The application of harm reduction to methamphetamine use during pregnancy: a call to arms

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Compared with opioid use disorder, methamphetamine use is a public health crisis that has limited evidence-based pharmacologic interventions for long-term treatment. The prevalence of methamphetamine use during pregnancy is growing and contributes to adverse maternal and neonatal outcomes. Because of widespread stigma and social complexities associated with methamphetamine use during pregnancy, these patients often experience limited prenatal care, further contributing to poor outcomes. In public health circles, harm reduction describes a framework for conceptualizing substance use by championing health promotion and the safest use of substances, as opposed to the unachievable goal of abstinence. There is limited evidence supporting the application of harm reduction in this population. We call for action and research to investigate how the progressive concept of harm reduction might be applied to mitigate adverse outcomes for obstetrical patients who use methamphetamine.

Key words: harm reduction, methamphetamine use, perinatal substance use, public health approach to substance use, stimulant use, substance use in pregnancy

Scope of the problem

Methamphetamine (MA) use is an epidemic that contributes to multiple public health challenges.[1] It is part of a larger group of drugs known as amphetamine-type stimulants (ATSs).[2] There are several forms of MA, including crystal, "ice," "crystal meth," or "crank." Other derivatives include "base" (an oily substance) and powdered "speed."[3] "Crystal meth" is the purest or most potent substance and has the highest incidence of dependence. MA is more frequently inhaled (smoked) followed by intravenous and intranasal use[4] with a time to peak effect of <20 minutes.[3] Rarely, MA can be ingested; however, the time to peak effect is lengthy, approximately 180 minutes.[3] MA acts as an indirect agonist at the neurotransmitter receptors of dopamine, noradrenaline, and serotonin, resulting in stimulation of these postsynaptic receptors. MA accumulation at the synapse is enhanced by the inhibition of monoamine oxidase, which diminishes the neurotransmitter's degradation. The metabolism of MA occurs primarily in the liver, and the excretion of MA is via the urine.[3]

EDITOR'S CHOICE

In 2017, the prevalence of MA use within the United States was estimated at 0.6%, most commonly within the Western states.[5] Illicitly manufactured MA continues to be the primary stimulant driving amphetamine use disorders, compared with pharmaceuticals. In 2017, manufactured illicit MA constituted 96% of treatment admissions for ATS use.[6] We note that prescription drugs, such as amphetamine or dextroamphetamine (common trade name Adderall, Teva Pharmaceutical Industries Ltd, Israel), lisdexamfetamine dimesylate (Vyvanse, Takeda Pharmaceuticals U.S. A., Inc Lexington, MA), and methylphenidate (Ritalin, Novartis Pharmaceuticals Corporation, East Hanover, NJ) are increasingly being prescribed to reproductive-aged women.[1] These stimulants are similarly understudied in pregnancy.[7] The safety of prescription amphetamine derivatives in pregnancy has not been proven, and the Centers for Disease Control and Prevention cites some concerns regarding routine use.[7]

MA's growth has been fueled by its desirable effects, low cost, and accessibility,[1] with increasing use by reproductive-aged women.[8,9] The estimated prevalence of MA use during pregnancy ranges from 0.7% to 5.2%.[9] In 2014, ATSs became the second most common primary drugs reported on admission for treatment services during pregnancy, second only to opioids.[6] Such a dramatic increase in use during pregnancy demands better recognition and availability of appropriate care and treatment options.[10]

Effects on pregnancy outcomes

A detailed review of the adverse outcomes reported in pregnancies complicated by MA use is beyond the scope of this article. Studies assessing outcomes associated with MA use in pregnancy have been inconsistent. Adverse perinatal outcomes are thought to be secondary to the vasoconstrictive effects of stimulants, reducing blood flow and impairing placental perfusion.[11] However, contributions from insufficient prenatal care and socioeconomic adversity cannot be underestimated. The most commonly reported maternal and

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neonatal adverse outcomes associated with MA use include gestational hypertension,[12] preeclampsia,[12,13] eclampsia,[12] placental abruption,[12–14] preterm delivery,[12–16] perinatal demise,[12,14,16] lower gestational age at birth,[15] lower Apgar scores,[14,16] and reduced birthweight.[12,14,15] The methodologies in many of the studies are imperfect. They are commonly obfuscated by a low number of participants, lack of a dose-response and temporal relationship evaluation of the substance, and ill accountancy for added confounding factors, such as polysubstance use, poverty, and other socioeconomic factors.[17]

Contextual considerations in prenatal care

MA is a stimulant that promotes wakefulness and reduced appetite,[3] leading to sleep disturbance[18,19] and malnutrition.[20,21] Impairments in sleep can contribute to preterm labor[22] and have been linked to greater incidences of depression.[23] In addition to arousal, MA produces an adrenergic response causing hypertension and tachycardia and has been linked to various cardiac pathologies.[24] A case series was published discussing several reports of MA-associated cardiomyopathy occurring in pregnancy.[24] In addition, women using MA frequently engage in polysubstance use, including alcohol and tobacco.[9,17,25] When used intravenously, there is an increased risk of blood-borne diseases secondary to needle sharing.[26,27]

Women who use substances are more likely to have experienced childhood emotional, physical, or sexual abuse.[28–31] They are more likely to suffer from psychiatric disorders, such as anxiety, depression, and posttraumatic stress disorder.[32] Furthermore, MA use can lead to psychosis.[33] In addition, there is an increased incidence of engagement in high-risk sexual behavior, which increases the possibility of physical and sexual violence.[34] It is challenging for healthcare teams to address the many biopsychosocial factors that complicate the narrative of these patients.

Stigma is a widely known barrier to healthcare utilization for individuals with substance use disorders, particularly reproductive-aged women. Females who engage in substance use are more likely than their male counterparts to suffer from perceived judgment from their community[35] and healthcare workers.[36] Structural racism and bias in an obstetrical setting and mandatory reporting and involvement with child protective services can reinforce initial negative experiences and aversion to participating in clinical care. From an obstetrical standpoint, substance use leads to substandard engagement in prenatal care or no prenatal care, which is an independent risk factor for adverse pregnancy outcomes.[37]

Finally, a 2017 report by Amnesty International describes a concerning trend in legislation within the United States, which criminalizes substance use in pregnancy. Although such policies purportedly promote "fetal health," they inevitably harm women and families by destabilizing the overall well-being of the maternal-infant dyad. The criminalization of substance use disorder in pregnancy further marginalizes a vulnerable population and can decrease access to prenatal care, social services, and support.[38] A visual summary of the factors contributing to maternal and fetal well-being is presented in the Figure.

Identification of substance use in pregnancy

To provide appropriate and holistic prenatal care, obstetrical providers must screen for and identify prenatal substance use. Although no screening test

FIGURE
Factors associated with maternal and fetal health and well-being

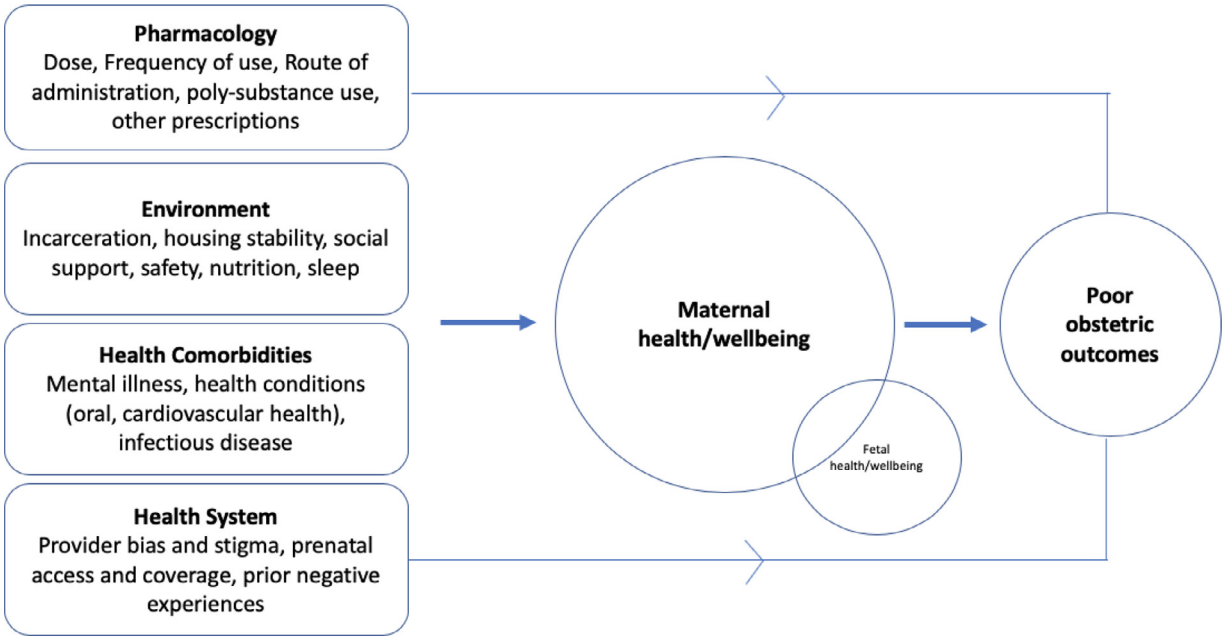

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TABLE 1
Summary of screening tools

Tool	Sensitivity	Limitations	Access information
4 P's Plus	87%[40] 90.2%[39,a]	• Must be purchased	https://www.ntiupstream.com/4psabout
SURP-P	Low-risk: 80%–100%[40] High-risk: 48%–100%[40] 92.4%[39,a]	• Only asks about marijuana and alcoholic drinks	https://journals.lww.com/greenjournal/fulltext/2010/10000/Screening_for_Prenatal_Substance_Use__Development.7.aspx
NIDA Quick Screen and ASSIST	79.7%[39,a]	• Potentially a 2-part questionnaire; can be lengthy • Not initially validated for prenatal screening	https://www.drugabuse.gov/sites/default/files/pdf/nmassist.pdf

NIDA, National Institute on Drug Abuse; *SURP-P*, Substance Use Risk Profile–Pregnancy.

[a] From the combined reference standard test results.

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is perfect, there are multiple screening instruments or tools that are validated for prenatal care to allow for rapid screening of multiple substances in a clinical environment. Research conducted by Coleman-Cowger et al[39] evaluated and validated 3 common prenatal screening tools. These tools have been referenced by the World Health Organization in their published guidelines for identifying and managing substance use during pregnancy.[40] Efficacious screening tools should have high sensitivities to identify true-positive individuals. Of the 3 tools evaluated, all had similar negative predictive values; however, the 4 P's Plus and Substance Use Risk Profile–Pregnancy had higher sensitivity.[39] Table 1 provides a summary of the 3 common screening tools along with the major limitations. In general, screening for substance use should be universal and asked for every patient to avoid bias in determining who should be screened. Even asking an abbreviated version of the first 2 questions of the 4 Ps—such as "Have you used alcohol or drugs during this pregnancy?" and "Have you had a problem with alcohol or drug use in the past?"—can be helpful in starting a conversation.

Current treatment for methamphetamine use

In contrast to opioid use disorder, there is limited evidence-based pharmacologic therapy for MA use disorder.[41] A recent systematic review by Siefried et al[42] examined 43 studies investigating the use of pharmacotherapies in people who used amphetamine or MA. The most common primary outcomes evaluated were abstinence and cravings, with 5 studies specifically examining withdrawal. Limitations of the studies included underrepresentation of women, small sample size, low participant retention, and low treatment adherence rates. The pharmacologic categories investigated include antidepressants (including tricyclics), atypical antipsychotics, anticonvulsants, central nervous system (CNS) stimulants, $GABA_B$ agonist or GABAergic agents, opioid agonists or antagonists, $5HT_3$ receptor antagonist, partial cholinergic nicotinic agonist, glutamatergic agents, CRF1 antagonist, and a combination of benzodiazepine antagonist, GABA agonist, and H1 histamine receptors.[42] CNS stimulants, such as dexamphetamine and methylphenidate; the opioid antagonist naltrexone; and the anticonvulsant topiramate demonstrated the most consistent positive findings.[42] Treatment with antidepressants, bupropion and mirtazapine, were shown to be less consistent.[42] A recent study investigating the combination of bupropion and naltrexone for moderate to severe MA use disorder showed an 11% response rate compared with placebo.[43]

Current expert opinion for treatment revolves around psychosocial interventions, with few studies in the obstetrics population.[40] This includes behavioral therapies, such as contingency management reward systems coupled with either community reinforcement or cognitive behavioral therapy.[40,44] Thus far, a combination of psychosocial interventions mentioned above has proven best for long-term abstinence.[44] Unfortunately, behavioral interventions, such as cognitive behavioral therapy, and contingency management carry suboptimal attrition rates and high-risk of relapse.[45,46] Given the current evidence, when a patient presents for prenatal care in the setting of ongoing MA use, what counseling can be provided?

Introduction to harm reduction

Harm reduction is a public health approach to substance use.[47] The goal of harm reduction is the attenuation of adverse effects associated with drug use through the emphasis on health and well-being.[47,48] Motivation to seek help is often secondary to the negative consequences of drug use.[48] Harm reduction acknowledges abstinence as ideal for reducing drug use harms and accepts any forward steps in which risks with drug use are mitigated.[47,48] Harm reduction aims to improve outcomes by increasing engagement with the healthcare system, to ultimately pave a path to

effective substance use disorder treatment.[47]

There are several harm reduction principles that can be applied within a clinical setting. Pragmatism is a key component of harm reduction; it is a provider's understanding that abstinence is not immediately achievable for many individuals.[49] Harm reduction focuses on identifying the high-risk behaviors associated with drug use and employs techniques to reduce the harms acknowledged without necessarily changing the drug use itself.[48] Obstetrical providers should seek to understand each person's individual needs and promote autonomy in decision making,[49] which effectively empowers the person[50,51] instead of modeling paternalism.[48] This builds a therapeutic partnership and may promote honesty about substance use.[52] Harm reduction emphasizes humanism with compassionate[49] and adaptive care[51] and a nonjudgmental approach in which small reductions in drug-associated risks are celebrated as a success.[48,53] In addition, there is a strong effort to address social needs and foster social enrichment.[53]

Obstetricians are quite inured to the shortcomings of abstinence-only expectations in other reproductive settings,[47,48] and harm reduction is encountered regularly in other applications. A harm reduction mainstay for tobacco use consists of nicotine replacement therapy (NRT).[48,54] NRT not only can act as a full replacement for tobacco use but also can help reduce smoking.[54] The treatment of opioid use disorders during pregnancy incorporates the harm reduction-aligned pharmacotherapies, methadone or buprenorphine,[55] to treat withdrawal and promote healthy behaviors.[56] Maintenance therapy is commonly paired with evidence-based behavioral interventions for maximal changes at sustained recovery.[55]

Application of harm reduction

An important consideration for the application of harm reduction involves attention to state legislation in the United States. Recent legislation that incorporates harm reduction strategies has made strides, such as the decriminalization of substance use in Oregon in 2020.[57] This progress continues to be undermined by widespread regressive state laws that insist on criminalizing substance use in pregnancy.[38] Obstetrical providers who care for pregnant women using substances should understand the legal climate of their state and consider participating in public policy or legislative advocacy efforts on a state or local level.

There has been considerable growth in the adaptation of harm reduction techniques in response to drug use.[58] However, limited data exist regarding the application of harm reduction in pregnancy that is specific to MA use. A study conducted by Wright et al[59] at a specialized, state-funded clinic in Hawaii employed several harm reduction techniques, in addition to contingency management, to improve adverse substance use-related outcomes in pregnancy. In 3 years, the clinic cared for 132 pregnancies with 86% of the women reporting MA use. Services provided by the clinic included transportation to and childcare during appointments, psychiatric and social services, group classes, and healthy food. Prenatal visits and ultrasounds were scheduled frequently to promote maternal-fetal bonding.[59] Harm reduction interventions demonstrated similarity in the rate of preterm delivery at the clinic (12.6%) vs the non-MA using cohort at the local hospital (15.0%), and there was no substantial difference in the rate of low birthweight at the clinic compared with the local hospital (13.6% vs 9.7%, respectively). Such outcomes were discordant (ie, improved) from the expected outcomes associated with MA use in pregnancy.[59] Regarding substance use, patients who engaged in repeat prenatal visits had improved abstinence rates, despite not requiring abstinence to use the services, and reduced relapse up to 6 months after delivery.[59] A study later conducted by Wright et al[15] evaluating the effects of MA use on pregnancy outcomes with women at the Hawaiian clinic found that outcomes related to birthweight and gestational age could be improved with the cessation of MA use during pregnancy.

Similar to the clinic in Hawaii, the Sheway program in Vancouver, British Columbia, provides comprehensive and coordinated services to pregnant and parenting women who use substances and alcohol.[60] The clinic uses a harm reduction approach to provide services that aim to meet the biopsychosocial needs of their clients through support and stability to break the cycle of substance use, poverty, and child protective services involvement. The comprehensive prenatal services provided by Sheway include food, counseling (nutrition, addiction, and legal), and social work to help secure housing and other various social needs.[60] A study conducted by Marshall et al[60] attempted to evaluate the effectiveness of Sheway's services by assessing pregnancy and infant outcomes. Since opening, client use of Sheway's services has increased annually; however, it is unknown whether this is because of the increased credibility of the program, the increased social needs, or both. Although no clear conclusions can be drawn from the data, 1 important finding was that increased engagement in prenatal care at Sheway was associated with higher neonatal birthweight (1 indicator of infant health), likely related to accessing food bags as needed.[60]

In addition, 1 qualitative study conducted by Rosenbaum et al[18] interviewing women engaging in substance use, either pregnant or recently pregnant, found that many women self-initiated harm reduction methods. Such techniques include reducing drug use, substituting for drugs perceived as less harmful (such as marijuana), remembering to eat and sleep, and changing their lifestyle, including moving away from family, friends, or neighbors who use drugs.[18]

Taking the focus off the drug use and concentrating on the care that promotes health and well-being during the prenatal period could be valuable in reducing adverse pregnancy outcomes.[37] The application of harm reduction techniques for MA use incorporates a biopsychosocial approach that aims to provide

TABLE 2
Harm reduction practices proposed for MA use in pregnancy

Harm associated with MA use in pregnancy	Application of harm reduction practices	Screening tools and guides
General MA consumption	• Accept ongoing drug use[47,50] • Discuss reduction in consumption frequency or dosing[61] • Assess behavior—if binging, schedule planned breaks and use a friend to help support their efforts[21]	
Adverse childhood experiences	• Screening[62]	ACOG Committee Opinion no. 498: screening for sexual violence
Intimate partner violence	• Screening: minimum once per trimester of pregnancy and once after delivery[63]	ACOG Committee Opinion no. 518: sample intimate partner violence screening questions
Mental health needs	• Screening for psychiatric comorbidities with a full assessment of mood and emotional well-being[40,64] • Access or referral to mental healthcare providers[64]	Edinburgh Postnatal Depression Scale
Polysubstance use	• Nicotine replacement therapy[65] • Opioid medication-assisted treatment[55,56] • Education in alcohol consumption[66]	4 P's Plus, SURP-P, NIDA Quick Screen and ASSIST
Poor social support and basic social needs	• Enquire about social and structural determinants of health: employment, immigration status, and access to safe and secure housing[67] • Screen for food insecurities[67] • Refer to relevant social support services[40,67] • Partnership with social workers, local community advocates, medical-legal teams[67]	ACOG Committee no. 729: sample screening tool; Health Leads Screening Toolkit
Social stigma	• Interventions should be provided in a nonstigmatizing fashion[40] • Healthcare worker training on bias[68]	
Infectious risk from IVDU	• Education on safe injection practices[21] • Utilization of needle and syringe programs[21] • Infectious disease testing—HIV, syphilis, HCV • Abstaining from intravenous MA use and changing consumption methods[21,59]	National Harm Reduction Coalition training guide: Getting off right: a safety manual for injection drug users
Unsafe sexual practices	• Safe sex education[21,59] • Distribution of condoms[21] • Sexually related infectious disease testing[26]	
Lack of sleep	• Education on the importance of sleep during pregnancy[21]	
Poor nutrition	• Consumption of healthy foods, such as vegetables and fruits[21] • Regular consumption of water[21] • Education on the importance of nutrition during pregnancy[21,61]	
Oral health	• Education on the importance of basic dental health[21,61] • Encourage brushing of teeth and water consumption[21]	

ACOG, American College of Obstetricians and Gynecologists; *HCV*, hepatitis C virus; *IVDU*, intravenous drug user; *MA*, methamphetamine; *SURP-P*, Substance Use Risk Profile—Pregnancy.

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TABLE 3
Future research considerations

Research category	Topic
Antenatal care and environmental factors	• Assessment of engagement in prenatal care and access to community services when harm reduction is applied for MA • Assessment of maternal and neonatal outcomes when harm reduction is applied during prenatal care • Distinguishing long-term outcomes of harm reduction interventions
Pharmacologic considerations	• Assessment of the routes safest for the consumption of manufactured MA and whether risks are cumulative, dose, or time dependent for the obstetrical population • Evaluating promising pharmacologic therapies for treatment of MA use disorders within the obstetrical population
Healthcare systems and providers	• Improving healthcare provider education regarding principles of harm reduction • Interventions to mitigate provider bias and stigma surrounding MA use in pregnancy • Cost analyses of harm reduction or pharmacologic interventions for the obstetrical population with MA use • Studies investigating the sequelae of harm reduction legislation at state or local levels

MA, methamphetamine.

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holistic care during the prenatal care visit. A proposal for the application of harm reduction practices is outlined in Table 2.

A call to arms

In conclusion, harm reduction is a theoretical framework that de-emphasizes abstinence and seeks to mitigate the harms associated with continued substance use. Harm reduction emphasizes patient autonomy and humanism in medicine. Unfortunately, there are few clinical studies regarding the application of harm reduction in patients with ongoing MA use during pregnancy. The lack of robust clinical evidence is a barrier to improving care related to MA use during pregnancy. The authors of this paper applaud specialized programs and clinics, such as Vancouver's Sheway, for their progressive use of harm reduction in an attempt to mitigate the negative impact of drug use while respecting the autonomy of pregnant individuals. We believe that the framework of harm reduction has the potential to encourage engagement in prenatal care for this marginalized population and deserves more attention. Specific questions have been identified, which include the following:

1 Can pragmatic harm reduction practices, such as acceptance of ongoing MA use, improve engagement in prenatal care? What are the short- and long-term maternal and perinatal outcomes of harm reduction? Which specific service interventions within a comprehensive program most contribute to perinatal well-being? Which interventions are cost-effective?
2 Which routes of MA consumption are most harmful to a pregnancy? Can recommending changes in frequency, route, or dosing of MA use improve perinatal outcomes?
3 Which of the current pharmacologic interventions undergoing investigation for MA use would be most appropriate to recommend in the obstetrical population?
4 Can healthcare provider education in harm reduction mitigate the effects of perceived healthcare provider bias and stigma regarding substance use? How does a harm reduction-focused legislation impact public health?

A summary of the recommendations is listed in Table 3. Answering such questions can reduce gaps in the literature for substance use in pregnancy and identify better therapies. This is an urgent call for further investigation of the application of harm reduction for MA use during pregnancy. ■

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