


Concurrent Opioid and Alcohol Use Among Women Who Become Pregnant: Historical, Current, and Future Perspectives

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Substance Abuse: Research and Treatment
Volume 13: 1–7
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DOI: 10.1177/1178221819852637



ABSTRACT: The numbers of women using opioids who become pregnant have captured the attention of media, research, policy, and community. At the same time, there is an ever-growing use of alcohol among women who continue drinking during pregnancy that has received less focus. Although both untreated opioid use disorder and alcohol misuse pose risks for maternal, fetal, and child morbidities, alcohol is the substance with the most significant documentation of harms. As we focus on the opioid epidemic in the United States, it is critical that we do not overlook alcohol use during pregnancy. Both opioid use and alcohol use during pregnancy are important public health challenges and often happen concurrently. Thus, this commentary aims to (1) highlight the historical and current context of opioid and alcohol use during pregnancy; (2) summarize the current knowledge of opioids and alcohol use during pregnancy; and (3) detail future directions in how health care providers can help identify and therapeutically respond to women with concurrent opioid and alcohol use disorder.

KEYWORDS: pregnancy, opioid, neonatal abstinence syndrome, neonatal opioid withdrawal, alcohol, fetal alcohol spectrum disorder

RECEIVED: April 23, 2019. **ACCEPTED:** May 2, 2019.

TYPE: Commentary

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) received no financial support for the research, authorship, and/or publication of this article.

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The United States is in the midst of an opioid epidemic, which has taken a tremendous toll on women and their children. Opioid use by pregnant women represents a significant public health concern. The rate of opioid use disorder (OUD) diagnoses among women during labor and delivery from 30 states has more than quadrupled over a 15-year period ending in 2014, increasing from 1.5 to 6.5 per 1000 deliveries per year.¹

Concurrently, in the United States, the escalation of alcohol use among women during the past decade has led to an increase in the prevalence of alcohol use disorder (AUD),² which in turn has been associated with a rise in alcohol-induced deaths. According to recent national data, the prevalence estimate of women aged 15 to 44 who self-reported past month alcohol use was 53%, of which 11.5% were pregnant.³ Furthermore, nearly 5 million women are estimated to have AUD.³ Although both untreated OUD and alcohol use pose risks for maternal, fetal, and child morbidities, alcohol is the substance with the most significant documentation of harms.⁴ Thus, alcohol use during pregnancy deserves focus as the attention on the opioid epidemic continues to intensify.

This commentary aims to (1) highlight the historical and current context of opioid and alcohol use during pregnancy; (2) summarize the current knowledge of opioids and alcohol use during pregnancy; and (3) detail future directions in how health care providers can help identify and therapeutically respond to women with concurrent OUD and AUD.

Women and Opioid Use in the United States: Historical Context

Substance use in women is not a new problem. In the United States, it dates back at least 150 years.⁵ During the late 19th century, the typical individual using opioids in the United States was an upper/middle-class white woman.⁶ Physicians and pharmacists prescribed and dispensed opioids to relieve many female patients' menstrual cramps, morning sickness, and emotional complaints (eg, "neurasthenia" or nervous character diseases).⁵ Opioid overuse commonly led to addiction. By the end of the 19th century, women made up 66% to 75% of individuals using opium and morphine.⁶

By the early 20th century, society's views about those using substances grew increasingly negative. Public perception might have been influenced by the striking shift in the demographics of substance use across the country from the late 1870s through 1920.⁵ Trends in substance use changed from female to male, from white to people of color, from southern rural to northern urban, and from high-income to low-income.⁵ During this period, legislation against substance use ensued. The United States moved toward a national drug policy that supported the restriction of substances. The Harrison Narcotics Tax Act of 1914 was a federal law that restricted and placed a tax on the import, production, distribution, or sales of narcotics, including opiates. An interpretation of the Harrison Narcotics Tax Act prevented physicians from prescribing opiates as medication maintenance treatment for patients with substance use



problems.⁶ In 1919, the United States Supreme Court upheld this interpretation.⁵ As a result, affluent women continued to access opioids through private clinics or their physicians.⁵ However, women who could not afford to maintain their opioid use through these channels often turned to prostitution and crime to access opiates.⁵

Throughout the 20th century, the spectrum of women who used opioids spanned beyond those typically portrayed as the mothers and caretakers in society. In the 1920s, Hollywood combined sexuality and substance use and found it to be a profitable enterprise.⁵ During the 1950s and 1960s, women were frequently and inappropriately prescribed psychoactive drugs (eg, stimulants, sedatives, antidepressants) and made up most of the psychoactive prescription drug users.⁵ By the 1980s, media attention and public outrage over increased numbers of substance-exposed newborns led to greater condemnation and prosecutions of the so-called “unfit mothers,” stereotyped as poor, urban, minorities.⁵ Consequently, many women avoided the health care system for fear of stigma, discrimination, and involvement by child protective services.⁶

Opioid Use During Pregnancy: Current Context

Although the history of women with OUD in the United States dates back more than 150 years, concerns regarding OUD in pregnancy have received considerable attention recently. Since 2002, prescription opioid use and misuse have significantly increased among pregnant women.⁷ Risk factors for substance use, including opioid use, among reproductive-age women include a lifetime prevalence of gender-based violence (GBV).^{8,9} Women who have experienced any GBV have an increased likelihood of a substance use disorder relative to women without GBV.¹⁰ Women are also more likely to use substances when their partners use. A family history of addiction is associated with the risk of developing substance use dependency.¹¹ According to the 2017 National Survey on Drug Use and Health (NSDUH), the prevalence of women aged 15 to 44 who were pregnant and self-reported past month misuse opioids (heroin or prescription-type pain relievers) was 1.4%.³ This reflects a nearly 17% increase over the prevalence of women who were pregnant and self-reported misusing opioids in the 2016 NSDUH.³ Such an increase in opioid use is of concern given the potential harms associated with untreated opioid misuse during pregnancy that may include poor fetal growth, preterm birth, congenital abnormalities, and neonatal abstinence syndrome (NAS).¹²

NAS: Historical Context

NAS is an array of signs and symptoms that some newborns experience after the sudden discontinuation of in utero exposure to substances such as opioids.¹¹ The first documented case of NAS in infants was in 1875, named congenital morphinism, and it was often fatal to newborns because there was no known treatment.¹³ In 1903, *The Journal of the American Medical*

Association published a physician’s letter that reported successfully treating congenital morphinism with morphine in an infant.¹⁴

Nearly a century after congenital morphinism was first reported, studies about the recognition, assessment, diagnosis, and scoring systems for NAS were published. In 1971, Zelson et al¹⁵ reported that of 384 infants born to mothers addicted to opioids, 67% showed signs of withdrawal within the first 4 days of life. In 1975, Desmond and Wilson¹⁶ first published their recognition and diagnosis of a generalized disorder that they termed NAS. And, in the same year, Finnegan et al¹⁷ published the Finnegan Neonatal Abstinence Scoring System (FNASS), which is the most commonly used tool to score an affected infant’s behaviors and signs/symptom of severity. The signs and symptoms of NAS usually occur within the first 24 to 72 hours after birth and can affect an infant’s neurologic, autonomic, gastrointestinal, and respiratory systems.^{16–18}

NAS: Current Context

As opioid use and misuse increase among the general population and women of childbearing age who get pregnant in the United States, so does NAS. The incidence of NAS increased more than fivefold from 2004 to 2014, from 1.5 to 8.0 per 1000 hospital births.¹⁹ This increase was driven in large part by a substantial increase in NAS among Medicaid-covered births, which rose from 2.8 to 14.4 per 1000 hospital births.¹⁹

The term neonatal opioid withdrawal syndrome (NOWS) has more recently been applied when NAS results specifically from women using opioids during pregnancy. The term NOWS was used by the Food and Drug Administration (FDA) to describe withdrawal from opioid exposure in utero and clarifies that infants cannot meet the definition of abstinence.²⁰ Screening and treatment procedures can be used to promote the best outcomes for infants with NOWS (see, for example, the Substance Abuse and Mental Health Services Administration *Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants*),²¹ whereas infants not exposed to opioids may require different assessment and management. However, most pregnant women struggling with substance misuse have prenatal polysubstance exposure, so infants usually experience withdrawal from more than just opioids. This commentary will continue to use the term NAS, as it is the term most commonly used in the literature.

More than half of prenatally opioid-exposed newborns exhibit NAS.¹⁸ Affected newborns have substantially more extended hospital stays and increased risk for developing problems than healthy newborns.¹⁸ The vulnerability NAS creates in an infant can be a risk factor for poor early bonding between mother and infant, and this can have potential long-term effects. Challenging behaviors frequently displayed by an infant undergoing NAS, such as irritability, dysregulated sleep-awake patterns, and autonomic signs of stress can affect and influence

maternal responses to the newborn's cues.²² Maternal opioid misuse, mood disorders, and adverse childhood experiences can also affect the mother's emotional and physical availability to help regulate and organize her newborn exhibiting NAS.²²

There is renewed interest in questions about the longitudinal effects of in utero opioid exposure and NAS on children. A literature review of prenatal opioid exposure reported behavioral effects but no consensus on cognition and noted that when positive results were reported they were usually confounded by environmental factors.²³ Recent studies of retrospective samples comparing a sample of children with NAS to control samples have found lower scores on language, cognition, and school performance.^{24,25} Among children prenatally exposed to methadone or buprenorphine, a randomized blinded study showed that neither NAS nor pharmacologic treatment for NAS had long-term effects.²⁶ Future research may help inform the extent to which NAS contributes to developmental differences between children who were diagnosed with NAS and a normative sample of children who were not, as such differences are likely due to multiple prenatal and postnatal causes.²⁷ Future research would benefit from using refined definitions and exacting methods for diagnosing NAS, well-defined criteria for selecting matching control and comparison groups, and statistical analyses that provide practical and clinically meaningful results.^{20,28}

Women and Alcohol Use in the United States: Historical Context

Similar to opioid use among women, alcohol use among women is not a new problem. Alcohol was a fundamental part of American dietary and social customs during the 17th and 18th centuries.²⁹ Women, men, and children of all classes consumed alcoholic beverages.³⁰ However, by the early 19th century, the temperance movement, a social movement, promoted moderation and, more often, complete abstinence from alcohol use.³⁰ Participants in the temperance movement believed that excessive alcohol use was a threat to family life and to women who were raising children to be good citizens.³¹ Still, during the late 19th century, male physicians prescribed alcohol, similar to opioids, to their mostly white, middle-class, married female patients. Alcohol came in the form of medicines, tonics, commercial remedies, and teas for pain relief from repeated pregnancies or other female complaints.³¹

Alcohol became illegal in 1920 with the passage of the Eighteenth Amendment to the United States Constitution. Although the amendment outlawed the manufacture, sale, or transportation of alcohol, it did not prohibit consumption.³² Before prohibition, women drank at home. However, prohibition created a substantial illegal market for alcohol. New social spaces made public drinking for women more acceptable.³³ For many single, working- and middle-class women, drinking and frequenting speakeasies, nightclubs, and roadhouses were ways of rebelling against traditional female stereotypes.³³ Many

Americans continued to view women's drinking as threatening family stability and social order. Women's recreational drinking was met with severe criticism and stigma.³¹ Although prohibition ended in 1933,³² the stigma against women who consume alcohol continued.

By the late 1950s and early 1960s, various professional groups, including the American Medical Association, declared alcoholism a disease.³⁴ However, no diagnosis, treatment regimen, or definition of cure was agreed upon. To this day, among all substances (eg, heroin, cocaine, and marijuana) alcohol remains the only substance yielding a constitutional amendment.³¹

Alcohol Use During Pregnancy: Current Context

Americans, especially women, are drinking more alcohol. Prevalence estimates from the Centers for Disease Control and Prevention's (CDC) 2006 to 2010 Behavioral Risk Factor Surveillance System (BRFSS) that show any alcohol use and binge drinking in the past 30 days among pregnant women aged 18 to 44 years, based on self-report, were 7.6% and 1.4%, respectively.³⁵ However, from 2011 to 2013, prevalence estimates of any alcohol use and binge drinking in the past 30 days among pregnant women aged 18 to 44, again based on self-report, increased to 10.2% and 3.1%, respectively.³⁶ Furthermore, compared with non-pregnant women who reported binge drinking from 2011 to 2013, pregnant women had a significantly higher frequency of binge drinking (3.1 vs 4.6, respectively)³⁶ with self-reported alcohol use among pregnant women increasing from 1 in 13 to 1 in 10, respectively.

Furthermore, according to a 2016 CDC analysis of data from the 2011 to 2013 National Survey of Family Growth, the United States prevalence estimate of the past month alcohol-exposed pregnancy risk among women 15 to 44 years old was 7.3%. Factors considered to put women at risk included sex with a man, drank any alcohol, no use of contraception by her or her partner, able to conceive, and partner(s) being fertile.³⁷ From 2006 to 2013, it appears that more women are consuming alcohol during pregnancy; are they? Is it possible that the same numbers of women are consuming alcohol during pregnancy, but they feel less stigmatized reporting use?

Fetal Alcohol Syndrome and Fetal Alcohol Spectrum Disorder: Historical Context

It is well known that drinking alcohol can harm the development of a fetus during pregnancy and may lead to fetal alcohol syndrome (FAS). The clinical characteristics of FAS were first described in the 1957 doctoral thesis of French pediatrician, Jacqueline Rouquette.³⁸ Rouquette described the influences of parental alcoholism on the physical and psychological development of 100 Parisian children. In 1968, another French pediatrician, Paul Limoine, published a longitudinal study describing a characteristic pattern of congenital abnormalities in 127 children affected by parental alcoholism from 69 families.³⁹

Five years later, in the United States, Jones and Smith, dysmorphologists at the University of Washington Medical School, published studies of 11 children affected by maternal alcoholism.⁴⁰ They coined the term “fetal alcohol syndrome” and identified diagnostic criteria based on 3 features: (1) prenatal and/or postnatal growth deficiency; (2) a distinct pattern of craniofacial malformations; and (3) central nervous system dysfunction.^{40,41} Despite clinical evidence, there was resistance within the scientific and clinical communities to the idea of alcohol as a teratogen.^{41,42} As animal studies began to establish credibility for the conclusion that alcohol is a teratogen, researchers worked to define better the diagnostic criteria for FAS set forth by Jones and Smith in 1973.⁴¹

Fetal Alcohol Spectrum Disorder: Current Context

By the early 2000s, FAS was recognized as one of several related syndromes under the umbrella term fetal alcohol spectrum disorder (FASD).⁴³ FASD encompasses a range of lifelong physical, neurodevelopmental, and behavioral disabilities that may affect a child following prenatal alcohol exposure.⁴³ There are 4 diagnosed conditions associated with prenatal alcohol exposure. Fetal alcohol syndrome has the most visible criteria of the 4 conditions. Individuals with FAS exhibit abnormal facial features, below average height and/or weight, and abnormalities of the central nervous system. Individuals with partial fetal alcohol syndrome (PFAS) exhibit two-thirds of the FAS criteria. Individuals with alcohol-related neurodevelopmental disorder (ARND) experience only the brain or central nervous system abnormalities. Individuals with neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE) mostly experience behavioral effects and have difficulty with executive functions such as motor control, regulation of emotions, time perception, and memory.⁴⁴

Between 1% and 5% of school-aged children in the United States may be affected by FASD, yet such prevalence has received relatively little attention.^{45,46} The CDC has concluded, “there is no known safe amount of alcohol use during pregnancy or while trying to get pregnant.”⁴³ Alcohol remains the most widely studied prenatal substance of misuse.⁴⁷ Evidence is strong for lifelong consequences of prenatal alcohol exposure on growth, behavior, cognition, language, and achievement. Thus, in the midst of the opioid epidemic in the United States that has drawn the attention of the public as well as federal, state, local, and tribal leaders,⁴⁸ prenatal alcohol use must also receive attention.

The Concurrent Use of Opioids and Alcohol Among Pregnant Women

Little research has been published about the concurrent use of opioids and alcohol during pregnancy. A simplified PubMed search using major search terms, “opioid use disorder” and “pregnancy,” and then the search terms, “alcohol use disorder” and “pregnancy,” yielded more than 1000 and 5000 publications, respectively, since the 1960s, inclusive of all countries. A

PubMed search using the major search terms, “opioid use disorder,” “alcohol use disorder,” and “pregnancy,” yielded 54 publications to date. Of these publications, 25 did not mention alcohol in the abstract, 17 were not pregnancy related, 11 did not focus on concurrent use, 7 were focused on the effects of prenatal exposure on infants/children, 3 called for treatment guidelines on the concurrent use, and 2 focused on concurrent use. The 2 publications that focused on concurrent use found a high prevalence of prenatal alcohol use in pregnant women with substance/opioid use disorder.^{49,50} Overall, the lack of research is surprising given that aggregate data from the 2005 to 2014 NSDUH indicate that, among pregnant women who used opioids non-medically, almost half reported alcohol use and nearly one-third binge drinking in the past 30 days.⁵¹

In one of the two studies (mentioned above) that focused on the concurrent use of opioids and alcohol during pregnancy, Bakhireva et al⁴⁹ analyzed data from the ENRICH (Ethanol, Neurodevelopment, Infant and Child Health) prospective birth cohort study, which compared the prevalence of self-reported alcohol use among women receiving prenatal care from general obstetrics clinics (n=365) with women receiving prenatal care from an OUD program (n=295), and found significant differences in the intensity of alcohol consumption between the two study cohorts. The median number of drinks consumed per individual per week during the periconceptional period (defined as 2 weeks before and 2 weeks after the last menstrual period) was 3.5 drinks in the general obstetrics cohort versus 5.5 drinks in the OUD cohort, a statistically significant difference.⁴⁹ Similarly, the median number of binge drinking episodes in early pregnancy (defined as the last menstrual period to pregnancy recognition) was 1 episode in the general obstetrics cohort versus 3 episodes in the OUD cohort, also statistically significant.⁴⁹

Given the risks of NAS and FAS, studies such as the one by Bakhireva et al, further underscore the need for screening and intervention for alcohol use during pregnancy, perhaps especially for women with OUD. Screening and intervention are important because pregnant women with OUD may (1) delay prenatal care and miss more health care visits than women who do not use opioids⁵²; (2) face a diverse set of barriers to seeking prenatal care, including fear of child custody issues⁵²; and (3) return to a dysfunctional home environment after childbirth that may be detrimental to a child’s psychological growth and development.⁵³

Tobacco’s Role: Opioid and Alcohol Use During Pregnancy

Tobacco products and alcohol are the two most common substances used by both pregnant and non-pregnant women, followed by any illicit drug, marijuana, pain relievers, cocaine, and heroin.⁵⁴ Among women who have an OUD and are pregnant, 97% also use tobacco.⁵⁵ Among women who use alcohol daily during pregnancy, 19% also use tobacco.⁵⁶ Tobacco and alcohol are licit substances. There are well-known health risks

associated with smoking and alcohol consumption during pregnancy for both women and their infants. For pregnant women, smoking increases the likelihood of preterm delivery, preterm premature rupture of membranes, placental complications of pregnancy, and miscarriage.⁵⁷ For the fetus and infant, smoking increases the risk of low birth weight, prematurity, placental abruption, sudden infant death syndrome, and an increase in childhood respiratory illnesses.^{55,58} Among pregnant women in medication-assisted treatment for OUD, the rate of smoking is 4 times higher than in the general population of pregnant women.⁵⁹ Furthermore, heavier cigarette smoking during pregnancy has been found to exacerbate NAS symptoms in infants.⁵⁵

Future Directions

Pregnancy provides a significant opportunity to identify and treat women with concurrent OUD and AUD. The obstetrical provider is in a vital position for screening, early diagnosis, counseling, and initiating treatment of pregnant women who use opioids⁶⁰ and/or alcohol. Because these disorders affect women across all racial and ethnic groups, socioeconomic groups, and geographical locations, it is essential that verbal/self-report screening be universal.⁶¹ Screening should take place during the first prenatal visit in partnership with the pregnant woman.⁶¹ Multidisciplinary long-term follow-up should include medical, developmental, and social support.⁶¹ However, pregnant women might not seek prenatal care because of fear, guilt, and shame, as well as concerns about medical and legal interventions.⁶² Furthermore, women who use opioids may not even realize that they are pregnant if they are not planning a pregnancy and misinterpret the early signs of pregnancy as opioid withdrawal signs/symptoms (eg, nausea, vomiting, cramping).⁶³ Unintended pregnancy is common in this population⁶⁴; therefore, intervention is most effective if it takes place before conception.

There are several areas in which future research directions should focus to help health care providers identify and therapeutically respond to women with concurrent opioid and alcohol use. It is important to remember that there is a continuum of both opioid use and alcohol use. For example, patients may have an OUD and concurrent use of alcohol that does not meet a use disorder threshold. Alternatively, patients may have an AUD and be prescribed opioids for pain or to treat OUD. Thus, providers need to know the best approaches for addressing opioid and alcohol use before, during, and after pregnancy tailored to the patient's life circumstances.

The Institute of Medicine, the United States Preventive Services Task Force (USPSTF), and the American College of Obstetricians and Gynecologists recommend alcohol screening in primary care and obstetric or gynecologic care settings.^{65–67} Although a 2016 cross-sectional study of more than 1500 primary care providers, including family practitioners and obstetrician/gynecologists, demonstrated that 96% of providers

self-reported screening for alcohol misuse, only 38% used a USPSTF-preferred screening tool.⁶⁸ Furthermore, compared with other providers in the study, the prevalence of USPSTF-preferred screening tools was significantly lower among obstetrician/gynecologists.⁶⁸ Overall, more than half of the providers might not be identifying patients who drink excessively, do not meet the AUD criteria, or could benefit from a brief intervention.⁶⁸ However, brief intervention is a challenging skill to learn and sustain, and rates of implementation are low.⁶⁹ The CDC reports that less than 1 in 6 United States adults, and only 17% of pregnant women, report discussing drinking with a health care professional.⁷⁰

Thus, what can be done to help support all obstetricians/gynecologists regularly asking and responding to women if they use opioids and alcohol? Future research could identify and test innovative questioning and interventions and staffing models, such as using technology to ask questions or using nurses or health educators, to screen women for opioid and alcohol use during obstetric/gynecologic appointments.⁷¹ This has already shown promising results in adult primary care, where screening rates for alcohol use were higher among non-physician providers, compared with physicians.⁷² Other studies could examine how obstetrician/gynecologists respond to a positive response from pregnant women about opioid and alcohol use, what public health messages about opioid and alcohol use do women hear from their social network, television, social media, and their health care providers, and what do women believe about opioid and alcohol use. Developing provider accountability measures and adequate reimbursement for asking and appropriately responding to positive substance use screens among pregnant women is needed to advance the field.⁷³

There is also a fundamental need for improved understanding of, and response to, women with OUD and AUD over the life course.⁷⁴ Studies that consider a life course perspective could examine the ways in which an accumulation of risk and/or protective factors, rather than at one point in time,⁷⁴ foreshadows the course of a woman's path from opioid and alcohol use initiation to disorder. The fabric of early-life social environments may be interwoven with adverse childhood events (ACEs), cultural norms that negatively impact women, chronic health and mental health conditions, food insecurity, intimate partner violence, and cross-generational transmission of substance use.⁷⁵ Furthermore, coming from neighborhoods with concentrated disadvantages such as economic impoverishment, a lack of opportunities for educational attainment, and exposure to environmental hazards are also risk factors for contributing to OUD.^{75,76} Understanding OUD and AUD through the lens of a life course perspective is critical for future research aimed at designing and promoting effective interventions for this population of women.

As the opioid epidemic in the United States escalates, a more widespread substance use problem is quietly growing

much worse, alcohol. Over the past 50 years, a larger body of evidence has accumulated for the negative impact of prenatal substance exposure to licit substances (alcohol, tobacco) than for illicit substances (eg, opioids, methamphetamines).⁷⁷ The political, media, and lay communities need reminding that the treatment of alcohol use in pregnant women, like the treatment of opioid use in pregnant women, is also a very important clinical need.

Using alcohol and/or untreated OUD during pregnancy may increase the risk of pregnancy loss, preterm delivery, and infant death.^{78–80} Alcohol use is associated with a wide range of congenital abnormalities and developmental disabilities, including mental retardation, physical abnormalities, and visual and auditory impairments,⁸¹ and opioid use is associated with NAS/NOWS. For all these reasons, reproductive-age women should be screened regularly for alcohol and opioid use, from preconception, throughout pregnancy and during the postpartum period. And, when found to have a positive screen, women of all ages deserve to receive the best and most compassionate care. As the opioid epidemic dominates the headlines, it is important not to lose focus on both opioid and alcohol use and misuse in all women of reproductive age.

Author Contributions

SLK had the primary role in drafting the manuscript, with inputs from KA, EH, and HEJ. All authors read and approved the final manuscript.

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