Treatments for opioid use disorder among pregnant and reproductive-aged women

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The increased prevalence of opioid use disorder and access to medical insurance is subsequently increasing the likelihood that medical professionals will encounter individuals with opioid use disorder. Sharp increases in opioid use disorder among women mean that obstetricians, gynecologists, and other reproductive medicine providers may be especially likely to encounter such patients. Medical professionals' understanding of treatment for opioid use disorder and their roles in their patients' treatment may increase referrals to treatment, reduce stigma, and improve the quality of medical care. Treatment for opioid use disorder falls into four overlapping domains: medication management, medical care, behavioral/mental health care, and psychosocial support. In this review, we discuss these domains with an emphasis on pregnant women and women of reproductive age. Treatment for opioid use disorder is most effective when all providers coordinate care in an informed, nonjudgmental, patient-centered approach. (Fertil Steril® 2017;108:222–7. ©2017 by American Society for Reproductive Medicine.)

Key Words: Buprenorphine, methadone, medication-assisted treatment, opioid, substance use disorder

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Opioid use disorder (OUD) among pregnant women and women of reproductive age has been increasing since the 1990s with demographics shifting toward young, white females [1]. The increased prevalence means that medical practitioners who typically do not encounter women with OUD are now more likely to encounter patients who need or are receiving treatment for OUD. This article reviews how OUD is treated, with an emphasis on the unique needs of pregnant women and women of reproductive age.

In 1965, the first controlled trial demonstrating that a daily dose of methadone could provide a 24-hour reduction in withdrawal symptoms and craving revolutionized treatment for OUD [2]. Methadone clinics were created and quickly grew to become centers where patients could receive

their daily dose of methadone, counseling, and other needed services, and they demonstrated effectiveness in reducing illicit substance use and increasing social functioning [3]. More recently the introduction of the opioid partial agonist/antagonist buprenorphine and long-acting formulations of the opioid antagonist naltrexone have increased alternatives for medication-assisted treatment and the settings in which treatment can take place. Regardless of the pharmacologic intervention provided, an evidence-based biopsychosocial assessment helps determine placement of the patient into the most appropriate level of care.

The American Society of Addiction Medicine (ASAM) placement criteria [4] include five broad levels of care (Table 1) spread across a continuum of treatment intensity. Early intervention is the least intensive, involving brief

interventions with minimal follow-up observation. Outpatient treatment can range from occasional office visits for counseling and medication management to a more intensive outpatient program involving 9 or more hours per week of counseling and group therapy. In partial hospitalization, individuals receive services for several hours each day, and physicians are readily available to deal with emergent medical problems, such as dangerous withdrawal symptoms. In residential treatment, the individual resides at the treatment facility in a structured living environment and receives treatment services throughout their stay. Inpatient treatment is reserved for the most severe cases requiring constant medical supervision, such as a high likelihood of dangerous withdrawal symptoms or co-occurring medical or psychiatric issues that present a danger to self or others.

The level of care reflects the setting and intensity of treatment, but treatment across all levels is multifaceted and can be described as falling into four domains: medication management, medical care, behavioral/mental

TABLE 1

American Society of Addiction Medicine (ASAM) levels of care and descriptions.

Level of care	Description
0.5	Early Intervention: Brief motivational counseling or other brief interventions to prevent addiction from developing, further assessment to rule out addiction is recommended.
1.0	Outpatient Treatment: Clinical services provided for up to 5 hours per week.
2.0	Intensive Outpatient Treatment and Partial Hospitalization: Nine or more hours per week provided near-daily or daily with ready access to acute medical care.
3.0	Residential Treatment: Individuals reside in a facility with 24-hour staffing and clinical services are provided throughout the day.
4.0	Medically Managed Intensive Inpatient Services: Individuals reside in a facility with 24-hour staffing by medical professionals and receive clinical services throughout the day.

Hand. Treatments for opioid use disorder. Fertil Steril 2017.

health care, and psychosocial support (Fig. 1). Medication management includes detoxification, maintenance on methadone or buprenorphine, or the use of oral or injectable naltrexone as well as management of concomitant medications. Medical care involves addressing medical needs that may have arisen as a result of addiction or have gone untreated. In the context of pregnancy, coordination and provision of prenatal care improves pregnancy and infant outcomes among women with OUD (5). Behavioral/mental health care involves treatment of co-occurring psychiatric and behavioral issues, which are common among individuals with OUD. Finally, psychosocial support involves addressing the social determinants of health, such as poverty, housing, education, and employment. The four domains are not orthogonal, and integration between the domains is important to comprehensive care and relapse prevention; these domains are intended to serve as a conceptual framework for evidence-based treatment for OUD.

MEDICATION MANAGEMENT

All individuals with OUD will require some form of medication management as part of their treatment. Ceasing chronic opioid use produces extremely unpleasant withdrawal symptoms such as diarrhea, vomiting, sleeplessness, tachycardia, hypertension, all of which may be relieved by using an opioid. Depending on the severity of the problem, medication management options range from maintenance with full or partial opioid agonists, to medication-assisted withdrawal (often called detoxification).

In the context of pregnancy complicated by OUD, maintenance with full or partial opioid agonists is the current consensus guidance from ASAM (6) and the American College of Obstetricians and Gynecologists (7). Methadone

FIGURE 1
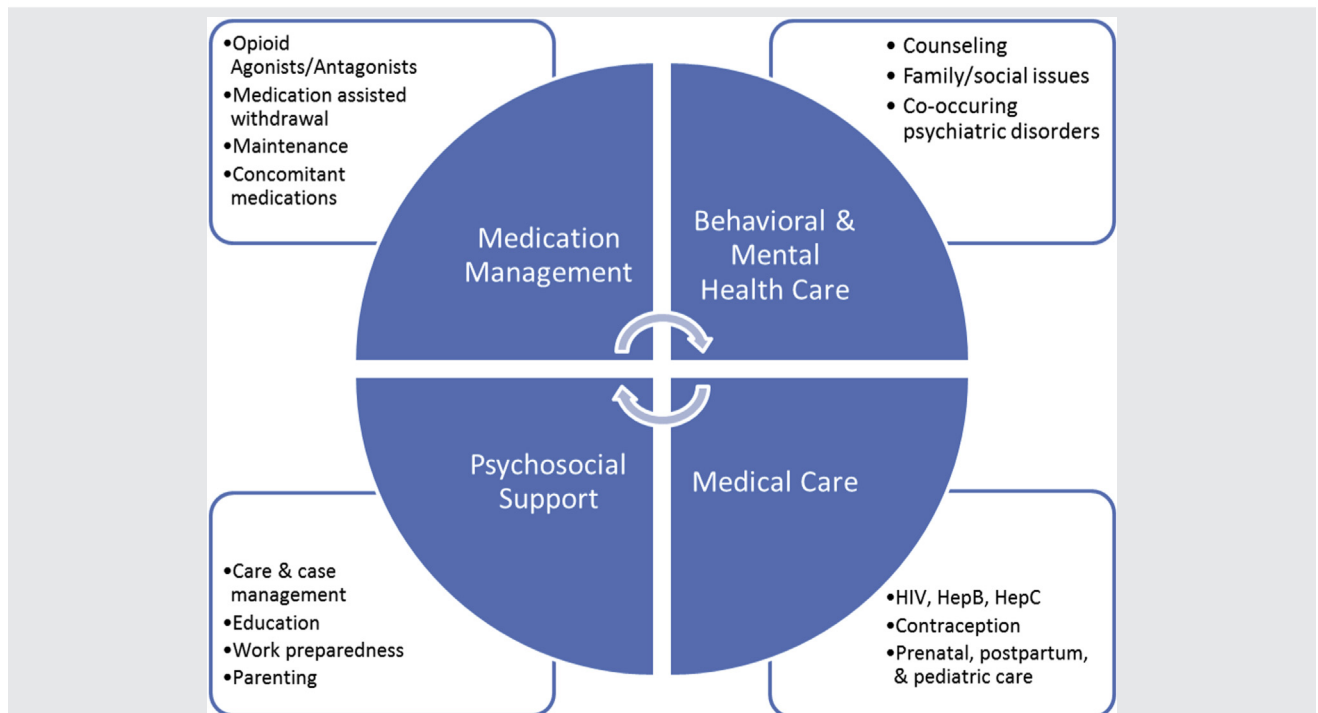
A conceptual framework for treatment of opioid use disorder.

Hand. Treatments for opioid use disorder. Fertil Steril 2017.

maintenance in pregnancy significantly reduces the risk of preterm birth and increases fetal growth when combined with a comprehensive treatment program (5). Buprenorphine, a partial opioid agonist and antagonist, is also an option for maintenance. Like methadone, buprenorphine is taken daily at a dose sufficient to prevent withdrawal symptoms and drug-seeking behavior. Methadone and buprenorphine are equally effective in controlling opioid withdrawal and preventing illicit opioid use among pregnant women, although methadone facilitates greater retention in treatment (8). Buprenorphine, however, tends to produce less severe neonatal withdrawal symptoms and improved obstetric and fetal outcomes (9). There is no clear clinical indication as to which medication is most appropriate for which person, thus other factors need to be considered.

Methadone and buprenorphine maintenance are often conducted in substantially different settings. Methadone is typically dispensed from a licensed opioid treatment program, and patients must attend the clinic daily to receive medication and comprehensive treatment for an extended period of time before take-home medication is permitted per federal regulations. Buprenorphine can also be used in a licensed opioid treatment program but is more typically prescribed by a physician in a primary care setting. The patient receives a prescription for up to 30 days of buprenorphine and self-administers the prescribed dose. These two modes of delivering the maintenance medication have their benefits and limitations, especially regarding the other three domains of OUD treatment. With methadone maintenance, it is more likely that a patient will engage with counseling, psychiatric care, and psychosocial services as a result of daily clinic attendance. Daily clinic attendance is a barrier for some patients, due to employment, education, or their proximity to a methadone clinic, which are typically located in urban centers. For such individuals, buprenorphine and office-based opioid treatment may be the only possible treatment with alternate counseling arrangements. The two medications also differ in their insurance coverage, with Medicaid/Medicare covering methadone in most states, while private insurance tends to only cover buprenorphine. Both public and private insurance typically reimburses for the other dimensions of OUD treatment, regardless of the medication used for maintenance.

Neonatal abstinence syndrome (NAS), a cluster of neurologic, autonomic, and gastrointestinal signs, is exhibited by almost half of neonates after gestational exposure to opioids (10). Neonatal abstinence syndrome has received much attention due to its increasing prevalence and the relatively higher costs associated with caring for opioid-exposed infants due to longer postdelivery hospital stays of up to several weeks and in neonatal intensive care units (11–13). The evaluation of NAS involves semiobjective observational tools such as the Finnegan Scoring Method (14); pharmacologic treatment with opioids is reserved for instances of relatively severe withdrawal. The percentage of opioid-exposed neonates requiring pharmacologic interventions for NAS varies widely between 50% and 90% due to differences in hospital procedures (15), maternal/infant bonding (16, 17), maternal cigarette smoking (18), benzodiazepine use (17, 19), and genetic factors

(20). Maternal opioid dosage is not associated with increased incidence of NAS (21, 22). It is important to keep in mind that NAS is a temporary, treatable condition, and decisions around maternal OUD treatment should take into account many other factors, such as the risks associated with acquiring and using illicit drugs and overdose. Nonetheless, pregnant women with OUD may seek opioid-free treatment in an attempt to avoid NAS.

Although medication-assisted withdrawal is not currently recommended in the setting of pregnancy, recent retrospective analyses of medication-assisted withdrawal in pregnancy have suggested the risks may be more limited than previously thought (23). However, there is a paucity of high-quality, controlled studies that support recommending withdrawal as a treatment in pregnancy (24). Outside of pregnancy, medication-assisted withdrawal is a frequent medication management strategy for OUD.

Medication-assisted withdrawal involves gradually reducing the dosage of opioids over a period of several days while monitoring and minimizing withdrawal symptoms. There are several validated measures of opioid withdrawal, such as the Clinical Opioid Withdrawal Scale and the Clinical Institute Narcotic Withdrawal Scale (25). Methadone is the most common opioid used for medication-assisted withdrawal. A typical methadone withdrawal protocol involves starting at 10 to 20 mg, increasing the dose up to 40 mg within the first 24 hours, followed by a gradual tapering of the daily dose over the following days (26). The length of the taper can be as short as 3 days, but short tapers are associated with higher relapse risk (27). Buprenorphine may also be used for medication-assisted withdrawal, with a similar pattern of increasing dose in small (e.g., 2 mg) increments until withdrawal symptoms are managed and then tapering over the following days. As with methadone, successful completion of withdrawal may be associated with a longer taper time (28, 29). To date, methadone- and buprenorphine-facilitated tapers have shown near equivalence (30).

Nonopioids that affect withdrawal symptoms may be used in addition to or even in place of opioid agonists during the withdrawal period. Alpha2-adrenergic agonists (e.g., clonidine, lofexidine, and guanfacine) can be used to control withdrawal symptoms while tapering an opioid or can be used in place of opioids altogether, and they have shown similar effectiveness to methadone tapers (31). Other symptomatic medications can be used as needed, such as hydroxyzine for anxiety and loperamide for diarrhea.

Generally, medication-assisted withdrawal results in minimal sustained opioid abstinence. For example, one study found that 80% of individuals had relapsed within 30 days of completing an inpatient detoxification (32). The opioid antagonist naltrexone can help to maintain abstinence after medication-assisted withdrawal by blocking the effects of subsequently used opioids (33). Oral naltrexone must be taken daily, and as a result compliance tends to be low (34). Long-acting injectable naltrexone avoids some of the compliance issues as injections are required monthly, and it produces greater retention in treatment and abstinence from opioids than placebo (35).

MEDICAL CARE

Infectious diseases, including hepatitis C virus (HCV) and human immunodeficiency virus (HIV), are common among women with OUD (36, 37) due to intravenous drug use (37) and high-risk sexual behaviors (38). Rates of HCV among pregnant women with OUD are between 50% and 62% (39). Intravenous opioid use also carries the risk of cellulitis and abscess formation at the injection site, sepsis, endocarditis, osteomyelitis, and hepatitis B infection (7). Given the high prevalence of HCV, pregnancy is a critical opportunity to identify and evaluate HCV infection in high-risk populations. Frequent prenatal care visits offer multiple opportunities to provide patient education and counseling regarding HCV transmission, disease course, and treatment options to prevent further transmission and encourage enrollment in HCV treatment after delivery.

Among pregnant women undergoing treatment for OUD, tobacco smoking rates are high (36, 40, 41) and concomitant use of other substances including alcohol, marijuana, benzodiazepines, and cocaine is not uncommon (42). Such use, however, can lead to adverse maternal and infant outcomes. For example, as in the general population, smoking among opioid-maintained pregnant women has been associated with lower neonatal birth weight and smaller birth length (43). Prenatal exposure to opioids combined with cocaine, benzodiazepines, or high levels of tobacco during pregnancy is associated with more severe neonatal withdrawal and longer newborn hospital stays (17–19, 44). Benzodiazepines in addition to opioids is associated with increased risks for overdose and overdose death (45, 46).

Although almost half of pregnancies in the United States are unintended (47), the proportion of unintended pregnancies in women with OUD may be greater than 85% (48). Women with OUD also become pregnant more often than women in the general population. In a study examining the reproductive health of opioid-dependent women, 54% reported having four or more pregnancies in their lifetime compared to 14% of a nationally representative sample of U.S. women (49). There are also low rates of contraceptive use among women with OUD. Results of a recent systematic review suggest that only about half of women with opioid and other substance use disorders use any contraception (38). Results also indicate that condoms are the most commonly used contraceptive method (approximately 62%), while the use of more effective methods (e.g., tubal ligation, implants, and intrauterine devices) is considerably lower (approximately 8%) (38). Integrating family planning services into substance use disorder treatment clinics substantially increases the use of effective contraception (50, 51).

BEHAVIORAL/MENTAL HEALTH CARE

It is generally required that all individuals receiving treatment for OUD receive counseling as part of their treatment, and counseling is associated with improved treatment outcomes (52). Individual counseling occurring several times per week, weekly, or monthly enables the patient to process and become aware of triggers of relapse, keeps the treatment plan concordant with the patient's needs, and allows for interventions for co-occurring social or family problems. Social and family relationships appear to be relatively more influential in substance use disorders among women, as a perceived need to maintain even unhealthy, abusive relationships significantly complicates recovery (53). Cognitive behavioral therapies are the most common counseling interventions, and trauma-informed techniques are especially important among pregnant women and women of reproductive age as this population has a high incidence of traumatization (54–56), which is associated with poorer substance use disorder treatment outcomes (57, 58).

Group counseling is an effective component of treatment. In groups of peers facilitated by a senior peer or therapist, patients can share experiences, learn from each other's behaviors, and provide support. Peer support may be especially important for pregnant women and women of reproductive age given the stigmatization of mothers with substance use disorders (59). Group settings can also be used to convey cognitive behavioral therapies, parenting training, and other psychosocial supports as discussed herein.

Mental/behavioral health comorbidities are present in upward of half of individuals with OUD, with anxiety, depression, and antisocial personality disorders being most common (60–62). Additionally, these disorders are differentially represented between the genders, with women more likely to exhibit posttraumatic stress disorder (63), anxiety disorders (64), depression, and borderline personality disorder (60). Thus, proper screening and treatment for such disorders is a necessary component of OUD treatment. If psychiatric medications are required, integration with the medication management component of treatment is critical.

PSYCHOSOCIAL SUPPORT

Psychosocial support in OUD treatment is an essential component of successful recovery. State of the art treatment and care are necessary, but what determines adherence to care and relapse prevention begins with the support necessary to participate in treatment. Care management provides a structured process for which psychosocial support is delivered. Care management consists of working with the patient to enable her to access the services and care she may need outside of substance use treatment.

Case management is the act of working with the individual to identify and link specific care services and activities needed to help patients manage their substance abuse treatment by identifying the care and services needed to improve an individual's or her children's health and well-being. It includes a single point of contact for the multiple systems that the patient may need (e.g., housing, child care, legal advocacy, food, employment, and other programs that would assist with recovery), assisting and advocating with systems on the behalf of and with the patient. Case management is community-based and patient centered. Enhanced case management, which combines care management for medical care for the mother and child and social service linkages for women with substance misuse disorders, is essential to recovery. Women are centered in the families, and their families have unmet needs as well. These stressors have a direct impact on recovery, and when stressors are not addressed they affect relapse.

Women with substance use disorders who are pregnant or have children have parenting deficits (65). The deficits may include ambivalent feelings about parenting, harsh punitive responses expressed through yelling and threatening, a lack of understanding about basic developmental issues, and perception of infant communications as demanding and inappropriate (66). Parenting stress may further complicate treatment adherence. Studies have shown that parenting support (i.e., child care services, parenting education, parenting and family counseling) is needed in this population (67). An example of a parenting intervention that has recently demonstrated improvements in the quality of parenting and decreases in parental stress is mindfulness-based parenting adapted to substance misuse treatment and adapted to be trauma informed (55).

SUMMARY

A coordinated, multidisciplinary approach is essential for providing optimal care to pregnant women and women of reproductive age with OUD. Components of OUD treatment should include medication management to stabilize illicit drug use, medical care to secure the patient's physical health, behavioral/mental health care to address underlying cognitive and behavioral factors and co-occurring psychiatric disorders, and psychosocial support including parenting support and education, childcare, and transportation, reproductive health, and nutrition (68). A pregnant woman's treatment plan should also include coordinated prenatal care co-managed by obstetricians, gynecologists, and addiction medicine specialists to reduce obstetric and neonatal morbidity. Obstetric and labor-and-delivery providers caring for pregnant women with OUD should coordinate and communicate with pediatric staff responsible for the care of neonates with neonatal abstinence syndrome (68). Successful treatment of OUD among pregnant women and women of reproductive age requires the combined, coordinated efforts of medical and addiction professionals providing services within and across each of these domains to meet the specific needs of each woman.

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