

8-1-2017

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

Dennis J. Hand
Thomas Jefferson University

Vanessa L. Short
Thomas Jefferson University

Diane J. Abatemarco
Thomas Jefferson University

Follow this and additional works at: <https://jdc.jefferson.edu/obgynfp>



Part of the [Obstetrics and Gynecology Commons](#)

[Let us know how access to this document benefits you](#)

Recommended Citation

Hand, Dennis J.; Short, Vanessa L.; and Abatemarco, Diane J., "Treatments for opioid use disorder among pregnant and reproductive-aged women." (2017). *Department of Obstetrics and Gynecology Faculty Papers*. Paper 58.

<https://jdc.jefferson.edu/obgynfp/58>

This Article is brought to you for free and open access by the Jefferson Digital Commons. The Jefferson Digital Commons is a service of Thomas Jefferson University's [Center for Teaching and Learning \(CTL\)](#). The Commons is a showcase for Jefferson books and journals, peer-reviewed scholarly publications, unique historical collections from the University archives, and teaching tools. The Jefferson Digital Commons allows researchers and interested readers anywhere in the world to learn about and keep up to date with Jefferson scholarship. This article has been accepted for inclusion in Department of Obstetrics and Gynecology Faculty Papers by an authorized administrator of the Jefferson Digital Commons. For more information, please contact: JeffersonDigitalCommons@jefferson.edu.

Running head: TREATMENTS FOR OPIOID USE DISORDER

Treatments for Opioid Use Disorder Among Pregnant and Reproductive-Aged Women

Dennis J. Hand, Ph.D., Vanessa L. Short, Ph.D., M.P.H., & Diane J. Abatemarco, Ph.D., M.S.W.

Department of Obstetrics & Gynecology, Sidney Kimmel Medical College, Thomas Jefferson University, 1233 Locust St., Suite 401, Philadelphia, PA, USA

Corresponding Author:

Dennis J. Hand, Ph.D

MATER

1233 Locust St.

Suite 401

Philadelphia, PA 19107

Dennis.hand@jefferson.edu

Ph. +1 215-955-8419

Vanessa L. Short, Ph.D, MPH

Vanessa.short@jefferson.edu

Diane J. Abatemarco, Ph.D, MSW

Diane.abatemarco@jefferson.edu

Abstract

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, non-judgmental, patient-centered approach.

Keywords: opioid, methadone, buprenorphine, medication assisted treatment, substance use disorder

Introduction

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 opioid use disorder are now more likely to encounter patients who need, or are receiving treatment for OUD. The aim of the present article is to review 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 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 pharmacological 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. Outpatient treatment can range from occasional office visits for counseling and medication management to a more intensive outpatient program involving nine 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.

Table 1. American Society of Addiction Medicine (ASAM) Levels of care and descriptions.

ASAM Level of Care	Description
Level 0.5	Early Intervention – Brief motivational counseling or other brief interventions to prevent addiction from developing, further assessment to rule out addiction is recommended.
Level 1.0	Outpatient Treatment – Clinical services provided for up to 5 hours per week.
Level 2.0	Intensive Outpatient Treatment and Partial Hospitalization – 9 or more hours per week provided near-daily or daily with ready access to acute medical care.
Level 3.0	Residential Treatment – Individuals reside in a facility with 24-hr staffing and clinical services are provided throughout the day.
Level 4.0	Medically Managed Intensive Inpatient Services – Individuals reside in a facility with 24-hr staffing by medical professionals and receive clinical services throughout the day.

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 health care, and psychosocial support (Figure 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 the ASAM (6) and the American College of Obstetricians and Gynecologists (7). Methadone 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 obstetrical 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 neurological, autonomic, and gastrointestinal signs, is exhibited by almost half of neonates following gestational exposure to opioids (10). NAS has received much attention due to its increasing prevalence and the relatively higher costs associated with caring for opioid-exposed infants due to longer post-delivery hospital stays of up to several weeks and in neonatal intensive care units (11–13). NAS is evaluated using semi-objective observational tools, such as the Finnegan Scoring Method (14), and pharmacologic treatment with opioids is reserved for instances of relatively severe

withdrawal. The percentage of opioid-exposed neonates requiring pharmacological interventions for NAS varies widely between 50-90% 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.

While 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 10-20 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).

Non-opioids 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 be used in place of opioids altogether and 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 following 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 produces greater retention in treatment and abstinence from opioids than placebo (35).

Medical Care

Infectious diseases, including Hepatitis C Virus (HCV) and 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 50-62% (39). Intravenous opioid use also carries the risk of cellulitis and abscess formation at the injection site, sepsis, endocarditis, osteomyelitis, and hepatitis B (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).

While almost half of pregnancies in the U.S. 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 IUDs) 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 below.

Mental/behavioral health comorbidities are present in upwards 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. While state of the art treatment and care are necessary, 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 care and services needed to improve their or their 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 that combines care management to medical care for the mother and child and social service linkages for women with substance misuse disorders, are 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 as well.

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 which 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 to provide optimal care for 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 obstetrician–gynecologists and addiction medicine specialists to reduce obstetrical and neonatal morbidity. Obstetrical 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.

References

1. Martin CE, Longinaker N, Terplan M. Recent trends in treatment admissions for prescription opioid abuse during pregnancy. *J Subst Abuse Treat*. 2015 Jan;48(1):37–42.
2. Dole VP, Nyswander M. A Medical Treatment for Diacetylmorphine (Heroin) Addiction: A Clinical Trial With Methadone Hydrochloride. *JAMA*. 1965 Aug 23;193(8):646–50.
3. Ball JC, Ross A. *The Effectiveness of Methadone Treatment: Patients, Programs, Services, and Outcome*. New York: Springer-Verlag; 1991.
4. Mee-Lee D, editor. *The ASAM Criteria: Treatment Criteria for Addictive, Substance-Related, and Co-Occurring Conditions*. 2013.
5. Kaltenbach K, Berghella V, Finnegan L. Opioid dependence during pregnancy. Effects and management. *Obstet Gynecol Clin North Am*. 1998 Mar;25(1):139–51.
6. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. *J Addict Med*. 2015 Oct;9(5):358–67.
7. ACOG Committee on Health Care for Underserved Women, American Society of Addiction Medicine. ACOG Committee Opinion No. 524: Opioid abuse, dependence, and addiction in pregnancy. *Obstet Gynecol*. 2012 May;119(5):1070–6.
8. Jones HE, Kaltenbach K, Heil SH, Stine SM, Coyle MG, Arria AM, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med*. 2010 Dec 9;363(24):2320–31.
9. 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. *Addict Abingdon Engl*. 2016 Dec;111(12):2115–28.
10. Kocherlakota P. Neonatal Abstinence Syndrome. *Pediatrics*. 2014 Aug;134(2):e547–61.
11. Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *JAMA J Am Med Assoc*. 2012 May 9;307(18):1934–40.
12. Tolia VN, Patrick SW, Bennett MM, Murthy K, Sousa J, Smith PB, et al. Increasing Incidence of the Neonatal Abstinence Syndrome in U.S. Neonatal ICUs. *N Engl J Med*. 2015 Apr 26;
13. Patrick SW, Davis MM, Lehman CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. *J Perinatol Off J Calif Perinat Assoc*. 2015 Apr 30;
14. Jansson LM, Velez M, Harrow C. The opioid-exposed newborn: assessment and pharmacologic management. *J Opioid Manag*. 2009 Feb;5(1):47–55.

15. Holmes AV, Atwood EC, Whalen B, Beliveau J, Jarvis JD, Matulis JC, et al. Rooming-In to Treat Neonatal Abstinence Syndrome: Improved Family-Centered Care at Lower Cost. *Pediatrics*. 2016 May 18;
16. O'Connor AB, Collett A, Alto WA, O'Brien LM. Breastfeeding rates and the relationship between breastfeeding and neonatal abstinence syndrome in women maintained on buprenorphine during pregnancy. *J Midwifery Womens Health*. 2013 Jul;58(4):383–8.
17. Abdel-Latif ME, Pinner J, Clews S, Cooke F, Lui K, Oei J. Effects of breast milk on the severity and outcome of neonatal abstinence syndrome among infants of drug-dependent mothers. *Pediatrics*. 2006 Jun;117(6):e1163-1169.
18. Jones HE, Heil SH, Tuten M, Chisolm MS, Foster JM, O'Grady KE, et al. Cigarette smoking in opioid-dependent pregnant women: neonatal and maternal outcomes. *Drug Alcohol Depend*. 2013 Aug 1;131(3):271–7.
19. 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 Oct;199(4):396.e1-396.e7.
20. Wachman EM, Hayes MJ, Brown MS, et al. Association of *oprm1* and *comt* single-nucleotide polymorphisms with hospital length of stay and treatment of neonatal abstinence syndrome. *JAMA*. 2013 May 1;309(17):1821–7.
21. 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(12):2071–2084.
22. Berghella V, Lim PJ, Hill MK, Cherpes J, Chennat J, Kaltenbach K. Maternal methadone dose and neonatal withdrawal. *Am J Obstet Gynecol*. 2003 Aug;189(2):312–7.
23. Bell J, Towers CV, Hennessy MD, Heitzman C, Smith B, Chattin K. Detoxification from opiate drugs during pregnancy. *Am J Obstet Gynecol*. 2016 Sep;215(3):374.e1-6.
24. Jones HE, Terplan M, Meyer M. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. *J Addict Med*. 2017 Jan 11;
25. Tompkins DA, Bigelow GE, Harrison JA, Johnson RE, Fudala PJ, Strain EC. Concurrent validation of the Clinical Opiate Withdrawal Scale (COWS) and single-item indices against the Clinical Institute Narcotic Assessment (CINA) opioid withdrawal instrument. *Drug Alcohol Depend*. 2009 Nov 1;105(1–2):154–9.
26. Amato L, Davoli M, Minozzi S, Ferroni E, Ali R, Ferri M. Methadone at tapered doses for the management of opioid withdrawal. *Cochrane Database Syst Rev*. 2013 Feb 28;(2):CD003409.
27. Senay EC, Dorus W, Goldberg F, Thornton W. Withdrawal from methadone maintenance. Rate of withdrawal and expectation. *Arch Gen Psychiatry*. 1977 Mar;34(3):361–7.

28. Dunn KE, Sigmon SC, Strain EC, Heil SH, Higgins ST. The association between outpatient buprenorphine detoxification duration and clinical treatment outcomes: a review. *Drug Alcohol Depend.* 2011 Dec 1;119(1–2):1–9.
29. Sigmon SC, Dunn KE, Saulsgiver K, Patrick ME, Badger GJ, Heil SH, et al. A randomized, double-blind evaluation of buprenorphine taper duration in primary prescription opioid abusers. *JAMA Psychiatry.* 2013 Dec;70(12):1347–54.
30. Gowing L, Ali R, White JM, Mbewe D. Buprenorphine for managing opioid withdrawal. *Cochrane Database Syst Rev.* 2017 21;2:CD002025.
31. Gowing L, Farrell M, Ali R, White JM. Alpha₂-adrenergic agonists for the management of opioid withdrawal. *Cochrane Database Syst Rev.* 2016 May 3;(5):CD002024.
32. Smyth BP, Barry J, Keenan E, Ducray K. Lapse and relapse following inpatient treatment of opiate dependence. *Ir Med J.* 2010 Jun;103(6):176–9.
33. Shufman EN, Porat S, Witztum E, Gandacu D, Bar-Hamburger R, Ginath Y. The efficacy of naltrexone in preventing reabuse of heroin after detoxification. *Biol Psychiatry.* 1994 Jun 15;35(12):935–45.
34. Tennant FS, Rawson RA, Cohen AJ, Mann A. Clinical experience with naltrexone in suburban opioid addicts. *J Clin Psychiatry.* 1984 Sep;45(9 Pt 2):42–5.
35. Comer SD, Sullivan MA, Yu E, Rothenberg JL, Kleber HD, Kampman K, et al. Injectable, sustained-release naltrexone for the treatment of opioid dependence: a randomized, placebo-controlled trial. *Arch Gen Psychiatry.* 2006 Feb;63(2):210–8.
36. Almario CV, Seligman NS, Dysart KC, Berghella V, Baxter JK. Risk factors for preterm birth among opiate-addicted gravid women in a methadone treatment program. *Am J Obstet Gynecol.* 2009 Sep;201(3):326.e1-6.
37. Holbrook AM, Baxter JK, Jones HE, Heil SH, Coyle MG, Martin PR, et al. Infections and obstetric outcomes in opioid-dependent pregnant women maintained on methadone or buprenorphine. *Addict Abingdon Engl.* 2012 Nov;107 Suppl 1:83–90.
38. 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 Nov;80:23–31.
39. Latt NC, Spencer JD, Beeby PJ, McCaughan GW, Saunders JB, Collins E, et al. Hepatitis C in injecting drug-using women during and after pregnancy. *J Gastroenterol Hepatol.* 2000 Feb;15(2):175–81.
40. Chisolm MS, Fitzsimons H, Leoutsakos J-MS, Acquavita SP, Heil SH, Wilson-Murphy M, et al. A Comparison of Cigarette Smoking Profiles in Opioid-Dependent Pregnant Patients Receiving Methadone or Buprenorphine. *Nicotine Tob Res Off J Soc Res Nicotine Tob.* 2013 Jan 3;
41. Jones HE, Heil SH, O'Grady KE, Martin PR, Kaltenbach K, Coyle MG, et al. Smoking in pregnant women screened for an opioid agonist medication study compared to related

- pregnant and non-pregnant patient samples. *Am J Drug Alcohol Abuse*. 2009;35(5):375–80.
42. Hand DJ, Short VL, Abatemarco DJ. Substance use, treatment, and demographic characteristics of pregnant women entering treatment for opioid use disorder differ by United States census region. *J Subst Abuse Treat*. 2017 May;76:58–63.
 43. Winklbaur B, Baewert A, Jagsch R, Rohrmeister K, Metz V, Aeschbach Jachmann C, et al. Association between prenatal tobacco exposure and outcome of neonates born to opioid-maintained mothers. Implications for treatment. *Eur Addict Res*. 2009;15(3):150–6.
 44. Cleary BJ, Eogan M, O’Connell MP, Fahey T, Gallagher PJ, Clarke T, et al. Methadone and perinatal outcomes: a prospective cohort study. *Addict Abingdon Engl*. 2012 Aug;107(8):1482–92.
 45. Chan GM, Stajic M, Marker EK, Hoffman RS, Nelson LS. Testing positive for methadone and either a tricyclic antidepressant or a benzodiazepine is associated with an accidental overdose death: analysis of medical examiner data. *Acad Emerg Med Off J Soc Acad Emerg Med*. 2006 May;13(5):543–7.
 46. Lee SC, Klein-Schwartz W, Doyon S, Welsh C. Comparison of toxicity associated with nonmedical use of benzodiazepines with buprenorphine or methadone. *Drug Alcohol Depend*. 2014 May 1;138:118–23.
 47. Finer LB, Zolna MR. Declines in Unintended Pregnancy in the United States, 2008-2011. *N Engl J Med*. 2016 Mar 3;374(9):843–52.
 48. Heil SH, Jones HE, Arria A, Kaltenbach K, Coyle M, Fischer G, et al. Unintended pregnancy in opioid-abusing women. *J Subst Abuse Treat*. 2011 Mar;40(2):199–202.
 49. Armstrong KA, Kennedy MG, Kline A, Tunstall C. Reproductive health needs: comparing women at high, drug-related risk of HIV with a national sample. *J Am Med Womens Assoc* 1972. 1999;54(2):65–70, 78.
 50. Armstrong KA, Kenen R, Samost L. Barriers to family planning services among patients in drug treatment programs. *Fam Plann Perspect*. 1991 Dec;23(6):264–6, 270–1.
 51. Heil SH, Hand DJ, Sigmon SC, Badger GJ, Meyer MC, Higgins ST. Using behavioral economic theory to increase use of effective contraceptives among opioid-maintained women at risk of unintended pregnancy. *Prev Med*. 2016 Jun 23;
 52. Magura S, Nwakeze PC, Kang SY, Demsky S. Program quality effects on patient outcomes during methadone maintenance: a study of 17 clinics. *Subst Use Misuse*. 1999 Jul;34(9):1299–324.
 53. Price A, Simmel C. Partners’ influence on women’s addiction and recovery: The connection between substance abuse, trauma and intimate relationships. University of California at Berkeley; 2002.

54. Substance Abuse and Mental Health Services Administration. SAMHA's Concept of Trauma and Guidance for a Trauma-Informed Approach. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014. (HHS Publication No. (SMA) 14-4884).
55. Short VL, Gannon M, Weingarten W, Kaltenbach K, LaNoue M, Abatemarco DJ. Reducing Stress Among Mothers in Drug Treatment: A Description of a Mindfulness Based Parenting Intervention. *Matern Child Health J.* 2017 Jan 11;
56. Liebschutz J, Savetsky JB, Saitz R, Horton NJ, Lloyd-Travaglini C, Samet JH. The relationship between sexual and physical abuse and substance abuse consequences. *J Subst Abuse Treat.* 2002 Apr;22(3):121–8.
57. Sacks JY, McKendrick K, Banks S. The impact of early trauma and abuse on residential substance abuse treatment outcomes for women. *J Subst Abuse Treat.* 2008 Jan;34(1):90–100.
58. Bernstein DP. Childhood trauma and drug addiction: Assessment, diagnosis, and treatment. *Alcohol Treat Q.* 2000;18(3):19–30.
59. Terplan M, Kennedy-Hendricks A, Chisolm MS. Prenatal Substance Use: Exploring Assumptions of Maternal Unfitness. *Subst Abuse Res Treat.* 2015;9(Suppl 2):1–4.
60. Brooner RK, King VL, Kidorf M, Schmidt CW, Bigelow GE. Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. *Arch Gen Psychiatry.* 1997 Jan;54(1):71–80.
61. Kidorf M, Disney ER, King VL, Neufeld K, Beilenson PL, Brooner RK. Prevalence of psychiatric and substance use disorders in opioid abusers in a community syringe exchange program. *Drug Alcohol Depend.* 2004 May 10;74(2):115–22.
62. Naji L, Dennis BB, Bawor M, Varenbut M, Daiter J, Plater C, et al. The association between age of onset of opioid use and comorbidity among opioid dependent patients receiving methadone maintenance therapy. *Addict Sci Clin Pract.* 2017 Mar 28;12(1):9.
63. Villagómez RE, Meyer TJ, Lin MM, Brown LS. Post-traumatic stress disorder among inner city methadone maintenance patients. *J Subst Abuse Treat.* 1995 Aug;12(4):253–7.
64. Ward J, Mattick RP, Hall W. Psychiatric comorbidity among the opioid dependent. In: Ward J, Mattick RP, Hall W, editors. *Methadone Maintenance Treatment and Other Opioid Replacement Therapies.* Amsterdam: Harwood Academic Publishers; 1998. p. 419–40.
65. Chaffin M, Kelleher K, Hollenberg J. Onset of physical abuse and neglect: psychiatric, substance abuse, and social risk factors from prospective community data. *Child Abuse Negl.* 1996 Mar;20(3):191–203.
66. Suchman N, Mayes L, Conti J, Slade A, Rounsaville B. Rethinking parenting interventions for drug-dependent mothers: From behavior management to fostering emotional bonds. *J Subst Abuse Treat.* 2004 Oct;27(3):179–85.
67. Suchman NE, Luthar SS. The Mediating Role of Parenting Stress in Methadone-Maintained Mothers' Parenting. *Parent Sci Pract.* 2001 Oct;1(4):285–315.

68. American Society of Addiction Medicine. Substance Use, Misuse, and Use Disorders During and Following Pregnancy, with an Emphasis on Opioids [Internet]. 2017 [cited 2017 Mar 21]. Available from: <http://www.asam.org/advocacy/find-a-policy-statement/view-policy-statement/public-policy-statements/2017/01/19/substance-use-misuse-and-use-disorders-during-and-following-pregnancy-with-an-emphasis-on-opioids>

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

