.

98. Bouyer J, Coste J, Fernandez H, Job-Spira N. Tobacco and ectopic pregnancy. Arguments in favor of a causal relation [in French]. Rev Epidemiol Sante Publique 1998;46:93–9.

99. Aliyu MH, Lynch O, Wilson RE, Alio AP, Kristensen S, Marty PJ, et al. Association between tobacco use in pregnancy and placenta-associated syndromes: a population-based study. Arch Gynecol Obstet 2011;283:729–34. doi: 10.1007/s00404-010-1447-8

100. Ion R, Bernal AL. Smoking and preterm birth. Reprod Sci 2015;22:918–26. doi: 10.1177/1933719114556486

101. Dietz PM, England LJ, Shapiro-Mendoza CK, Tong VT, Farr SL, Callaghan WM. Infant morbidity and mortality attributable to prenatal smoking in the U.S. Am J Prev Med 2010;39:45–52. doi: 10.1016/j.amepre.2010.03.009

102. Ratnasiri AWG, Gordon L, Dieckmann RA, Lee HC, Parry SS, Arief VN, et al. Smoking during pregnancy and adverse

birth and maternal outcomes in California, 2007 to 2016. Am J Perinatol 2020;37:1364–76. doi: 10.1055/s-0039-1693689

103. Adams JM. Smoking cessation-progress, barriers, and new opportunities: the Surgeon general's report on smoking cessation. JAMA 2020;323:2470–1. doi: 10.1001/jama.2020.6647

104. World Health Organization. WHO recommendations for the prevention and management of tobacco use and second-hand smoke exposure in pregnancy. Accessed July 15, 2021. https://apps.who.int/iris/bitstream/handle/10665/94555/9789241506076_eng.pdf;jsessionid=C22738AEA7D8C5298D27A981B7E648C5?sequence=1.

105. Office on Smoking Health. Publications and reports of the Surgeon General. Women and smoking: a report of the Surgeon General. Centers for Disease Control and Prevention; 2001.

106. Tong VT, Dietz PM, Morrow B, D'Angelo DV, Farr SL, Rockhill KM, et al. Trends in smoking before, during, and after pregnancy–pregnancy risk assessment monitoring system, United States, 40 sites 2000-2010. MMWR Surveill Summ 2013;62:1–19.

107. Lumley J, Chamberlain C, Dowswell T, Oliver S, Oakley L, Watson L. Interventions for promoting smoking cessation during pregnancy. The Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD001055. doi: 10.1002/14651858.CD001055.pub3

108. Smith PH, Weinberger AH, Zhang J, Emme E, Mazure CM, McKee SA. Sex differences in smoking cessation pharmacotherapy comparative efficacy: a Network meta-analysis. Nicotine Tob Res 2017;19:273–81. doi: 10.1093/ntr/ntw144

109. McKee SA, Smith PH, Kaufman M, Mazure CM, Weinberger AH. Sex differences in varenicline efficacy for smoking cessation: a meta-analysis. Nicotine Tob Res 2016;18:1002–11. doi: 10.1093/ntr/ntv207

110. U.S. Food and Drug Administration. Want to quit smoking? FDA-approved products can help. Accessed. https://www.fda.gov/consumers/consumer-updates/want-quit-smoking-fda-approved-products-can-help.

111. Claire R, Chamberlain C, Davey MA, Cooper SE, Berlin I, Leonardi-Bee J, et al. Pharmacological interventions for promoting smoking cessation during pregnancy. The Cochrane Database of Systematic Reviews 2020, Issue 3. Art. No.: CD010078. doi: 10.1002/14651858.CD010078.pub3

112. Nanovskaya TN, Oncken C, Fokina VM, Feinn RS, Clark SM, West H, et al. Bupropion sustained release for pregnant smokers: a randomized, placebo-controlled trial. Am J Obstet Gynecol 2017;216:420.e1–9. doi: 10.1016/j.ajog.2016.11.1036

113. Stotts AL, Northrup TF, Cinciripini PM, Minnix JA, Blalock JA, Mullen PD, et al. Randomized, controlled pilot trial of bupropion for pregnant smokers: challenges and future directions. Am J Perinatol 2015;32:351–6. doi: 10.1055/s-0034-1386635

114. Turner E, Jones M, Vaz LR, Coleman T. Systematic review and meta-analysis to assess the safety of bupropion and varenicline in pregnancy. Nicotine Tob Res 2019;21:1001–10. doi: 10.1093/ntr/nty055

115. Aubin HJ, Bobak A, Britton JR, Oncken C, Billing CB, Jr., Gong J, et al. Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomised open-label trial. Thorax 2008;63:717–24. doi: 10.1136/thx.2007.090647

116. Schnoll RA, Patterson F, Lerman C. Treating tobacco dependence in women. J Womens Health (Larchmt) 2007;16:1211–8. doi: 10.1089/jwh.2006.0281

117. Fagerström K, Hughes J. Varenicline in the treatment of tobacco dependence. Neuropsychiatr Dis Treat 2008;4:353–63. doi: 10.2147/ndt.s927

118. Brandon TH, Drobes DJ, Unrod M, Heckman BW, Oliver JA, Roetzheim RC, et al. Varenicline effects on craving, cue reactivity, and smoking reward. Psychopharmacology (Berl) 2011;218:391–403. doi: 10.1007/s00213-011-2327-z

119. May PA, Baete A, Russo J, Elliott AJ, Blankenship J, Kalberg WO, et al. Prevalence and characteristics of fetal alcohol spectrum disorders. Pediatrics 2014;134:855–66. doi: 10.1542/peds.2013-3319

120. May PA, Hasken JM, Baete A, Russo J, Elliott AJ, Kalberg WO, et al. Fetal alcohol spectrum disorders in a midwestern city: child characteristics, maternal risk traits, and prevalence. Alcohol Clin Exp Res 2020;44:919–38. doi: 10.1111/acer.14314

121. Bertrand J, Floyd RL, Weber MK, O'Connor M, Riley EP, Johnson KA, et al. Fetal alcohol syndrome: guidelines for referral and diagnosis. Accessed July 15, 2021. https://www.cdc.gov/ncbddd/fasd/documents/FAS_guidelines_accessible-P.pdf.

122. Mai CT, Isenburg JL, Canfield MA, Meyer RE, Correa A, Alverson CJ, et al. National population-based estimates for major birth defects, 2010-2014. Birth Defects Res 2019;111:1420–35. doi: 10.1002/bdr2.1589

123. Abel EL. An update on incidence of FAS: FAS is not an equal opportunity birth defect. Neurotoxicol Teratol 1995;17:437–43. doi: 10.1016/0892-0362(95)00005-c

124. Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). N Engl J Med 2014;371:2109–13. doi: 10.1056/NEJMra1407298

125. Mayo-Smith MF, Beecher LH, Fischer TL, Gorelick DA, Guillaume JL, Hill A, et al. Management of alcohol withdrawal delirium. An evidence-based practice guideline. Arch Intern Med 2004;164:1405–12. doi: 10.1001/archinte.164.13.1405

126. Crotty K, Freedman KI, Kampman KM. Executive summary of the focused update of the ASAM national practice guideline for the treatment of opioid use disorder. J Addict Med 2020;14:99–112. doi: 10.1097/adm.0000000000000635

127. Campos J, Roca L, Gude F, Gonzalez-Quintela A. Long-term mortality of patients admitted to the hospital with alcohol withdrawal syndrome. Alcohol Clin Exp Res 2011;35:1180–6. doi: 10.1111/j.1530-0277.2011.01451.x

128. Pettinati HM, Weiss RD, Miller WR, Donovan D, Ernst DB, Rounsaville BJ, et al. Medical management treatment manual. A clinical research guide for medically trained clinicians providing pharmacotherapy as part of the treatment for alcohol dependence.U.S. Department of Health and Human Services; 2004.

129. Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA 2006;295:2003–17. doi: 10.1001/jama.295.17.2003

130. Smith EJ, Lui S, Terplan M. Pharmacologic interventions for pregnant women enrolled in alcohol treatment. The Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.: CD007361. doi: 10.1002/14651858.CD007361.pub2

131. DeVido J, Bogunovic O, Weiss RD. Alcohol use disorders in pregnancy. Harv Rev Psychiatry 2015;23:112–21. doi: 10.1097/HRP.0000000000000070

132. Alharbi YN. Current legal status of medical marijuana and cannabidiol in the United States. Epilepsy Behav 2020;112:107452. doi: 10.1016/j.yebeh.2020.107452

133. Young-Wolff KC, Sarovar V, Tucker LY, Avalos LA, Alexeeff S, Conway A, et al. Trends in marijuana use among pregnant women with and without nausea and vomiting in pregnancy, 2009-2016. Drug Alcohol Depend 2019;196: 66–70. doi: 10.1016/j.drugalcdep.2018.12.009

134. Ko JY, Coy KC, Haight SC, Haegerich TM, Williams L, Cox S, et al. Characteristics of marijuana use during pregnancy - eight states, pregnancy risk assessment monitoring system, 2017. MMWR Morb Mortal Wkly Rep 2020;69:1058–63. doi: 10.15585/mmwr.mm6932a2

135. Grywacheski V, Ali J, Baker MM, Gheorghe M, Wong SL, Orpana HM. Opioid and cannabis use during pregnancy and breastfeeding in relation to sociodemographics and mental health status: a descriptive study. J Obstet Gynaecol Can 2021;43:329–36. doi: 10.1016/j.jogc.2020.09.017

136. Jarlenski M, Barry CL, Gollust S, Graves AJ, Kennedy-Hendricks A, Kozhimannil K. Polysubstance use among US women of reproductive age who use opioids for nonmedical reasons. Am J Public Health 2017;107:1308–10. doi: 10.2105/ajph.2017.303825

137. Odom GC, Cottler LB, Striley CW, Lopez-Quintero C. Perceived risk of weekly cannabis use, past 30-day cannabis use, and frequency of cannabis use among pregnant women in the United States. Int J Womens Health 2020;12:1075–88. doi: 10.2147/ijwh.S266540

138. Chang JC, Tarr JA, Holland CL, De Genna NM, Richardson GA, Rodriguez KL, et al. Beliefs and attitudes regarding prenatal marijuana use: perspectives of pregnant women who report use. Drug Alcohol Depend 2019;196:14–20. doi: 10.1016/j.drugalcdep.2018.11.028

139. Cohen K, Weinstein A. The effects of cannabinoids on executive functions: evidence from cannabis and synthetic cannabinoids-a systematic review. Brain Sci 2018;8:40. doi: 10.3390/brainsci8030040

140. Adams AJ, Banister SD, Irizarry L, Trecki J, Schwartz M, Gerona R. "Zombie" outbreak caused by the synthetic cannabinoid AMB-FUBINACA in New York. N Engl J Med 2017; 376:235–42. doi: 10.1056/NEJMoa1610300

141. Kelkar AH, Smith NA, Martial A, Moole H, Tarantino MD, Roberts JC. An outbreak of synthetic cannabinoid-associated coagulopathy in Illinois. N Engl J Med 2018;379:1216–23. doi: 10.1056/NEJMoa1807652

142. Darke S, Duflou J, Farrell M, Peacock A, Lappin J. Characteristics and circumstances of synthetic cannabinoid-related death. Clin Toxicol (Phila) 2020;58:368–74. doi: 10.1080/15563650.2019.1647344

143. Alipour A, Patel PB, Shabbir Z, Gabrielson S. Review of the many faces of synthetic cannabinoid toxicities. Ment Health Clin 2019;9:93–9. doi: 10.9740/mhc.2019.03.093

144. Berry-Cabán C, Slack L, Huffman C, Whitecar P, Haley C. Synthetic cannabinoid and synthetic cocaine use during pregnancy in a soldier. J Subst Abuse Alcohol 2013;1:1002–4

145. Öztürk Z. Neonatal outcome after the use of synthetic cannabinoid Bonzai in pregnancy: a case report and brief review of literature. Acta Med 2017;48:25–7.

146. Marijuana use during pregnancy and lactation. Committee Opinion No. 722. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e205–9. doi: 10.1097/aog.0000000000002354

147. Office of the Surgeon General.US Surgeon general's advisory: marijuana use and the developing brain. Retrieved from https://www.hhs.gov/surgeongeneral/reports-and-publications/addiction-and-substance-misuse/advisory-on-marijuana-use-and-developing-brain/index.html.

148. Ryan SA, Ammerman SD, O'Connor ME; Committee on Substance Use and Prevention; Section on Breastfeeding. Marijuana use during pregnancy and breastfeeding: implications for neonatal and childhood outcomes [published erratum appears in Pediatrics 2018 Aug 27]. Pediatrics 2018;142: e20181889. doi: 10.1542/peds.2018-1889

149. Kondo KK, Morasco BJ, Nugent SM, Ayers CK, O'Neil ME, Freeman M, et al. Pharmacotherapy for the treatment of cannabis use disorder: a systematic review. Ann Intern Med 2020; 172:398–412. doi: 10.7326/m19-1105

150. Gray KM, Watson NL, Carpenter MJ, Larowe SD. N-acetylcysteine (NAC) in young marijuana users: an open-label pilot study. Am J Addict 2010;19:187–9. doi: 10.1111/j.1521-0391.2009.00027.x

151. Mason BJ, Crean R, Goodell V, Light JM, Quello S, Shadan F, et al. A proof-of-concept randomized controlled study of gabapentin: effects on cannabis use, withdrawal and executive function deficits in cannabis-dependent adults. Neuropsychopharmacology 2012;37:1689–98. doi: 10.1038/npp.2012.14

152. Sherman BJ, McRae-Clark AL. Treatment of cannabis use disorder: current science and future outlook. Pharmacother J Hum Pharmacol Drug Ther 2016;36:511–35. doi: 10.1002/phar.1747

153. Lind JN, Interrante JD, Ailes EC, Gilboa SM, Khan S, Frey MT, et al. Maternal use of opioids during pregnancy and congenital malformations: a systematic review. Pediatrics 2017; 139:e20164131. doi: 10.1542/peds.2016-4131

154. Zedler BK, Mann AL, Kim MM, Amick HR, Joyce AR, Murrelle EL, et al. Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: a systematic review and meta-analysis of safety in the mother, fetus and child. Addiction 2016;111:2115–28. doi: 10.1111/add.13462

155. Zuspan FP, Gumpel JA, Mejia-Zelaya A, Madden J, Davis R. Fetal stress from methadone withdrawal. Am J Obstet Gynecol 1975;122:43–6. doi: 10.1016/0002-9378(75)90613-4

156. Rementeriá JL, Nunag NN. Narcotic withdrawal in pregnancy: stillbirth incidence with a case report. Am J Obstet Gynecol 1973;116:1152–6. doi: 10.1016/0002-9378(73)90953-8

157. Bell J, Towers CV, Hennessy MD, Heitzman C, Smith B, Chattin K. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1–6. doi: 10.1016/j.ajog.2016.03.015

158. Welle-Strand GK, Skurtveit S, Tanum L, Waal H, Bakstad B, Bjarkø L, et al. Tapering from methadone or buprenorphine during pregnancy: maternal and neonatal outcomes in Norway 1996-2009. Eur Addict Res 2015;21:253–61. doi: 10.1159/000381670

159. Jansson LM, Dipietro JA, Velez M, Elko A, Knauer H, Kivlighan KT. Maternal methadone dosing schedule and fetal neurobehaviour. J Matern Fetal Neonatal Med 2009;22:29–35. doi: 10.1080/14767050802452291

160. Jansson LM, Di Pietro JA, Elko A, Williams EL, Milio L, Velez M. Pregnancies exposed to methadone, methadone and other illicit substances, and poly-drugs without methadone: a comparison of fetal neurobehaviors and infant outcomes. Drug Alcohol Depend 2012;122:213–9. doi: 10.1016/j.drugalcdep.2011.10.003

161. Jansson LM, Dipietro JA, Velez M, Elko A, Williams E, Milio L, et al. Fetal neurobehavioral effects of exposure to methadone or buprenorphine. Neurotoxicol Teratol 2011;33:240–3. doi: 10.1016/j.ntt.2010.09.003

162. Salisbury AL, Coyle MG, O'Grady KE, Heil SH, Martin PR, Stine SM, et al. Fetal assessment before and after dosing with

buprenorphine or methadone. Addiction (Abingdon, England) 2012;107(suppl 1):36–44. doi: 10.1111/j.1360-0443.2012.04037.x

163. Ramirez-Cacho WA, Flores S, Schrader RM, McKay J, Rayburn WF. Effect of chronic maternal methadone therapy on intrapartum fetal heart rate patterns. J Soc Gynecol Investig 2006;13:108–11. doi: 10.1016/j.jsgi.2005.11.001

164. Leeman LM, Brown SA, Albright B, Skipper B, Hsi A, Rayburn WF. Association between intrapartum fetal heart rate patterns and neonatal abstinence syndrome in methadone exposed neonates. J Matern Fetal Neonatal Med 2011;24:955–9. doi: 10.3109/14767058.2010.536863

165. Kocherlakota P. Neonatal abstinence syndrome. Pediatrics 2014;134:e547–61. doi: 10.1542/peds.2013-3524

166. Wachman EM, Schiff DM, Silverstein M. Neonatal abstinence syndrome: advances in diagnosis and treatment. JAMA 2018;319:1362–74. doi: 10.1001/jama.2018.2640

167. Patrick SW, Kaplan HC, Passarella M, Davis MM, Lorch SA. Variation in treatment of neonatal abstinence syndrome in US children's hospitals, 2004-2011. J Perinatol 2014;34:867–72. doi: 10.1038/jp.2014.114

168. Disher T, Gullickson C, Singh B, Cameron C, Boulos L, Beaubien L, et al. Pharmacological treatments for neonatal abstinence syndrome: a systematic review and Network meta-analysis. JAMA Pediatr 2019;173:234–43. doi: 10.1001/jamapediatrics.2018.5044

169. Burnette T, Chernicky L, Towers CV. The effect of standardizing treatment when managing neonatal abstinence syndrome. J Matern Fetal Neonatal Med 2019;32:3415–9. doi: 10.1080/14767058.2018.1465038

170. McCarthy JJ. Methadone and buprenorphine for opioid dependence during pregnancy: a retrospective cohort study: Re: Meyer et al. J Addict Med 2016;10:133–4. doi: 10.1097/ADM.0000000000000183

171. Cleary BJ, Donnelly J, Strawbridge J, Gallagher PJ, Fahey T, Clarke M, et al. Methadone dose and neonatal abstinence syndrome-systematic review and meta-analysis. Addiction 2010;105:2071–84. doi: 10.1111/j.1360-0443.2010.03120.x

172. Seligman NS, Almario CV, Hayes EJ, Dysart KC, Berghella V, Baxter JK. Relationship between maternal methadone dose at delivery and neonatal abstinence syndrome. J Pediatr 2010;157:428–33, 433.e1. doi: 10.1016/j.jpeds.2010.03.033

173. O'Connor AB, O'Brien L, Alto WA. Maternal buprenorphine dose at delivery and its relationship to neonatal outcomes. Eur Addict Res 2016;22:127–30. doi: 10.1159/000441220

174. Wong J, Saver B, Scanlan JM, Gianutsos LP, Bhakta Y, Walsh J, et al. Does maternal buprenorphine dose affect severity or incidence of neonatal abstinence syndrome? J Addict Med 2018;12:435–41. doi: 10.1097/ADM.0000000000000427

175. National Academies of Sciences Engineering, and Medicine. Medications for opioid use disorder save lives. National Academies Press; 2019.

176. Dugosh K, Abraham A, Seymour B, McLoyd K, Chalk M, Festinger D. A systematic review on the use of psychosocial interventions in conjunction with medications for the treatment of opioid addiction. J Addict Med 2016;10:93–103. doi: 10.1097/adm.0000000000000193

177. Carroll KM, Weiss RD. The role of behavioral interventions in buprenorphine maintenance treatment: a review. Am J Psychiatry 2017;174:738–47. doi: 10.1176/appi.ajp.2016.16070792

178. Carroll KM, Onken LS. Behavioral therapies for drug abuse. Am J Psychiatry 2005;162:1452–60. doi: 10.1176/appi.ajp.162.8.1452

179. Wakeman SE, Larochelle MR, Ameli O, Chaisson CE, McPheeters JT, Crown WH, et al. Comparative effectiveness of different treatment pathways for opioid use disorder. JAMA Netw Open 2020;3:e1920622. doi: 10.1001/jamanetworkopen.2019.20622

180. Wilder C, Lewis D, Winhusen T. Medication assisted treatment discontinuation in pregnant and postpartum women with opioid use disorder. Drug Alcohol Depend 2015;149:225–31. doi: 10.1016/j.drugalcdep.2015.02.012

181. Schiff DM, Nielsen T, Terplan M, Hood M, Bernson D, Diop H, et al. Fatal and nonfatal overdose among pregnant and postpartum women in Massachusetts. Obstet Gynecol 2018;132:466–74. doi: 10.1097/AOG.0000000000002734

182. Substance Abuse and Mental Health Services Administration. Substance abuse treatment: addressing the specific needs of women. Treatment improvement protocol (TIP) series 51. Health and Human Services Publication; 2009.

183. Patrick SW, Buntin MB, Martin PR, Scott TA, Dupont W, Richards M, et al. Barriers to accessing treatment for pregnant women with opioid use disorder in Appalachian states. Subst Abus 2019;40:356–62. doi: 10.1080/08897077.2018.1488336

184. Sufrin C, Sutherland L, Beal L, Terplan M, Latkin C, Clarke JG. Opioid use disorder incidence and treatment among incarcerated pregnant women in the United States: results from a national surveillance study. Addiction 2020;115:2057–65. doi: 10.1111/add.15030

185. Knittel AK, Zarnick S, Thorp JM, Jr., Amos E, Jones HE. Medications for opioid use disorder in pregnancy in a state women's prison facility. Drug and alcohol dependence 2020;214:108159. doi: 10.1016/j.drugalcdep.2020.108159

186. Saia KA, Schiff D, Wachman EM, Mehta P, Vilkins A, Sia M, et al. Caring for pregnant women with opioid use disorder in the USA: expanding and improving treatment. Curr Obstet Gynecol Rep 2016;5:257–63. doi: 10.1007/s13669-016-0168-9

187. Krans EE, Patrick SW. Opioid use disorder in pregnancy: health policy and practice in the midst of an epidemic. Obstet Gynecol 2016;128:4–10. doi: 10.1097/aog.0000000000001446

188. World Health Organization. Training manual for clinical guidelines for withdrawal management and treatment of drug dependence in closed settings. Accessed July 15, 2021. https://apps.who.int/iris/handle/10665/207034.

189. Cleary EM, Smid MC, Charles JE, Jones KM, Costantine MM, Saade G, et al. Buprenorphine X-waiver exemption - beyond the basics for the obstetrical provider. Am J Obstet Gynecol MFM 2021;3:100451. doi: 10.1016/j.ajogmf.2021.100451

190. Kleinman MB, Felton JW, Johnson A, Magidson JF. I have to be around people that are doing what I'm doing": the importance of expanding the peer recovery coach role in treatment of opioid use disorder in the face of COVID-19 health disparities. J Subst Abuse Treat 2021;122:108182. doi: 10.1016/j.jsat.2020.108182

191. Schottenfeld RS, Moore B, Pantalon MV. Contingency management with community reinforcement approach or twelve-step facilitation drug counseling for cocaine dependent pregnant women or women with young children. Drug Alcohol Depend 2011;118:48–55. doi: 10.1016/j.drugalcdep.2011.02.019

192. Mills Huffnagle S, Brennan G, Wicks K, Holden D, Kawasaki S. A comparison of patients with opioid use disorder receiving buprenorphine treatment with and without peer recovery support services. J Substance Use 2021:1–6. doi: 10.1080/14659891.2021.1938265

193. Fallin-Bennett A, Elswick A, Ashford K. Peer support specialists and perinatal opioid use disorder: someone that's been there, lived it, seen it. Addict Behav 2020;102:106204. doi: 10.1016/j.addbeh.2019.106204

194. Langabeer JR, II, Yatsco A, Champagne-Langabeer T. Telehealth sustains patient engagement in OUD treatment during COVID-19. J Subst Abuse Treat 2021;122:108215. doi: 10.1016/j.jsat.2020.108215

195. Galanter M, White WL, Hunter B. Virtual twelve step meeting attendance during the COVID-19 period: a study of members of narcotics anonymous. J Addict Med 2021 Apr 15 [Epub ahead of print]. doi: 10.1097/adm.0000000000000852

196. Blandthorn J, Bowman E, Leung L, Bonomo Y, Dietze P. Managing opioid overdose in pregnancy with take-home naloxone. Aust N Z J Obstet Gynaecol 2018;58:460–2. doi: 10.1111/ajo.12761

197. Bell A, Bennett AS, Jones TS, Doe-Simkins M, Williams LD. Amount of naloxone used to reverse opioid overdoses outside of medical practice in a city with increasing illicitly manufactured fentanyl in illicit drug supply. Subst Abus 2019;40:52–5. doi: 10.1080/08897077.2018.1449053

198. Haffajee RL, Cherney S, Smart R. Legal requirements and recommendations to prescribe naloxone. Drug Alcohol Depend 2020;209:107896. doi: 10.1016/j.drugalcdep.2020.107896

199. Sohn M, Brinkman R, Wellman GS. Coprescription of opioid and naloxone in office-based practice and emergency department settings in the United States. Public Health 2020;180:82–4. doi: 10.1016/j.puhe.2019.11.014

200. Terplan M, Laird HJ, Hand DJ, Wright TE, Premkumar A, Martin CE, et al. Opioid detoxification during pregnancy: a systematic review. Obstet Gynecol 2018;131:803–14. doi: 10.1097/aog.0000000000002562

201. Coles CD. Saying "goodbye" to the "crack baby". Neurotoxicology and teratology 1993;15:290–2. doi: 10.1016/0892-0362(93)90024-i

202. Terplan M, Kennedy-Hendricks A, Chisolm MS. Prenatal substance use: exploring assumptions of maternal unfitness. Substance Abuse 2015;9:1–4. doi: 10.4137/sart.S23328

203. Lutiger B, Graham K, Einarson TR, Koren G. Relationship between gestational cocaine use and pregnancy outcome: a meta-analysis. Teratology 1991;44:405–14. doi: 10.1002/tera.1420440407

204. Moore TR, Sorg J, Miller L, Key TC, Resnik R. Hemodynamic effects of intravenous cocaine on the pregnant Ewe and fetus. Am J Obstet Gynecol 1986;155:883–8. doi: 10.1016/s0002-9378(86)80044-8

205. Woods JR, Jr, Plessinger MA, Clark KE. Effect of cocaine on uterine blood flow and fetal oxygenation. JAMA 1987;257:957–61. doi: 10.1001/jama.1987.03390070077027

206. Patel TG, Laungani RG, Grose EA, Dow-Edwards DL. Cocaine decreases uteroplacental blood flow in the rat. Neurotoxicology and teratology 1999;21:559–65. doi: 10.1016/s0892-0362(99)00022-7

207. McCord J, Jneid H, Hollander JE, de Lemos JA, Cercek B, Hsue P, et al. Management of cocaine-associated chest pain and myocardial infarction: a scientific statement from the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. Circulation 2008;117:1897–907. doi: 10.1161/circulationaha.107.188950

208. Afonso L, Mohammad T, Thatai D. Crack whips the heart: a review of the cardiovascular toxicity of cocaine. Am J Cardiol 2007;100:1040–3. doi: 10.1016/j.amjcard.2007.04.049

209. Chan B, Kondo K, Freeman M, Ayers C, Montgomery J, Kansagara D. Pharmacotherapy for cocaine use disorder-a systematic review and meta-analysis. J Gen Intern Med 2019;34:2858–73. doi: 10.1007/s11606-019-05074-8

210. Chan B, Kondo K, Freeman M, Ayers C, Montgomery J, Kansagara D. Pharmacotherapy for cocaine use disorder–a systematic review and meta-analysis. J Gen Intern Med 2019;34:2858–73. doi: 10.1007/s11606-019-05074-8

211. Terplan M, Ramanadhan S, Locke A, Longinaker N, Lui S. Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions. The Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD006037. doi: 10.1002/14651858.CD006037.pub3

212. Wright TE, Schuetter R, Fombonne E, Stephenson J, Haning WF, III. Implementation and evaluation of a harm-reduction model for clinical care of substance using pregnant women. Harm Reduction J 2012;9:5. doi: 10.1186/1477-7517-9-5

213. Lewis D, Kenneally M, van denHeuvel C, Byard RW. Methamphetamine deaths: changing trends and diagnostic issues. Med Sci L 2021;61:25802420986707. doi: 10.1177/0025802420986707

214. Admon LK, Bart G, Kozhimannil KB, Richardson CR, Dalton VK, Winkelman TNA. Amphetamine- and opioid-affected births: incidence, outcomes, and costs, United States, 2004-2015. Am J Public Health 2019;109:148–54. doi: 10.2105/ajph.2018.304771

215. Smith LM, LaGasse LL, Derauf C, Grant P, Shah R, Arria A, et al. The infant development, environment, and lifestyle study: effects of prenatal methamphetamine exposure, polydrug exposure, and poverty on intrauterine growth. Pediatrics 2006;118:1149–56. doi: 10.1542/peds.2005-2564

216. Smith LM, Lagasse LL, Derauf C, Grant P, Shah R, Arria A, et al. Prenatal methamphetamine use and neonatal neurobehavioral outcome. Neurotoxicol Teratol 2008;30:20–8. doi: 10.1016/j.ntt.2007.09.005

217. Kiblawi ZN, Smith LM, Diaz SD, LaGasse LL, Derauf C, Newman E, et al. Prenatal methamphetamine exposure and neonatal and infant neurobehavioral outcome: results from the IDEAL study. Subst Abus 2014;35:68–73. doi: 10.1080/08897077.2013.814614

218. Smith LM, LaGasse LL, Derauf C, Newman E, Shah R, Haning W, et al. Motor and cognitive outcomes through three years of age in children exposed to prenatal methamphetamine. Neurotoxicol Teratol 2011;33:176–84. doi: 10.1016/j.ntt.2010.10.004

219. Siefried KJ, Acheson LS, Lintzeris N, Ezard N. Pharmacological treatment of methamphetamine/amphetamine dependence: a systematic review. CNS drugs 2020;34:337–65. doi: 10.1007/s40263-020-00711-x

220. Bais B, Molenaar NM, Bijma HH, Hoogendijk WJG, Mulder CL, Luik AI, et al. Prevalence of benzodiazepines and benzodiazepine-related drugs exposure before, during and after pregnancy: a systematic review and meta-analysis. J affective Disord 2020;269:18–27. doi: 10.1016/j.jad.2020.03.014

221. Venkatesh KK, Pate V, Boggess KA, Jones HE, Funk MJ, Smid MC. Trends in opioid and psychotropic prescription in pregnancy in the United States from 2001 to 2015 in a privately insured population: a cross-sectional study. Ann Intern Med 2020;173:S19–28. doi: 10.7326/m19-3249

222. Hernandez I, He M, Brooks MM, Zhang Y. Exposure-response association between concurrent opioid and benzodiazepine use and risk of opioid-related overdose in medicare Part D beneficiaries. JAMA Netw Open 2018;1:e180919. doi: 10.1001/jamanetworkopen.2018.0919

223. Murphy Y, Wilson E, Goldner EM, Fischer B. Benzodiazepine use, misuse, and harm at the population level in Canada: a comprehensive narrative review of data and developments since 1995. Clin Drug Invest 2016;36:519–30. doi: 10.1007/s40261-016-0397-8

224. Ogawa Y, Takeshima N, Hayasaka Y, Tajika A, Watanabe N, Streiner D, et al. Antidepressants plus benzodiazepines for adults with major depression. The Cochrane Database of Systematic Reviews 2019, Issue 6. Art. No.: CD001026. doi: 10.1002/14651858.CD001026.pub2

225. Shinfuku M, Kishimoto T, Uchida H, Suzuki T, Mimura M, Kikuchi T. Effectiveness and safety of long-term benzodiazepine use in anxiety disorders: a systematic review and meta-analysis. Int Clin Psychopharmacol 2019;34:211–21. doi: 10.1097/yic.0000000000000276

226. Park TW, Larochelle MR, Saitz R, Wang N, Bernson D, Walley AY. Associations between prescribed benzodiazepines, overdose death and buprenorphine discontinuation among people receiving buprenorphine. Addiction 2020;115:924–32. doi: 10.1111/add.14886

227. U.S. Food and Drug Administration. FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks. Accessed July 15th, 2021. https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-urges-caution-about-withholding-opioid-addiction-medications.

228. Grigoriadis S, Graves L, Peer M, Mamisashvili L, Dennis CL, Vigod SN, et al. Benzodiazepine use during pregnancy alone or in combination with an antidepressant and congenital malformations: systematic review and meta-analysis. J Clin Psychiatry 2019;80:18r12412. doi: 10.4088/JCP.18r12412

229. Enato E, Moretti M, Koren G. The fetal safety of benzodiazepines: an updated meta-analysis. J Obstet Gynaecol Can 2011;33:46–8. doi: 10.1016/s1701-2163(16)34772-7

230. Rementería JL, Bhatt K. Withdrawal symptoms in neonates from intrauterine exposure to diazepam. J Pediatr 1977;90:123–6. doi: 10.1016/s0022-3476(77)80785-3

231. Iqbal MM, Sobhan T, Ryals T. Effects of commonly used benzodiazepines on the fetus, the neonate, and the nursing infant. Psychiatr Serv (Washington, DC) 2002;53:39–49. doi: 10.1176/appi.ps.53.1.39

232. Seligman NS, Salva N, Hayes EJ, Dysart KC, Pequignot EC, Baxter JK. Predicting length of treatment for neonatal abstinence syndrome in methadone-exposed neonates. Am J Obstet Gynecol 2008;199:396.e1–7. doi: 10.1016/j.ajog.2008.06.088

233. McElhatton PR. The effects of benzodiazepine use during pregnancy and lactation. Reprod Toxicol 1994;8:461–75. doi: 10.1016/0890-6238(94)90029-9

234. Voshaar RC, Couvée JE, van Balkom AJ, Mulder PG, Zitman FG. Strategies for discontinuing long-term benzodiazepine use: meta-analysis. Br J Psychiatry 2006;189:213–20. doi: 10.1192/bjp.189.3.213

235. Gopalan P, Moses-Kolko E, Valpey R, Shenai N, Smith E. Benzodiazepine withdrawal in pregnant women with opioid use disorders: an observational study of current clinical practices at a tertiary obstetrical hospital. Gen Hosp Psychiatry 2019;57:29–33. doi: 10.1016/j.genhosppsych.2018.12.005

236. O'Connor K, Marchand A, Brousseau L, Aardema F, Mainguy N, Landry P, et al. Cognitive-behavioural, pharmacological and psychosocial predictors of outcome during tapered discontinuation of benzodiazepine. Clin Psychol psychotherapy 2008;15:1–14. doi: 10.1002/cpp.556

237. Romisher R, Hill D, Cong X. Neonatal abstinence syndrome: exploring nurses' attitudes, knowledge, and practice. Adv neonatal Care 2018;18:E3–11. doi: 10.1097/anc.0000000000000462

238. Schiff DM, Zuckerman B, Wachman EM, Bair-Merritt M. Trainees' knowledge, attitudes, and practices towards caring for the substance-exposed mother-infant dyad. Substance abuse 2017;38:414–21. doi: 10.1080/08897077.2017.1356423

239. Meyer M, Paranya G, Keefer Norris A, Howard D. Intrapartum and postpartum analgesia for women maintained on buprenorphine during pregnancy. Eur J pain (London, England) 2010;14:939–43. doi: 10.1016/j.ejpain.2010.03.002

240. Meyer M, Wagner K, Benvenuto A, Plante D, Howard D. Intrapartum and postpartum analgesia for women maintained on methadone during pregnancy. Obstet Gynecol 2007;110:261–6. doi: 10.1097/01.AOG.0000275288.47258.e0

241. Jones HE, Deppen K, Hudak ML, Leffert L, McClelland C, Sahin L, et al. Clinical care for opioid-using pregnant and postpartum women: the role of obstetric providers. Am J Obstet Gynecol 2014;210:302–10. doi: 10.1016/j.ajog.2013.10.010

242. Tsui JI, Herman DS, Kettavong M, Alford D, Anderson BJ, Stein MD. Physician introduction to opioids for pain among patients with opioid dependence and depressive symptoms. J substance abuse Treat 2010;39:378–83. doi: 10.1016/j.jsat.2010.06.012

243. Buresh M, Ratner J, Zgierska A, Gordin V, Alvanzo A. Treating perioperative and acute pain in patients on buprenorphine: narrative literature review and practice recommendations. J Gen Intern Med 2020;35:3635–43. doi: 10.1007/s11606-020-06115-3

244. Reif S, Braude L, Lyman DR, Dougherty RH, Daniels AS, Ghose SS, et al. Peer recovery support for individuals with substance use disorders: assessing the evidence. Psychiatr Serv (Washington, DC) 2014;65:853–61. doi: 10.1176/appi.ps.201400047

245. Gruß I, Firemark A, Davidson A. Motherhood, substance use and peer support: benefits of an integrated group program for pregnant and postpartum women. J Subst Abuse Treat 2021;131:108450. doi: 10.1016/j.jsat.2021.108450

246. Alexander K, Short V, Gannon M, Goyal N, Naegle M, Abatemarco DJ. Identified gaps and opportunities in perinatal healthcare delivery for women in treatment for opioid use disorder. Subst Abus 2020:1–7. doi: 10.1080/08897077.2020.1803178

247. American Society of Addiction Medicine. Definition of addiction. Accessed July 1, 2021. https://www.asam.org/Quality-Science/definition-of-addiction.

248. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013.

249. Substance Abuse Mental Health Services Administration. SAMHSA's working definition of recovery. Accessed. https://store.samhsa.gov/sites/default/files/d7/priv/pep12-recdef.pdf.

250. Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, et al. Interventions for tobacco smoking cessation in adults, including pregnant persons: US preventive services task force recommendation statement. JAMA 2021;325:265–79. doi: 10.1001/jama.2020.25019

251. Tobacco and nicotine cessation during pregnancy. ACOG Committee Opinion No. 807. American College of Obstetricians and Gynecologists. Obstet Gynecol 2020;135:e221–9. doi: 10.1097/AOG.0000000000003822

252. Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, et al. Interventions for tobacco smoking

cessation in adults, including pregnant persons: US preventive services task force recommendation statement. JAMA 2021; 325:265–79. doi: 10.1001/jama.2020.25019

253. Bradley KA, Bush KR, Epler AJ, Dobie DJ, Davis TM, Sporleder JL, et al. Two brief alcohol-screening tests from the alcohol use disorders identification test (AUDIT): validation in a female veterans affairs patient population. Arch Intern Med 2003;163:821–9. doi: 10.1001/archinte.163.7.821

254. Sokol RJ, Martier SS, Ager JW. The T-ACE questions: practical prenatal detection of risk-drinking. Am J Obstet Gynecol 1989;160:863–8. doi: 10.1016/0002-9378(89)90302-5

255. Chasnoff IJ, McGourty RF, Bailey GW, Hutchins E, Lightfoot SO, Pawson LL, et al. The 4P's Plus screen for substance use in pregnancy: clinical application and outcomes. J Perinatol 2005;25:368–74. doi: 10.1038/sj.jp.7211266

256. National Institute on Drug Abuse. Resource guide: screening for drug use in general medical settings. Accessed July 15, 2021. https://archives.drugabuse.gov/publications/resource-guide-screening-drug-use-in-general-medical-settings.

257. Yonkers KA, Gotman N, Kershaw T, Forray A, Howell HB, Rounsaville BJ. Screening for prenatal substance use: development of the Substance Use Risk Profile-Pregnancy scale. Obstet Gynecol 2010;116:827–33. doi: 10.1097/AOG.0b013e3181ed8290

258. Knight JR, Shrier LA, Bravender TD, Farrell M, Vander Bilt J, Shaffer HJ. A new brief screen for adolescent substance abuse. Arch Pediatr Adolesc Med 1999;153:591–6. doi: 10.1001/archpedi.153.6.591

259. Ondersma SJ, Svikis DS, LeBreton JM, Streiner DL, Grekin ER, Lam PK, et al. Development and preliminary validation of an indirect screener for drug use in the perinatal period. Addiction 2012;107:2099–106. doi: 10.1111/j.1360-0443.2012.03982.x

260. Coleman-Cowger VH, Oga EA, Peters EN, Trocin KE, Koszowski B, Mark K. Accuracy of three screening tools for prenatal substance use. Obstet Gynecol 2019;133:952–61. doi: 10.1097/aog.0000000000003230

261. Ondersma SJ, Chang G, Blake-Lamb T, Gilstad-Hayden K, Orav J, Beatty JR, et al. Accuracy of five self-report screening instruments for substance use in pregnancy. Addiction 2019; 114:1683–93. doi: 10.1111/add.14651

262. McCarthy JJ, Leamon MH, Parr MS, Anania B. High-dose methadone maintenance in pregnancy: maternal and neonatal outcomes. Am J Obstet Gynecol 2005;193:606–10. doi: 10.1016/j.ajog.2005.03.072

263. Shiu JR, Ensom MH. Dosing and monitoring of methadone in pregnancy: literature review. Can J Hosp Pharm 2012;65:380–6. doi: 10.4212/cjhp.v65i5.1176

264. McCarthy JJ, Leamon MH, Willits NH, Salo R. The effect of methadone dose regimen on neonatal abstinence syndrome. J Addict Med 2015;9:105–10. doi: 10.1097/adm.0000000000000099

265. Morgan JR, Schackman BR, Weinstein ZM, Walley AY, Linas BP. Overdose following initiation of naltrexone and buprenorphine medication treatment for opioid use disorder in a United States commercially insured cohort. Drug Alcohol Depend 2019;200:34–9. doi: 10.1016/j.drugalcdep.2019.02.031

266. Caulfield MDG, Brar R, Sutherland C, Nolan S. Transitioning a patient from injectable opioid agonist therapy to sublingual buprenorphine/naloxone for the treatment of opioid use disorder using a microdosing approach. BMJ Case Rep 2020;13:e233715. doi: 10.1136/bcr-2019-233715

267. Brar R, Fairbairn N, Sutherland C, Nolan S. Use of a novel prescribing approach for the treatment of opioid use disorder: buprenorphine/naloxone micro-dosing - a case series. Drug Alcohol Rev 2020;39:588–94. doi: 10.1111/dar.13113

268. Azar P, Nikoo M, Miles I. Methadone to buprenorphine/-naloxone induction without withdrawal utilizing transdermal fentanyl bridge in an inpatient setting-Azar method. Am J Addict 2018;27:601–4. doi: 10.1111/ajad.12809

269. Lee KP, Chromey NC, Culik R, Barnes JR, Schneider PW. Toxicity of N-methyl-2-pyrrolidone (NMP): teratogenic, subchronic, and two-year inhalation studies. Fundam Appl Toxicol 1987;9:222–35. doi: 10.1016/0272-0590(87)90045-5

270. Saillenfait AM, Gallissot F, Morel G. Developmental toxicity of N-methyl-2-pyrrolidone in rats following inhalation exposure. Food Chem Toxicol 2003;41:583–8. doi: 10.1016/s0278-6915(02)00300-9

271. Link HM, Jones H, Miller L, Kaltenbach K, Seligman N. Buprenorphine-naloxone use in pregnancy: a systematic review and metaanalysis. Am J Obstet Gynecol MFM 2020;2:100179. doi: 10.1016/j.ajogmf.2020.100179

272. Wiegand SL, Stringer EM, Stuebe AM, Jones H, Seashore C, Thorp J. Buprenorphine and naloxone compared with methadone treatment in pregnancy. Obstet Gynecol 2015;125:363–8. doi: 10.1097/AOG.0000000000000640

273. Mullins N, Galvin SL, Ramage M, Gannon M, Lorenz K, Sager B, et al. Buprenorphine and naloxone versus buprenorphine for opioid use disorder in pregnancy: a cohort study. J Addict Med 2020;14:185–92. doi: 10.1097/ADM.0000000000000562

274. Nguyen L, Lander LR, O'Grady KE, Marshalek PJ, Schmidt A, Kelly AK, et al. Treating women with opioid use disorder during pregnancy in Appalachia: initial neonatal outcomes following buprenorphine+naloxoneexposure. Am J Addict 2018;27:92–6. doi: 10.1111/ajad.12687

275. Hulse G, O'Neil G. Using naltrexone implants in the management of the pregnant heroin user. Aust N Z J Obstet Gynaecol 2002;42:569–73. doi: 10.1111/j.0004-8666.2002.548_14.x

276. Hulse GK, O'Neill G, Pereira C, Brewer C. Obstetric and neonatal outcomes associated with maternal naltrexone exposure. Aust N Z J Obstet Gynaecol 2001;41:424–8. doi: 10.1111/j.1479-828x.2001.tb01322.x

277. Hulse GK, Arnold-Reed DE, O'Neil G, Hansson RC. Naltrexone implant and blood naltrexone levels over pregnancy. Aust N Z J Obstet Gynaecol 2003;43:386–8. doi: 10.1046/j.0004-8666.2003.00121.x

278. Towers CV, Katz E, Weitz B, Visconti K. Use of naltrexone in treating opioid use disorder in pregnancy. Am J Obstet Gynecol 2020;222:83.e1–8. doi: 10.1016/j.ajog.2019.07.037

279. Jones CW, Terplan M. Pregnancy and naltrexone pharmacotherapy. Obstet Gynecol 2018;132:923–5. doi: 10.1097/AOG.0000000000002864

280. Kelty E, Hulse G. A retrospective cohort study of obstetric outcomes in opioid-dependent women treated with implant naltrexone, oral methadone or sublingual buprenorphine, and non-dependent controls. Drugs 2017;77:1199–210. doi: 10.1007/s40265-017-0762-9

281. Wachman EM, Saia K, Miller M, Valle E, Shrestha H, Carter G, et al. Naltrexone treatment for pregnant women with opioid use disorder compared with matched buprenorphine control subjects. Clin Ther 2019;41:1681–9. doi: 10.1016/j.clinthera.2019.07.003

282. Hulse GK, O'Neil G, Arnold-Reed DE. Methadone maintenance vs. implantable naltrexone treatment in the pregnant heroin user. Int J Gynaecol Obstet 2004;85:170–1. doi: 10.1016/j.ijgo.2003.10.001

283. Geraghty S, Dixon C. The use of naltrexone in pregnancy in opiate-dependent mothers. Br J Midwifery 2012;20:503–6.

PEER REVIEW HISTORY

Received July 28, 2021. Received in revised form September 24, 2021. Accepted October 1, 2021. Peer reviews and author correspondence are available at http://links.lww.com/AOG/C560.

CME FOR THE CLINICAL EXPERT SERIES

Learning Objectives for "What Obstetrician–Gynecologists Should Know About Substance Use Disorders in the Perinatal Period"

After completing this continuing education activity, you will be able to:

- Describe the prevalence of pregnancy-associated substance use and substance use disorder in the United States;
- Discuss the role of the obstetrician–gynecologists in the identification and management of substance use disorder during pregnancy; and
- Implement suitable strategies in your own practice to address these issues.

Instructions for Obtaining *AMA PRA Category 1 Credits*™

Continuing Medical Education credit is provided through joint providership with The American College of Obstetricians and Gynecologists.

Obstetrics & Gynecology *includes CME-certified content that is designed to meet the educational needs of its readers. This article is certified for 2 AMA PRA Category 1 Credits*.™ This activity is available for credit through February 28, 2025.

Accreditation Statement

ACCME Accreditation

The American College of Obstetricians and Gynecologists is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

AMA PRA Category 1 Credit(s)™

The American College of Obstetricians and Gynecologists designates this **journal-based CME activity** for a maximum of 2 *AMA PRA Category 1 Credits*.™ Physicians should claim only the credit commensurate with the extent of their participation in the activity.

College Cognate Credit(s)

The American College of Obstetricians and Gynecologists designates this **journal-based CME activity** for a maximum of 2 Category 1 College Cognate Credits. The College has a reciprocity agreement with the AMA that allows *AMA PRA Category 1 Credits*™ to be equivalent to College Cognate Credits.

Disclosure of Faculty and Planning Committee Industry Relationships

In accordance with the College policy, all faculty and planning committee members have signed a conflict of interest statement in which they have disclosed any financial interests or other relationships with industry relative to article topics. Such disclosures allow the participant to evaluate better the objectivity of the information presented in the articles.

How to Earn CME Credit

To earn CME credit, you must read the article in *Obstetrics & Gynecology* and complete the quiz, answering at least 70 percent of the questions correctly. For more information on this CME educational offering, visit the Lippincott CMEConnection portal at https://cme.lww.com/browse/sources/196 to register and to complete the CME activity online. ACOG Fellows will receive 50% off by using coupon code, **ONG50**.

Hardware/software requirements are a desktop or laptop computer (Mac or PC) and an Internet browser. This activity is available for credit through February 28, 2025. To receive proper credits for this activity, each participant will need to make sure that the information on their profile for the CME platform (where this activity is located) is updated with 1) their date of birth (month and day only) and 2) their ACOG ID. In addition, participants should select that they are board-certified in obstetrics and gynecology.

The privacy policies for the *Obstetrics & Gynecology* website and the Lippincott CMEConnection portal are available at http://www.greenjournal. org and https://cme.lww.com/browse/sources/196, respectively.

Contact Information

Questions related to transcripts may be directed to educationcme@acog.org. For other queries, please contact the *Obstetrics & Gynecology* Editorial Office, 202-314-2,317 or obgyn@greenjournal.org. For queries related to the CME test online, please contact ceconnection@wolterskluwer.com or 1-800-787-8985.