

(NIDA, 2012).

Studies involving tobacco users have demonstrated a 1.2 to 3.6 relative risk for infertility in the preconception period. Moreover, there is an increased prevalence of smoking among younger pregnant women (less than 20 years of age) and older pregnant women (over the age of 35). Up to 15 percent of all women continue to smoke during their pregnancy. However, tobacco use is linked to more complications during pregnancy. Spontaneous abortion runs 20 to 80 percent higher in women who smoke during pregnancy than in nonsmokers. Fetuses that survive are more likely to be preterm and of low birth weight. On average, newborns exposed to tobacco during pregnancy weigh 200 to 500 grams lighter. Research further suggests that births for these newborns tend to be violent (Keegan, Parva, Finnegan, Gerson, & Belden, 2010; NIDA, 2014). A number of studies have reported a higher risk of ectopic pregnancy for women who smoke cigarettes. This is a very serious complication where the developing fetus grows outside of the uterus, typically in the fallopian tubes (OTIS, 2014b).

Withdrawal symptoms, such as tremors, increased muscle tone (rigid muscles) and irritability have been observed in newborns of mothers who smoked during the last weeks of pregnancy. These neonates also demonstrate a higher risk of asthma, bronchitis, and respiratory infections during their childhood. Smoking during pregnancy has further been linked to sudden infant death syndrome (SIDS) (OTIS, 2014b). It is possible that the newborns that survive infancy may later experience language delays or physical control and coordination problems (NAIARC, 2012). Associations have been found between behavior and learning problems and smoking during pregnancy (OTIS, 2014b).

Smokeless Tobacco.

A number of women look for a way to stop smoking cigarettes during pregnancy because they know of the problems for the developing fetus. However, some women choose to replace the cigarette with smokeless tobacco. They assume it is safer for the developing fetus. Unfortunately, it is the nicotine and not the mode of delivery that is problematic for newborn (Mann, 2011).

Using snuff during pregnancy can elevate a newborn's risk for brief pauses in breathing during sleep (i.e., sleep apnea) to a greater extent than smoking cigarettes. It is believed that other smokeless tobacco products, as well as nicotine replacement products, may carry the same risks.

Women who are pregnant should use a cold turkey approach to quit using tobacco products (Mann, 2011).

As a consequence, a number of health care professionals are asking women who are pregnant to implement a cold turkey approach to quit using tobacco products (Mann, 2011).

A study conducted in Sweden examined sleep apnea in newborns whose mothers used snuff during pregnancy, compared to those who did not use any tobacco products. The snuff used by the mothers contained nicotine, though such is not true of all types. The researchers found that the newborns of mothers who used snuff during pregnancy were two times as likely to have apnea, compared to newborns of mothers who did not use tobacco products. Moreover, it was observed that the risk was higher among snuff users than smokers. The study involved nearly 7,600 women who reported using snuff during pregnancy and close to 500 women who reported using both snuff

and smoking cigarettes (Mann, 2011).

Treatment Summary.

Pharmacological treatments have been considered a mainstay for cessation of cigarette smoking. First-line therapies, as recommended by the FDA because of their evidence of effectiveness consist of nicotine replacement therapies (NRT), bupropion, and varenicline (Douaihy, Kelly, & Sullivan, 2013). On the whole, findings from studies investigating pharmacological treatments for users of smokeless tobacco have not been as promising as desired (Ebbert & Fagerstrom, 2012). Behavioral treatments can be used in conjunction with medication or alone. They incorporate a variety of methods to assist users of tobacco products to quit, ranging from self-help materials to individual cognitive-behavioral therapy. Typically these interventions teach persons to recognize high-risk tobacco-using situations, develop new coping strategies, manage stress, improve problem solving skills, and increase social support (NIDA, 2012).

Opioid Use during Pregnancy

In the nineteenth century, pain relievers such as morphine and heroin were deemed as helpful in everyday life. However, people were not initially aware of the adverse effects associated with these and similar substances, especially the abuse potential (Musto, 1991). Over the past several decades, however, flexibility in laws governing the prescribing of opioids for the treatment of chronic non-cancer pain is said to cause the dramatic increases in opioid use. Moreover, opioid analgesics are now responsible for more deaths than the number of deaths from heroin and cocaine combined or from both motor vehicle crashes and suicide (Manchikanti et al., 2012). Some recent studies have reported nearly 22 percent of pregnant women on Medicaid and 14 percent of pregnant women with private health insurance filled a prescription for opioids during pregnancy (Government Accountability Office [GAO], 2015).

The ideal time to intervene and prevent a pregnancy in which the baby is exposed to opioids is during the preconception period. Education and awareness in advance of pregnancy is critical. Besides having conversations about the risks and benefits of exposing infants to opioids in utero, prescribing clinicians should also review a state's prescription drug monitoring program to assist in assessing the pregnant woman's history of exposure to prescription opioids (astho, 2014). Nevertheless, screening is highly recommended in early pregnancy as well (ACOG, 2014; Wong et al., 2011). Many women are unaware of their pregnancy for four to six weeks (CDC, 2014).

Opioid use in pregnancy can result in major problems for mother and her newborn (ACOG, 2012; WHO, 2014). Illicit use of opiates (e.g., heroin) can cause the pregnant woman to engage in risky and/or unhealthy activities, such as theft, prostitution, and violence, to support herself and/or her addiction. These activities, in turn, expose the woman to legal consequences, including loss of child custody, incarceration, or criminal proceedings; becoming a victim of violence; and sexually transmitted infections (ACOG, 2012). The newborns of these mothers typically experience withdrawal symptoms referred to as neonatal abstinence syndrome (NAS). NAS can also occur in newborns of mothers receiving medication-assisted treatment (MAT) in the form of methadone and/or buprenorphine for their opioid addiction (Wong et al., 2011). All newborns exposed to opioids should be monitored and treated for NAS if needed (ACOG, 2012). (NAS is discussed in greater detail in its own module in this tool guide.)

Similar to the biological method of screening for cocaine use, the urine toxicology screen is used to confirm opioid use during pregnancy. Urine screening is efficient and often the most rapid tool available, especially following findings on the physical examination (e.g., track marks) or patient self report. Methadone may be detected in urine for as long as two weeks after use. Heroin remains detectable for up to 72 hours following use. The fentanyl metabolite, norfentanyl, can be detected for a longer period of time than methadone (Bhuvaneshwar et al., 2008). (Some studies have detected norfentanyl for up to 96 hours [See Silverstein, Rieders, McMullin, Schulman, & Zahl, 1993, e.g.]). However, similar to methadone, it may not be part of the “drugs of use/misuse” urine toxicology screen in all facilities. Tests involving neonatal meconium are not yet widely available despite being shown to have at least equivalent and often greater sensitivity for maternal opioid use, when compared to urine toxicology. Though not validated in screening for opioid use, the DAST is still a widely used screening tool for opioid use in pregnancy (Bhuvaneshwar et al., 2008).

A seminal study of the reproductive health of women dependent on opioids by Armstrong, Kennedy, Kline, & Tunstall (1999) revealed the high rate at which these women become pregnant compared to women in the general population. Results indicated 54 percent of women with opioid dependence reported having at least four pregnancies in their lifetime compared to 14 percent of a nationally representative sample of women (Heil et al., 2011).

Heil et al. (2011) further studied estimates of the prevalence of unintended pregnancy for its three subtypes: mistimed pregnancy, unwanted pregnancy, and ambivalent pregnancy. Pregnancy intention of current pregnancy was measured by the question “When did you intend to become pregnant?” Response options consisted of “sooner”, “now”, “later”, “never”, and “don’t know/unsure”. “Sooner” and “now” responses classified the pregnancies as intended. “Later” responses classified the pregnancies as mistimed. Responses of “never” classified pregnancies as unwanted while “don’t know/unsure” responses resulted in an ambivalent pregnancies classification. Nearly 1,000 women with opioid dependence were included in the study.

Results indicated that nearly nine of every 10 pregnancies were unintended. This finding, thus, supported the need to develop interventions to address the extremely high rate of unintended pregnancies among women dependent on opioids (Heil et al., 2011). Similar results have been found in our state.

Voluntary, reversible long-acting contraceptives are being promoted for women of childbearing potential, including those with opioid dependence (Dreyzehner, 2015; Warren & Luskin, 2012).

The Pregnancy Risk Assessment Measurement System (PRAMS) data from 2009 showed that 86 percent of pregnant women that use opioids have unintended pregnancies compared to 50 percent of the general population of pregnant women (Dreyzehner, 2015).

Tennessee Department of Health (TDH) officials have recommended that use of voluntary, reversible long-acting contraceptives (VRLACs) be promoted for women of childbearing potential, including those with opioid dependence. (See Dreyzehner (2015) and Warren & Luskin (2012). Included among the VRLACs are intrauterine devices and subdermal implants. These strategies are much aligned with the recommendation of Heil et al. (2011) to promote interventions to address the extremely high rate of unintended pregnancies among women dependent on opioids.

Skin-to-skin contact between mother and newborn should be actively encouraged unless the new mom is unable to respond to the newborn's needs. Such contact is important regardless of the feeding choice (WHO, 2014).

Prescription Opioids and Pregnancy.

Data for 1999 to 2009 show there has been a 33 percent increase in nonmedical use of prescription opioid medications among pregnant women. This means that more women are using narcotic pain

There has been a 33 percent increase in nonmedical use of prescription opioid medications among pregnant women (astho, 2014, e.g.).

relievers in one or more of the following ways during pregnancy: without a prescription, for the experience or feeling the drug provides, or in a way other than as medication was prescribed (astho, 2014; Desai, Hernandez-Diaz, Bateman, & Huybrechts, 2014).

The most commonly used prescription medications during pregnancy are codeine (as found with Tylenol), fentanyl (Duragesic), hydrocodone (as Locet, Lortab, or Vicodin), hydromorphone (Dilaudid), morphine (Kadian or Avinza, MSIT, or MSContin), oxycodone (OxyContin or Percodan, Percocet), oxymorphone (Opana), and propoxyphene (Darvon or Darvocet) (The Partnership at Drugfree.org, n.d.)

As of March 1, 2014, Tennessee was one of 18 states to consider substance use/misuse during pregnancy to be child abuse under civil child-welfare statutes. In addition, the state is one of 10 that gives priority access in general programs to pregnant women (Guttmacher Institute, 2016; Thigpen & Melton, 2014).

It should also be noted that 50-75 percent of pregnant women dependent on opioids also have a major psychiatric disorder or mood disorder (astho, 2014; Thigpen & Melton, 2014). Among the pregnant women dependent on opioids, those with:

- Anxiety disorders are more likely to adhere to treatment.
- Mood disorders are more likely to test positive for substances while in treatment (astho, 2014).

It has also been reported that these women are heavy smokers and tend to be polydrug users (astho, 2014). Their pregnancies are often fraught with a host of medical problems including an elevated risk for obstetric complications such as stroke, premature birth, and drug withdrawal (NAIARC, 2012).

Older (2010) reported on the success of the MOTHER (i.e., Maternal Opioid Treatment: Human Experimental Research) study. Pregnant women dependent on opioids were followed a minimum of 28 days out from giving birth. The moms were addicted to opioids and rarely used other illegal drugs. Sixteen percent of moms were screened in and consented to participate in the study. These moms were further randomly assigned to either a buprenorphine or methadone treatment group.

The study supported the usefulness and safety of methadone treatments for moms dependent on opioids (Jones et al., 2010). Comparable findings were observed in a more comprehensive review of buprenorphine versus methadone treatment for pregnant mothers. In addition to the MOTHER study, the PROMISE (Pregnancy and Reduction of Opiates: Medication Intervention Safety and Efficacy) study and a second small-scale study by Fischer et al. have been examined. PROMISE was the small-scale, randomized, single site clinical trial that provided pilot data for the MOTHER study (Jones et al., 2012).

In a randomized European study, mothers who received long-acting morphine used less additional street opiates than mothers who received methadone though newborns in both groups were healthy (Kelly, Minty, Madden, Dooley, & Antone, 2011).

Baldacchino, Arbuckle, Petrie, & McCowan (2014) conducted a comprehensive meta-analysis of the consequences of opioid use by moms during pregnancy on the neurodevelopment of infants and children. They observed no significant impairments in cognitive, behavioral, or psychomotor outcomes. Nevertheless, there was a trend toward poorer outcomes for the infants and children that were exposed to opioids during pregnancy than for their non-exposed counterparts.

Treatment.

The ideal time to intervene and prevent a pregnancy in which the baby is exposed to opioids is during the preconception period. Education and awareness in advance of pregnancy is critical. Besides having conversations about the risks and benefits of exposing infants to opioids in utero, prescribing clinicians should also review a state's prescription drug monitoring program to assist in assessing the pregnant woman's history of exposure to prescription opioids (astho, 2014).

Methadone maintenance treatment (MMT) has been the most widely available treatment for opioid addiction. For pregnant women, MMT is associated with improved adherence to prenatal care, decreased exposure to illicit drugs and other high-risk behaviors, improved neonatal outcomes, and better relapse prevention. The goal is to prevent withdrawal during pregnancy and to the newborn at birth. Despite its effectiveness for pregnant women, methadone works best when applied as part of a comprehensive treatment program involving obstetric care, counseling, and wraparound services (astho, 2014). It should also be mentioned that breast feeding is safe for women in MMT and their infants unless the women are HIV-1 positive, which means they have the human immunodeficiency virus type 1. (**Women who are HIV-1 positive should never breastfeed.**) Prior to initiating MMT, efforts must be taken to determine that the pregnant female is indeed opioid dependent. Methadone must be used with extreme care in pregnant women that have compromised respiratory function (Kreek, Borg, Ducat, & Ray, 2010).

Research suggests that a large proportion of female admissions to MMT programs tend to be childbearing potential. Women in New York City's MMT program in 2007, for example, ranged in age from 18-34 years and constituted 62 percent of all the female admissions. Thus, MMT programs have the opportunity to address contraception and pregnancy planning with these women during intake and throughout their treatment (Kreek, Borg, Ducat, & Ray, 2010). It is not surprising to find that a third of the women who are sexually active report that they do not use contraception (Harding & Ritchie, 2003; Kreek, Borg, Ducat, & Ray, 2010). A CY 2013 report from TennCare indicates that only 15 percent of the women of childbearing potential prescribed narcotics were also prescribed contraceptives. Yet public health experts in the state highly recommend offering voluntary, reversible long-acting contraceptives to this category of women, particularly when they use or have a

dependence on opioids (Dreyzehner, 2015; Warren & Luskin, 2012). As many as 86 percent of women using opioids report unintended pregnancies compared to 50 percent for the general population of women (Dreyzehner, 2015).

In the event of a methadone overdose, an opioid antagonist such as naloxone is recommended. Naloxone only has a 30-minute-half-life, so more than a single dose will be needed (Kreek, Borg, Ducat, & Ray, 2010).

Increasing research on buprenorphine has resulted in greater use of this medication- assisted treatment (MAT) for the pregnant woman and fetus. There is evidence of lower risk of overdose with buprenorphine because of the ceiling effect on respiratory suppression. Subutex, the single-agent buprenorphine formulation without naloxone, continues to be promoted as the preferred medication-assisted treatment for pregnant women with opioid dependence, e.g., see the 2016 SAMHSA Advisory on buprenorphine for OUD. However, Subutex has a higher abuse or diversion risk potential.

Newer research is showing the success of buprenorphine/naloxone with pregnant women. For example, a 2013 study observed unremarkable maternal findings, comparable to what might be found after treatment with the mono-buprenorphine product. Neither were there any significant adverse neonatal outcomes during pregnancy (Deblak, Morrone, O'Grady, & Jones, 2013). Another study of pregnant women on opioids who were treated with the combination buprenorphine product versus methadone demonstrated unremarkable maternal and neonatal outcomes as well. Additionally, neonates exposed to maternal buprenorphine/naloxone had less frequent NAS and shorter overall hospitalization lengths (Wiegand et al., 2015). Despite positive maternal and neonate outcomes, buprenorphine/naloxone has not achieved preferred first-line pharmacotherapy status for pregnant women (e.g., see Berghella, Seligman, & Cleary, 2016).

There are also concerns about the benefits of buprenorphine for pregnant women that have high opiate needs. Nevertheless, it offers a different model of delivery from the highly regulated opioid treatment programs (OTPs). Buprenorphine can be prescribed in an office setting by physicians who have obtained a special SAMHSA waiver for prescribing. Further emerging research has suggested that buprenorphine exposure results in less severe NAS manifestation compared to methadone, which translates into less total morphine for treating withdrawal symptoms, shorter duration of treatment, and shorter hospital stay for the affected newborns. Data on infant and child outcomes in the long term following in utero exposure to buprenorphine are not yet available (astho, 2014). (Further discussion of the impact of opioid addiction on a prenatally exposed fetus can be found in the module on *Neonatal Abstinence Syndrome* found within this document.)

Mothers of the newborns and other family members likely need teaching and support. Mothers, in particular, may need support to deal with feelings of anxiety and/or guilt upon witnessing their newborn's withdrawal symptoms. In some cases, mothers of newborns likely need assistance dealing with distress or abusive or violent confrontations that can occur if partners or relatives communicate blame about her drug dependency. Mothers may also need positive role modeling from healthcare providers on how to recognize and respond appropriately to the newborn's cues, thereby helping to set the tone for mother-infant attachment and healthy interactions (astho, 2014).

Acupuncture for Opioid Use during Pregnancy.

This traditional method of health care with a long history of practice in China and other parts of Asia has been promoted as a supportive component of substance use treatment as well as a technique that can enable job readiness. Several thousand alcohol and drug treatment programs in the United States have added ear acupuncture to their protocol. Based on a 35-year experience at the Lincoln Hospital in Bronx, NY which delivered acupuncture treatments daily as part of its comprehensive substance disorder program, the technique serves to enhance an individual's overall functioning (Smith, 2012).

- As a nonverbal intervention, it aids in reaching resistant users/misusers of substances.
- It reduces agitation and anxiety while facilitating receptive behavior and calm.
- It helps in the development of an inner meditative core in even the most fearful and troubled individuals (Smith, 2012).

Ear acupuncture treatments are generally provided in large groups where group members sit together quietly for about 45 minutes. This process is known as the National Acupuncture Detoxification Association (NADA) protocol. Clinical personnel must be trained to use the protocol and state laws must include this training standard. The ear acupuncture protocol has been tested as a safe and inexpensive substance use treatment and/or adjunct to treatment (Smith, 2012). Dr. Wen developed the procedure, acupuncture combined with electrical stimulation at four body points and two ear points, reported relief of symptoms from opioid withdrawal in individuals with opiate addiction (Lin, Chan, & Chen, 2012).

Methamphetamine Use during Pregnancy

Methamphetamine is sometimes prescribed by a physician, but most often it is used illegally. Also known as “meth”, “speed”, “crank”, and “ice”, methamphetamine can be snorted, smoked, swallowed, inhaled, or injected (Petit, Karila, Chalmin & Lejoyeux, 2012). It works by exciting the brain with chemicals that can make people “feel good”. Methamphetamine acts as a stimulant and causes a fast heart rate, sweating, loss of appetite, hallucinations, paranoia, anxiety, trouble sleeping, and dizziness. Overdoses can lead to death or brain damage and long-term use can result in an array of health problems (OTIS, 2016).

The drug was discovered in Japan in 1919 (Narconon, n.d.). It could be injected but smoking methamphetamine created the same effects as injecting. While anyone who can read a recipe can manufacture it, today's increased abuse is the result of a new wave of extremely potent, high-purity, low-cost meth manufactured by advanced laboratories run by Mexican drug cartels. California is a favorite delivery location for the popular drug (Methamphetamines.com, 2013; Stewart, 2015).

Female users of methamphetamine tend to have high levels of psychiatric symptoms and psychological problems, in general. In addition, many of the women begin using methamphetamine to lose weight. It has been hypothesized that gender roles that stress the thin-ideal body image exacerbate use, especially among White, Pacific Islander, and Native American women (Wright, Schuetter, Fombonne, Stephenson, & Haning III, 2012).

It is extremely difficult to sort out the specific effects of methamphetamine because roughly 80 percent of the women who use the substance also use nicotine and/or alcohol. One study has tried to separate the effects and found that both methamphetamine and alcohol impair the part of the brain responsible for verbal memory and learning and attention. However, it was further observed that methamphetamine had a

negative impact even beyond that of alcohol alone (NAIARC, 2012).

Good, Solt, Acuna, Rotmensch, & Kim (2010) conducted a single site chart review from 2000 to 2006 where pregnant methamphetamine users were compared to the general obstetric population during the same period for various demographic factors and perinatal outcomes.

Methamphetamine use during pregnancy is complicated by more morbid neonatal and maternal outcomes when compared with the general obstetric population (Good, Solt, Acuna, Rotmensch, & Kim, 2010).

Factors significantly associated with methamphetamine use were preterm delivery, low Apgar scores, cesarean delivery, and neonatal mortality. Maternal demographic characteristics also indicated that these women were more likely to use other abusive substances, be unemployed, and have higher rates of domestic violence and adoption. It should also be noted that exposure to methamphetamine prenatally influences development of the verbal memory system above the effects of prenatal exposure to alcohol. Furthermore, these methamphetamine-exposed babies taxed hospital staff and ultimately burdened the foster care system. In short methamphetamine use during pregnancy is complicated by more morbid neonatal and maternal outcomes when compared with the general obstetric population.

A segment of the Infant Development Environment and Lifestyle (IDEAL) Study characterized methamphetamine usage patterns during pregnancy. Study sites in the United States included Tulsa, OK; Los Angeles, CA; Honolulu, HI; and Des Moines, IA. The researchers found variation in methamphetamine use during pregnancy. Some women consistently used the drug at a high rate throughout their pregnancy; some increased their use during pregnancy; some decreased their use; and some maintained a steady though not high level of use. Of the women showing decreased use during pregnancy, however, they were most likely to replace their diminished methamphetamine intake with alcohol. Thus, this group became polysubstance users during pregnancy, thereby increasing risks for themselves and their newborn (Grotta et al., 2010).

Methamphetamine use by women who are pregnant is not as well studied as use of alcohol, cocaine, and opiates. Moreover, women who use/misuse meth commonly use other drugs such as alcohol and tobacco, thus likely confounding birth outcomes. However, the increased risk of low birth weight and small for gestational age reported for newborns exposed to other substances of use/misuse during pregnancy also manifests in births associated with methamphetamine use (ACOG Committee on Health Care for Underserved Women, 2011; Wright et al, 2012). There is further evidence of increased rates of premature delivery and placental abruption (i.e., the separation of the placental lining from the uterus) (NIDA, 2013). Women that were actively using meth during their pregnancy should not breastfeed due to the inability to predict harmful effects associated with the ingredients used to cook it (ACOG Committee on Health Care for Underserved Women, 2011).

Neonates exposed to methamphetamine during pregnancy typically are being born too early and too small. They are also at risk for life-long breathing, vision, hearing, and learning problems. Some research suggests that methamphetamine can increase the chance for sudden infant death syndrome

(SIDS), even in neonates not born early (OTIS, 2016).

Evidence about whether methamphetamine increases the chance of birth defects is mixed. It is further not known whether prenatal exposure to methamphetamine can cause intellectual or behavioral problems in older children. A few studies have shown that if a mother uses methamphetamine later in her pregnancy, the newborn can show signs of withdrawal at birth. Symptoms include having very floppy or tight muscles, difficulty eating, sleeping too little or too much, and being very jittery. Withdrawal symptoms usually go away within a few weeks, but it is possible that the newborn will be admitted to the special care unit and have longer hospital stays. Some neonates have tremors and too much or too little muscle tone for many months after birth. These symptoms go away on their own in many cases, but these children might benefit from programs such as infant stimulation or physical therapy (OTIS, 2016).

At the time of this writing, there are no pharmacologic treatments that have shown to be effective in curbing methamphetamine use, prolonging abstinence, or counteracting the drug's special effects (ACOG Committee on Health Care for Underserved Women, 2011; NIDA, 2013). Three double-blind placebo-controlled trials using bupropion, naltrexone, and modafinil have shown positive results in reducing methamphetamine or amphetamine use. Two studies employing agonist replacement medications, one with methylphenidate and the other with d-amphetamine, have also shown promise. Continued efforts are being made to develop medications for the treatment of methamphetamine dependence (Karila, 2010).

Treatment for Methamphetamine Addiction.

Pharmacotherapy does not yet exist for treatment for methamphetamine use (ACOG Committee on Health Care for Underserved Women, 2011; Karila et al., 2010; NIDA, 2013; Petit et al., 2012). All treatments at this time are psychosocial and primarily behavioral.

1. First, every woman that reports using methamphetamine should receive counseling and be offered assistance in discontinuing use. Thus clinicians must ask the question(s) about alcohol and substance use.
2. Treatment outcomes are more positive when enrollment into residential care is voluntary.
3. Outpatient treatment, if used, must be very intensive during the first several weeks. This means three to five sessions per week early in the treatment phase and dropping to two to three sessions each week for the next 90 days.
4. Recommended treatment components include cognitive-behavioral therapy (CBT) that incorporates the Matrix model, family education, behavioral therapy, individual counseling, 12-step support, and random substance use testing. (The Matrix model typically runs for 16 weeks.)
5. Contingency management interventions that offer incentives for treatment engagement and abstinence have also shown effectiveness (ACOG Committee on Health Care for Underserved Women, 2011; NIDA, 2013; Petit et al., 2012).
6. Comprehensive prenatal care should be part of the treatment package. This means the women

should receive a nutritional assessment and linked to social support services.

7. Pregnant women using methamphetamine should further be tested for HIV and sexually transmitted infections (ACOG Committee on Health Care for Underserved Women, 2013).

Amphetamine Use during Pregnancy

Amphetamine use during pregnancy is increasing worldwide. Pregnant women that use amphetamines illegally tend to have lower household incomes, be socially deprived, younger, have less formal education, lack private insurance, have little support through a partner or family, less likely to obtain appropriate prenatal care, and be involved in a marginalized lifestyle, e.g., domestic violence situation. Very few studies abound for pregnant mothers legally prescribed amphetamines for conditions such as attention deficit hyperactivity disorder (ADHD) (Oei et al., 2012).

Prenatally, it is important to help the amphetamine user who is pregnant to secure adequate shelter and nutrition, treat any co-occurring psychiatric morbidities, and keep her prenatal care appointments. Research suggests these pregnant moms seek prenatal care less frequently than other known pregnant users of substances (Oei et al., 2012). Since there appears to be no detrimental effect associated with discontinuation of use during pregnancy, every reasonable effort should be undertaken to encourage known users/misusers who are pregnant to stop (Keegan et al., 2010).

Sedatives-Hypnotics and Anxiolytics Use during Pregnancy

Butalbital, the active ingredient in Fiorinal and Fiorocet, is a barbituate that is frequently used in the treatment of migraines which are more common in women. Both medications were Category C on the FDA's Fetal Risk Summary, meaning there were not any controlled studies of their harmful effects on fetuses. However, these medications should only be prescribed to pregnant women if the benefits outweigh the risks (Keegan, Parva, Finnegan, Gerson, & Belden, 2010).

Benzodiazepines, however, were Category D medications, indicative of positive evidence of human fetal risk based on adverse reaction data from marketing or investigational studies or experience in humans (Sanz & De las Cuevas, 2006). Again, the risk must be weighed against the medical condition for which the pregnant woman is being treated. Physicians should be on high alert if women are abusing benzodiazepines during pregnancy. There tends to be use/misuse of other substances in these cases (Keegan et al., 2010).

Alprazolam, a benzodiazepine commonly used in the treatment of anxiety, is contraindicated in pregnant women. The drug maker further warns that alprazolam could cause harm to the unborn baby and/or addiction or withdrawal symptoms at birth (Alprazolam, 2012; Sanz & De las Cuevas, 2006).

A rehabilitation program should be considered for women who are heavy users of sedative-hypnotics during pregnancy. An evaluation by a psychiatrist or migraine specialist might also be helpful as he or she may be able to help the woman transition away from the addictive medications. Newborns exposed to benzodiazepines or barbituates during pregnancy are further likely to experience significant withdrawal symptoms (Keegan et al., 2010).

Antiepileptic Drug (AEDs) Use during Pregnancy

No antiepileptic drug has proven safe in pregnancy in terms of teratogenesis at this time. Therefore, treatment for pregnant women must be individualized (Wilner, 2010).

Women with epilepsy who are considering pregnancy or currently pregnant should be carefully reassessed. Antiepileptic medication may no longer be necessary for women with persistent nonepileptic events, such as syncope or migraine that were misdiagnosed as epilepsy. A similar non-need might also be considered for women with ill-defined “spells” that have since gone away. Moreover, there are women that may have epilepsy that is sufficiently controlled (i.e., seizures have not been evident for several years) so that a trial off medication before conception could be warranted (Wilner, 2010).

Use of antiepileptic drugs (AEDs) by pregnant women has been linked to immediate withdrawal effects of the newborn, as well as to long-term neurologic dysfunctions (Sanz & Delas Cuevas, 2006). More current evidence suggests that women taking antiepileptic medication, in particular valproate, during the first trimester are at highest risk for congenital malformations. Phenobarbital and phenytoin also result in adverse cognitive outcomes for the children. Newer antiepileptic medications such as levetiracetam may not be safer. Much more research on these newer medications in terms of teratogenesis is needed (Wilner, 2010).

In short, use of antiepileptic medications with pregnant women should adhere to the following recommendations:

1. Start by assessing whether the patient really needs antiepileptic treatment.
2. Choose the drug that is well tolerated and controls the seizures (but avoid valproate).
3. Use as few drugs as possible at the lowest effective dose.
4. Regularly monitor drug levels during pregnancy (Wilner, 2010).

Selective Serotonin Reuptake Inhibitor (SSRI) Use during Pregnancy

Selective serotonin reuptake inhibitors (SSRIs) are frequently used during pregnancy, largely for the treatment of depressive disorders in the mothers. In fact, their use during pregnancy has increased because of the favorable risk to benefit ratio. However, short-term adverse outcomes in the form of a withdrawal syndrome similar to neonatal abstinence syndrome (NAS) have occurred in up to 30 percent of newborns exposed in utero to these medications. Among the short-term effects include signs of both central nervous system depression and excitation, decreased changes in behavioral states, autonomic symptoms, and abnormal sleep organization. These symptoms primarily affect the neonate’s respiratory and gastrointestinal systems. In addition there is some evidence of small head circumference at birth, but cognitive ability does not appear to be impacted (Klinger et al., 2011).

In 2011, the FDA updated its safety announcement on the use of SSRI antidepressants by pregnant women and the potential risk of a rare heart and lung condition known as persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs when a newborn does not adapt to breathing outside the womb and may require intensive care support including a mechanical ventilator to increase their oxygen level. In severe cases, PPHN can result in damage to multiple organs, including the brain, and even death.

The initial advisory was published in July 2006 and based on a single published study. Newer studies evaluating this potential risk have shown conflicting findings, thereby making it unclear whether use of SSRIs during pregnancy can cause PPHN. Hence, the FDA has recommended that health care providers treat depression during pregnancy as clinically appropriate (FDA, 2012).

Psychiatric Medication Use during Pregnancy

Mental illness can bring increased risks and difficulties during and after pregnancy, such as birth complications and a worsening of symptoms (Collingwood, 2010; Sanz & De las Cuevas, 2006). Serious mental illness such as schizophrenia is not as common but about 20 percent of women will experience clinically diagnosable anxiety or depression during pregnancy and the postpartum period (Collingwood, 2010).

Despite the lack of pregnancy safety data for many medications, some researchers have observed as many as 16 percent of women being treated for depression, for example, taking medications with potential for fetal harm. During pregnancy, the treatment plan should be based on the woman's current mental state and medication, as well as previous treatment, history of past mental illness, and family history of mental illness during pregnancy. Considerations should also be given to the woman's pregnancy-related fears, substance use, and support network (Collingwood, 2010). Discontinuing effective psychotropic treatments can worsen the mental health of the mother, causing secondary effects to the unborn child (Sanz & De las Cuevas, 2006). In addition, sudden stoppage of treatment can result in side effects and relapse (Collingwood, 2010).

Pregnancy outcomes for antipsychotic medications vary widely depending on the type of medication. Exposure to low-strength antipsychotics during the first trimester is associated with a small additional risk of congenital anomalies overall (Collingwood, 2010).

Management and treatment are complex and require careful consideration by the psychiatrist of any impact on mother and her fetus, in addition to the possibility of increased risk of obstetric complications and congenital malformations (Sanz & De las Cuevas, 2006). The National Institute of Mental Health (NIMH) affirms that medication decisions should be based on each woman's circumstances and needs. Further, medication selection should be based on available scientific research and prescriptions should be written for the lowest dose possible. Moreover, pregnant women on psychotropic medications should be watched closely throughout their pregnancy as well as after delivery (NIMH, 2012).

Substance Use, Pregnancy, and Birth Outcomes: General Summary

Many substances, if used during pregnancy produce teratogenic effects (e.g., facial and skeletal abnormalities). Such use further adversely affects developing neurological systems, brain organization and fetal growth and/or maturation.

Table 1 below summarizes the potential effects of prenatal exposure to the more commonly used substances on birth outcomes, central nervous system development cognitive function, and behavior. The table should be interpreted in conjunction with the fact that outcomes of newborns exposed to substances *in utero* depend, in part, upon the quality of care received by the mother during pregnancy (Jensen, 2014).

Table 1. Potential effects of prenatal substance exposure on birth outcomes, central nervous system development, cognitive function, and behavior

Substance	Birth Effects	Effects on CNS development, cognitive function, and behavior
Nicotine	<ul style="list-style-type: none"> ➤ Prematurity ➤ Decreased birth weight, height, head circumference ➤ Sudden infant death syndrome ➤ Increased infant mortality rate 	<ul style="list-style-type: none"> ➤ Excitability, hypertonia ➤ Conduct disorder, reduced IQ, aggression, impulsivity, ADHD, antisocial behavior
Marijuana	<ul style="list-style-type: none"> ➤ No fetal growth effects ➤ No physical abnormalities 	<ul style="list-style-type: none"> ➤ Prematurity ➤ Decreased birth weight, height, head circumference ➤ Intraventricular hemorrhage
Methamphetamine	<ul style="list-style-type: none"> ➤ Decreased birth weight ➤ Small for gestational age 	<ul style="list-style-type: none"> ➤ Poor movement quality, increased lethargy, lower arousal, increased physiological stress ➤ No motor or mental delay
Cocaine	<ul style="list-style-type: none"> ➤ No fetal growth effects ➤ No physical abnormalities 	<ul style="list-style-type: none"> ➤ Mild withdrawal symptoms; poor autonomic control, particularly of state regulation (the ability to adjust one's level of alertness as required for a task) ➤ Executive function impairment, reading and spelling difficulty
Heroin/Opioids	<ul style="list-style-type: none"> ➤ Prematurity ➤ Decreased birth weight, height, head circumference ➤ Sudden infant death syndrome 	<ul style="list-style-type: none"> ➤ NAS, strabismus, less rhythmic swallowing ➤ Possible delay in general cognitive function, aggression, anxiety, inattentive/disruptive behavior

Source: Jensen, 2014

It should be noted that pregnancy can serve as a motivating factor for entry into a treatment

program. Such a program might focus on improving prenatal care, optimizing maternal physical and mental health, and reducing withdrawal symptoms and cravings for substances, as well as behavioral problems (Jensen, 2014).

Treatment

While it is important to limit exposure to medications during pregnancy because of the potential harm to the developing fetus, untreated chronic illnesses, such as substance dependence, particularly to opioids, are linked to increased mortality and morbidity (Goodwin et al., 2007). Collaborative partnerships are essential to successfully serving pregnant women (BSAS, 2011). Yet, national data suggested almost 85 percent of women who needed substance use treatment during pregnancy and/or following childbirth either did not perceive the need for treatment or failed to receive treatment (Gibbons et al., 2010).

Withdrawal management (i.e., detoxification) during pregnancy is not recommended (Bhuvanewar et al., 2008; SAMHSA/CSAT/DPT, 2015). At least that's the position of the American Congress of Obstetricians and Gynecologists (ACOG) (IRETA, 2014). However, there are other recommendations. One approach allows the pregnant woman to withdraw from MAT and stay in the treatment program, but requires a mid-level practitioner, preferably a physician experienced in addiction medicine, to supervise the withdrawal process with regular fetal assessments, as appropriate, for the gestational age. Some experts specify that withdrawal, if implemented, should not be initiated before 14 weeks or after 32 weeks gestation (Bhuvanewar et al., 2008; SAMHSA/CSAT/DPT, 2015). Other experts recommend waiting until the end of the first trimester, which is very close in time frame to the former recommendation.

Limited data has shown miscarriage rates may be higher in the first trimester so waiting to employ detoxification may improve the fetus' survival chances. Some case reports of detoxification (i.e., withdrawal management) during pregnancy have reflected miscarriages, preterm births, meconium passage, stillbirth, and elevated norepinephrine and epinephrine levels, in addition to unsuccessful relapse rates of 50 percent or higher (Prasad, 2014). A more recent Tennessee study involving more

A Tennessee study involving more than 300 pregnant women dependent on opioids did not show detoxification to be harmful (Bell, Towers, Hennessy, Heitzman, Smith, & Chattin, 2016).

than 300 women detoxifying from opiates during pregnancy has shown some promising results. Nearly 75 percent of the women were younger than 30 years of age and 78 percent were multiparous, i.e., had given birth at least twice. **Overall the data did not show detoxification to be harmful to the fetus.** Compared to other

groups in the study, women who were fully detoxified and remained in long-term behavioral health settings had better relapse rates and their newborns had low NAS rates. The researchers acknowledged the need for further research but concluded that intense behavioral health follow-up is necessary for continued success once a woman has been fully detoxified (Bell, Towers, Hennessy, Heitzman, Smith, & Chattin, 2016).

The literature suggests that it is best to adopt a team approach with regard to withdrawal and/or replacement of substances used and/or misused by women during pregnancy. Incorporate a

system-based practice model involving neonatologists, psychiatrists, psychologists, and social workers (Keegan et al., 2010). Nonetheless, the best strategy for ameliorating many of the complications of substance use during pregnancy is prenatal care (Wright et al., 2012).

Maintenance therapy is recommended for pregnant opioid users, unless the maintenance drug is not well tolerated (Outcome is a function of person's social deprivation and the extent to which other substances, legal and/or illegal, are used concomitantly [Soyka, 2013].) Methadone maintenance treatment (MMT) is the most widely available treatment for opioid addiction. For pregnant women, MMT is associated with improved adherence to prenatal care, decreased exposure to illicit drugs and other high-risk behaviors, improved neonatal outcomes, and better relapse prevention. The goal is to prevent withdrawal during pregnancy and to the newborn at birth (astho, 2014). Hence, MMT goals for pregnant women include improved fetal as well as maternal outcomes (Fullerton et al., 2014). Despite its effectiveness for pregnant women, methadone works best when applied as part of a comprehensive treatment program involving obstetric care, counseling, and wraparound services (astho, 2014). It should also be mentioned that breast feeding is safe for women in MMT and their infants unless the women are HIV-1 positive, which means they have the human immunodeficiency virus type 1. (*Women who are HIV-1 positive should never breastfeed* [Kelly et al., 2011; Kreek, Borg, Ducat, & Ray, 2010].) Prior to initiating MMT, efforts must be taken to determine that the pregnant female is indeed opioid dependent. Methadone must be used with extreme care in pregnant women that have compromised respiratory function (Kreek et al., 2010).

Research suggests that a large proportion of female admissions to MMT programs tend to be childbearing potential. Women in New York City's MMT program in 2007, for example, ranged in age from 18-34 years and constituted 62 percent of all the female admissions. Thus, MMT programs have the opportunity to address contraception and pregnancy planning with these women during intake and throughout their treatment (Kreek et al., 2010). It is not surprising to find that a third of the women who are sexually active report that they do not use contraception (Harding & Ritchie, 2003; Kreek et al., 2010).

Increasing research on buprenorphine has resulted in greater use of this medication- assisted treatment (MAT) for the pregnant woman and fetus. There is evidence of lower risk of overdose with buprenorphine because of the ceiling effect on respiratory suppression (astho, 2014). Subutex, the single-agent buprenorphine formulation without naloxone, is preferred for pregnant women (astho, 2014; Federation of State Medical Boards, 2013), but it does have a higher abuse or diversion risk potential. There are also concerns about the benefits of buprenorphine for pregnant women that have high opiate needs. Nevertheless, it offers a different model of delivery from the highly regulated OTPs. Buprenorphine can be prescribed in an office setting by physicians who have obtained a special SAMHSA waiver for prescribing. Further emerging research has suggested that buprenorphine exposure results in less severe NAS manifestation compared to methadone, which translates into less total morphine for treating withdrawal symptoms, shorter duration of treatment, and shorter hospital stay for the affected newborns. Data on infant and child outcomes in the long term following in utero exposure to buprenorphine are not yet available (astho, 2014). Research has suggested that women be switched to buprenorphine monotherapy if they become pregnant because there is insufficient data to support the safety of the buprenorphine/naloxone combination (Soyak, 2013).

Mothers of newborns as well as other family members likely need teaching and support. The mothers, in particular, may need support to deal with feelings of anxiety and/or guilt upon witnessing their newborn's withdrawal

Mothers of newborns as well as other family members need teaching and support (astho, 2014).

symptoms. In some cases, mothers of newborns may need help dealing with distress or abusive or violent confrontations that can occur if partners or relatives communicate blame about her drug dependency. Mothers may also need positive role modeling from health care providers on how to recognize and respond appropriately to the newborn's cues, thereby helping to set the tone for mother- infant attachment and healthy interactions (astho, 2014). Best practice shows that babies born to women addicted to opioids fared better when the mothers received medication-assisted treatment in the form of buprenorphine or methadone, compared to babies whose mothers received no treatment (NIDA, 2010). Moreover, newer studies involving buprenorphine show the same clinical outcomes as methadone, but a reduction in withdrawal symptoms (e.g., Jones et al., 2012; Lacroix, Hammou, & Montastruc, 2011). NAS severity appears to be a greater function of the use of other drugs rather than the buprenorphine dose. Recent research has shown buprenorphine emerging as first-line treatment for opioid users who are pregnant (Soyka, 2013).

Other Treatments

The best strategy for reducing substance use complications during pregnancy is prenatal care (Wright et al., 2012).

Since prenatal care is the best strategy for reducing substance use complications during pregnancy, it follows that *harm-reduction programs* should be provided for pregnant women (Wright et al., 2012). Key components of such programs consist of:

- Improvements in nutrition
- Reduction in smoking
- Reduction in substance use including alcohol (Wright et al., 2012)
- Encouragement of breastfeeding, when appropriate (Thigpen & Melton, 2014; Wright et al., 2012)
- Promotion of dental health
- Encouragement of physical activity
- Encouragement of early and continuing prenatal care
- Promotion of social and community support (Wright et al., 2012)

A study of pregnant women in Hawaii who used methamphetamine during pregnancy demonstrated successful maternal and birth outcomes in such a program. There were increased prenatal visits that tended to be associated with better participation in other clinic services, which translated into increased abstinence. The abstinence rates were high despite not mandating an abstinence-only approach. Quality prenatal care involving four visits at minimum were shown to significantly improve birth outcomes. The findings suggest that providing a comprehensive approach to the treatment of women with addiction issues is paramount. All components of a woman's life must be addressed. This harm-reduction program further resulted in relatively low rates of postpartum depression (Wright et al., 2012).

Managing Relapse

Young and old alike run the risk of returning to substance use and/or at high rates following treatment. Estimates show between 67 percent and 80 percent thirds and four-fifths start using again in the six months after community-or hospital-based treatment (Ramo & Brown, 2008).

Ideally the individual's warning signs should be recognized in advance of any substance use while conducting regular drug screens. Carefully observe and review the person's behavior. For example, has the individual stopped attending sessions regularly? If showing up for scheduled appointments, note the person's clinical presentation at EACH visit. Look for any changes that might be precursors to relapse. Probing carefully will often shed light on patterns of substance use. In the case of detected or admitted substance use, acknowledge it in a nonjudgmental way, neither condoning nor punishing the behavior. Though any substance use is of concern, which substance a person is turning to since treatment is crucial in determining areas for revision in the treatment plan (Ramo & Brown, 2008).

Compared to women in the third trimester of pregnancy, mothers of children under three months of age in the household had much higher rates of past month cigarette use, marijuana use, alcohol use, and binge alcohol use. This finding suggests resumption of substance use among mothers in the three months following childbirth. Thus, there is a need to address use of effective interventions for women to prevent postpartum resumption of substance use and improve their overall health and wellbeing, as well as that of their young infants (SAMHSA/OAS, 2009).

A recent study examined the rates of abstinence in pregnancy and relapse postpartum for nicotine cigarettes, marijuana, cocaine, and alcohol. Self-reports and urine

toxicologies were collected during pregnancy and 24-months following delivery. The researchers observed that 83 percent of women achieved abstinence to at least one substance in pregnancy, with abstaining a more likely outcome for marijuana, cocaine, and alcohol than cigarettes. However, 80 percent of the women who were abstinent in the last month of their pregnancy have relapsed to at least one substance postpartum. Women using cocaine, however, were less likely to relapse after

There is a need to address the use of effective interventions for women to prevent postpartum resumption of substance use and improve their overall health and wellbeing, as well as that of their young infants (SAMHSA/OAS, 2009).

attaining abstinence compared to women who used marijuana, alcohol, or cigarettes (Forray, Merry, Haiqun, Ruger, & Yonkers, 2015).

More Contraindications

It is recommended that Naltrexone and Antabuse® be avoided during pregnancy.

Naltrexone has the ability to precipitate severe opioid withdrawal in patients taking buprenorphine or methadone, which could be fatal to the fetus. Antabuse® has teratogenic effects which means the developing fetus could develop an intellectual disability and/or some sort of growth deficiency, e.g. (Ramo & Brown, 2008).

Resources

Books/Curriculum.

Every Step of the Way (ESW).

- ✓ *Every Step of the Way (ESW)* is a thin, power-packed book designed for pregnant women. In particular, it has special value for women at risk of using substances during their pregnancy. Rather than focus on the hazards of substance use, it addresses the benefits of a healthy pregnancy. The substance focus of this book is alcohol, primarily because it is the most commonly used substance, even when other substances such as cocaine, heroin, or prescription pain relievers, might be the preferred substance of choice. The message to the women is to avoid any and all substance use during pregnancy.
- ✓ *Every Step of the Way: Parents' Guide* provides a month-by-month approach to what a healthy, developing baby looks like, as well as the risks alcohol (and/or other substances) may pose to the baby. The book is a blend of clinical research and imaginative writing exercises to connect the mother to her baby and foster healthy decision making throughout pregnancy. This guide is sold in a pack of 10.

I Am Concerned... (IAC).

- ✓ *I Am Concerned...* is a pre-treatment curriculum designed for use in the primary prenatal care setting for pregnant women who need some form of drug treatment, but refuse to get it. It is a brief intervention that focuses on the risks linked to continued substance use. The book contains background information on drug use among women, the brief intervention approach and drug-specific information on alcohol, cocaine, heroin, marijuana, methamphetamines, Oxycontin, PCP, and tobacco.

Video.

National Organization on Fetal Alcohol Syndrome (NOFAS) Web site.

Medical Experts on Light Drinking during Pregnancy – Short video clip in which various medical experts promote no drinking during pregnancy. However, they try reduce hysteria among women who have continued to drink during their pregnancy by getting them to embrace the benefits of abstinence, whenever that occurs during pregnancy. The YouTube link to this video is <http://www.nofas.org/light-drinking/>.

Web Source.

MotherToBaby Fact Sheets.

MotherToBaby is a service of the Organization of Teratology Information Specialists (OTIS), a nonprofit organization dedicated to providing evidence-based information to mothers, health care professionals, and the general public, with a focus on expectant mothers and their fetuses. The organization's experts have developed fact sheets to answer questions that are frequently asked in relation to exposures during pregnancy and breastfeeding. The fact sheets provide general information and are not meant to replace the advice health care providers. Nevertheless, fact sheets are available on medications (e.g., albuterol, tylenol), herbal products such as St. John's Wort, infections and vaccines (e.g., chicken pox and vaccine, hepatitis A), maternal medical conditions such as asthma and diabetes, illicit substances (e.g., cocaine), and other common exposures such as alcohol, caffeine, and carbon monoxide. Both English and Spanish versions of the fact sheets are accessible at no cost from <http://www.mothers-to-baby.org/otis-fact-sheets-s13037#5>. There is also a toll free number on the Web site that can be used to speak to a MotherToBaby expert.

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