National Institute on Drug Abuse | Research Report Series

Substance Use in Women

Summary

Women and men may face unique issues when it comes to substance use, as a result of both sex and gender. *Sex differences* result from biology, or being genetically female or male, while *gender differences* are based on culturally defined roles for men and women, as well as those who feel uncomfortable identifying with either category; such roles influence how people perceive themselves and how they interact with others (ORWH, 2015; Wizemann & Pardue, 2001). Sex and gender can also interact with each other to create even more complex differences between men and women.

Examples of Sex and Gender Influences in Smoking Cessation

Sex Difference: Women have a harder time quitting smoking than men do. Women metabolize nicotine, the active ingredient in tobacco, faster than men. Differences in metabolism may help explain why nicotine replacement therapies, like patches and gum, work better in men than in women. Men appear to be more sensitive to nicotine's pharmacologic effects related to addiction.

Gender Difference: Although men are more sensitive than women to nicotine's addiction-related effects, women may be more susceptible than men to non-nicotine factors, such as the sensory and social stimuli associated with smoking.

Source: ORWH, 2015

For example, women and men sometimes use drugs for different reasons and respond to them differently, and substance use disorders may manifest differently in women than in men. A substance use disorder occurs when a person needs alcohol or a drug to function normally and stopping use leads to withdrawal symptoms. Some of the unique issues women who use drugs face are further complicated during pregnancy and breastfeeding. Most new mothers and mothers-to-be realize that drugs, including tobacco and alcohol, can be passed on to their babies (both while in the womb and via mothers' milk) and cause them harm. Women should also know that some substances can impact their reproductive cycles, increasing the likelihood of infertility (Eggert et al., 2004; Joesoef et al., 1993; Tolstrup et al., 2003) and

early onset of menopause(Schoenbaum et al., 2005). (See "Substance Use While Pregnant and Breastfeeding" on page 8.)

Unfortunately, it can be difficult for a person with a substance use disorder to quit, and some women with such disorders fear that seeking help while pregnant or afterward could cause them legal or social problems. Communities can build support systems to help women access treatment as early as possible (SAMHSA, 2009), ideally before becoming pregnant. If a woman is unable to quit before becoming pregnant, treatment during pregnancy improves the chances of having a healthier baby at birth (Daley et al., 2001; Svikis et al., 1997).

Women have unique needs that should be addressed during substance use disorder treatment. Effective treatment should incorporate approaches that recognize sex and gender differences, understand the types of trauma women sometimes face, provide added support for women with child care needs, and use evidence-based approaches for the treatment of pregnant women (SAMHSA, 2011). (See "Sex and Gender Differences in Substance Use Disorder Treatment" on page 14.)

Despite the many differences between men and women, for many years most animal and human research has traditionally used male subjects. To find out more about how women might differ from men to inform better treatment approaches, federal agencies have developed guidelines to promote the inclusion of women in research (NIH, 2001; Clayton & Collins, 2014). (See "The Importance of Including Women in Research" on page 18.)

Despite the many differences between men and women, for many years most animal and human research has traditionally used male subjects. To find out more about how women might differ from men to inform better treatment approaches, federal agencies have developed guidelines to promote the inclusion of women in research (NIH, 2001; Clayton & Collins, 2014). (See "The Importance of Including Women in Research" on page 18.)

Sex and Gender Differences in Substance Use

Men are more likely than women to use almost all types of illicit drugs (SAMHSA, 2014), and illicit drug use is more likely to result in emergency department visits or overdose deaths for men than for women. "Illicit" refers to use of illegal drugs, including marijuana (according to federal law) and misuse of prescription drugs. For most age groups, men have higher rates of use or dependence on illicit drugs and alcohol than do women (TEDS, 2012a). However, women are just as likely as men to become addicted (Anthony et al., 1994). In addition, women may be more susceptible to craving (Robbins et al., 1999; Hitschfeld et al., 2015; Fox et al., 2014; Kennedy et al., 2013) and relapse (Kippin et al., 2005; Rubonis et al., 1994), which are key phases of the addiction cycle.

Research has shown that women often use drugs differently, respond to drugs differently, and can have unique obstacles to effective treatment as simple as not being able to find child care or being prescribed treatment that has not been adequately tested on women.

Women of color may face unique issues with regard to drug use and treatment needs. For example, African-American and American Indian/Alaska Native women are more likely than women of other racial and ethnic groups to be victims of rape, physical violence, and stalking by an intimate partner in their lifetime—issues that are risk factors for substance use and should be addressed during treatment. More information can be found in *Women of Color: Health Data Book*: http://orwh.od.nih.gov/resources/policyreports/pdf/WoC-Databook-FINAL.pdf (ORWH/NIH).

Illegal Drugs

Marijuana (Cannabis)

Similarly to other addictive drugs, fewer females than males use marijuana (SAMHSA, 2014). For females who do use marijuana, however, the effects can be different than for male users. Research indicates that marijuana impairs spatial memory in women more than it does in men (Makela et al., 2006; Pope et al., 1997). However, males show a greater marijuana-induced "high" (Haney, 2007; Penetar et al., 2005). Male high school students who smoke marijuana report poor family relationships and problems at school more often than female students who smoke marijuana (Butters, 2005). In contrast, animal studies show that female rats are more sensitive to the rewarding (Fattore et al., 2007; Craft et al., 2013), pain-relieving (Craft et al., 2012; Romero et al., 2002; Tseng & Craft, 2001), and activity-altering (Tseng & Craft, 2001; Craft et al., 2012; Wiley, 2003) effects of marijuana's main active ingredient *delta-9-tetrahydrocannabinol* (THC). Many of these differences have been attributed to the effects of sex hormones (Fattore et al., 2007; Craft & Leitl, 2008; Craft et al., 2012; Fattore et al., 2010; Winsauer et al., 2011), although rodent research also points to the possibility that there are sex differences in the functioning of the endocannabinoid system, the system of brain signaling where THC and other cannabinoids exert their actions (Krebs-Kraft et al., 2010; Craft et al., 2013). A few studies have suggested that teenage girls who use marijuana may have a higher risk of brain structural abnormalities as a result of regular marijuana exposure than teenage boys (Medina et al., 2009; McQueeny et al., 2011).

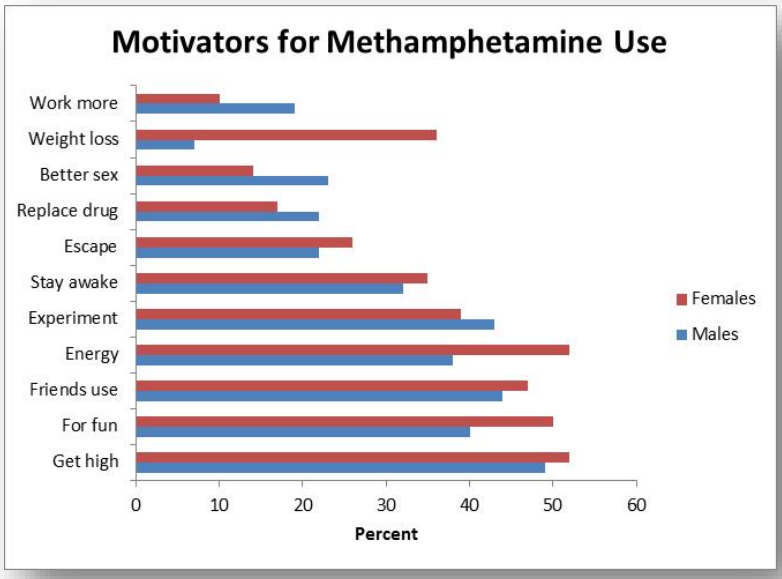
Cannabis Use Disorder

Men	Women
Similarities	
• At least one other mental health disorder • Low rate of seeking treatment	
Differences	
• Other substance use disorders • Antisocial personality disorder • Severity of disorder	• Panic attacks • Anxiety disorders • Disorder develops more quickly

For both sexes, addiction to marijuana is associated with an increased risk of at least one other mental health issue, such as depression or anxiety. However, men who are addicted to marijuana have higher rates of other substance use problems as well as antisocial personality disorders. By contrast, women who are addicted to marijuana have more panic attacks (Thomas, 1996) and anxiety disorders (Buckner et al., 2012; Buckner et al., 2006). Although the severity of cannabis use disorders is generally higher for men, women tend to develop these disorders more quickly after their first marijuana use (Hernandez-Avila et al., 2004). Rates of seeking treatment for marijuana addiction are low for both sexes (Khan et al., 2013).

Stimulants (Cocaine and Methamphetamine)

Research in both humans and animals suggests that women may be more vulnerable to the reinforcing (rewarding) effects of stimulants, with estrogen possibly being one factor for this increased sensitivity (Evans & Foltin, 2006; Justice & de Wit, 2000; Justice & de Wit, 1999; Anker & Carroll, 2011). In animal studies, females are quicker to start taking cocaine—and take it in larger amounts—than males. Women may also be more sensitive than men to cocaine's effects on the heart and blood vessels. In contrast, female and male cocaine users show similar deficits in learning, concentration, and academic achievement as a result of cocaine use, even if women had been using it longer. Female cocaine users are also less likely than male users to exhibit abnormalities of blood flow in the brain's frontal regions. These findings suggest a sex-related mechanism that may protect women from some of the damage cocaine inflicts on the brain (NIDA Notes, 2000).



Source: Brecht et al., 2004

Although some women report using methamphetamine to control weight, any effort to enhance physical appearance will disappear over time with the extensive physical damage caused to the skin and teeth. Women also report using methamphetamine because they believe it will increase energy and decrease exhaustion associated with work, home care, child care, and family responsibilities (Cretzmeyer et al., 2003; Brecht et al., 2004). Women who use methamphetamine also have high rates of co-occurring depression (Hser et al., 2005; Zweben et al., 2004; Rawson et al., 2005; Dluzen & Liu, 2008).

MDMA (Ecstasy, Molly)

Research suggests that MDMA produces stronger hallucinatory effects in women compared to men, although men show higher MDMA-induced blood pressure increases (Liechti et al., 2001). There is some evidence that, in occasional users, women are more prone than men to feeling depressed a few days after they last used MDMA (Verheyden et al., 2002). Both men and women show similar increases in aggression a few days after they stop using MDMA (Verheyden et al., 2002; Hoshi et al., 2006).

Research suggests that MDMA produces stronger hallucinatory effects in women compared to men.

MDMA can interfere with the body's ability to eliminate water and decrease sodium levels in the blood, causing a person to drink large amounts of fluid. In rare cases, this can lead to increased water in the spaces between cells, which may eventually produce swelling of the brain and even death. Young women are more likely than men to die from this reaction—with almost all reported cases of death occurring in young females between the ages of 15 and 30(Campbell & Rosner, 2008; Moritz et al., 2013). MDMA can also interfere with temperature regulation and cause acute hyperthermia leading to neurotoxic effects and even death (MDMA can be fatal in warm environments, 2014).

Heroin

Research suggests that women tend to use smaller amounts of heroin and for less time, and are less likely than men to inject it (Powis et al., 1996). Most women who inject heroin point to social pressure and sexual partner encouragement as factors (Bryant et al., 2010; Lum et al., 2005; Dwyer et al., 1994; Powis et al., 1996). One study indicates that women are more at risk than men for overdose death during the first few years of injecting heroin. It is unclear why this might be the case. One possibility is that women who inject heroin are more likely than their male counterparts to also use prescription drugs—a dangerous combination. Women who do not overdose within these first few years are more likely than men to survive in the long term. This could be due to differences in treatment and other environmental factors that impact heroin use (Gjersing & Bretteville-Jensen, 2014).

Compared with men, women who use heroin are:

- younger
- likely to use smaller amounts and for a shorter time
- less likely to inject the drug
- more influenced by drug-using sexual partners

Prescription Drugs

Prescription drug misuse is the use of a medication without a prescription, in a way other than as prescribed, or for the experience or feelings elicited. Prescription drugs can also be dangerous if mixed together without a physician's guidance, or mixed with other drugs or alcohol.

Pain Relievers (Opioids)

Some research indicates that women are more sensitive to pain than men (Riley et al., 1998) and more likely to have chronic pain (Gerdle et al., 2008), which could contribute to the high rates of opioid prescriptions among women of reproductive age (Ailes et al., 2015). In addition, women may be more likely to take prescription opioids without a prescription to cope with pain, even when men and women report similar pain levels. Research also suggests that women are more likely to misuse prescription opioids to self-treat for other problems such as anxiety or tension (McHugh et al., 2013).

A possible consequence of prescription opioid misuse is fatal overdose, which can occur because opioids suppress breathing. From 1999 to 2010, deaths from prescription pain reliever overdoses increased more rapidly for women (400 percent) than for men (265 percent) (CDC Vital Signs, 2013). In 2010, about 18 women per day (New CDC Vital Signs, 2013) compared to about 27 men (Mack et al., 2013) died from overdosing on prescription pain relievers. Women between the ages of 45 and 54 are more likely than women of other age groups to die from a prescription pain reliever overdose (CDC Vital Signs, 2013).

Anti-Anxiety Medications and Sleeping Aids

Women are more likely to seek treatment for misuse of barbiturates (TEDS, 2012), which includes sedatives sometimes prescribed to treat seizures, sleep disorders, and anxiety, and to help people fall asleep prior to surgery. Women are also more likely than men to die from overdoses of medicines for mental health conditions, like antidepressants. Antidepressants and benzodiazepines (anti-anxiety or sleep drugs) send more women than men to emergency departments (CDC Vital Signs, 2013). Because women are also more at risk than men for anxiety (Anxiety Disorders, n.d.), depression (NIMH, 2009), and insomnia (NHLBI, 1997), it is possible that women are being prescribed more of these types of medications; greater access can increase the risk of misuse and lead to addiction or overdose.

Other Substances

Alcohol

In general, men have higher rates of alcohol use, including binge drinking. However, teens are an exception: Teen boys and girls are similar in rates of current drinking (SAMHSA, 2014).

Drinking over the long term is more likely to damage a woman's health than a man's, even if the woman has been drinking less alcohol or for a shorter length of time (Holman et al., 1996; Piazza et al., 1989). Comparing people with alcohol use disorders, women have death rates 50 to 100 percent higher than do men, including deaths from suicides, alcohol-related accidents, heart disease, stroke, and liver disease (NIAAA, 2008). In addition, there are some health risks that are unique to female drinkers. For example, heavy drinking is associated with increased risk of having unprotected sex, resulting in pregnancy or disease (Rehm et al., 2012), and an increased risk of becoming a victim of violence and sexual assault. In addition, drinking as little as one drink per day can slightly raise the risk of breast cancer in some women, especially those who are postmenopausal or have a family history of breast cancer (NIAAA, 2008).

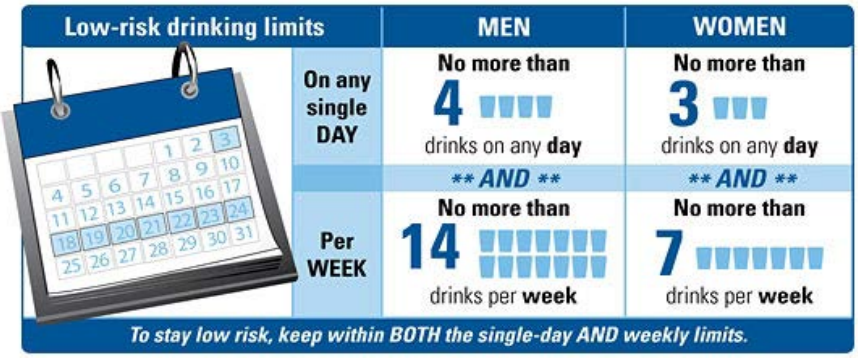


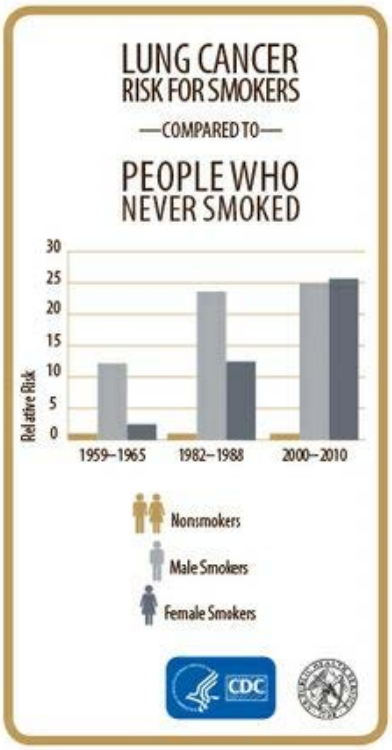
Image by NIAAA/http://rethinkingdrinking.niaaa.nih.gov/How-much-is-too-much/Is-your-drinking-pattern-risky/whats-Low-Risk-drinking.aspx

In addition, men and women metabolize alcohol differently due to differences in gastric tissue activity. In fact, after drinking comparable amounts of alcohol, women have higher blood ethanol concentrations (Frezza et al., 1990; NIAAA, 1999; NIAAA, 2008; Lieber, 2000). As a result, women become intoxicated from smaller quantities of alcohol than men (NIAAA, 1999).

More information on sex and gender differences in alcohol use is available from NIAAA at www.niaaa.nih.gov/alcohol-health/special-populations-co-occurring-disorders/women.

Nicotine (Tobacco)

Research indicates that men and women differ in their smoking behaviors. For instance, women smoke fewer cigarettes per day, tend to use cigarettes with lower nicotine content, and do not inhale as deeply as men (Melikian, 2007). Women also may smoke for different reasons than men, including regulation of mood and stress (Cosgrove et al., 2014). It is unclear whether these differences in smoking behaviors are because women are more sensitive to nicotine, because they find the sensations associated with smoking less rewarding, or because of social factors contributing to the difference; some research also suggests women may experience more stress and anxiety as a result of nicotine withdrawal than men (Torres & O'Dell, 2015).



Risk of death from smoking-associated lung cancer, chronic obstructive pulmonary disease, heart disease, and stroke continues to increase among women—approaching rates for men (Thun et al., 2013). According to data collected from 2005 to 2009, approximately 201,000 women die each year due to factors related to smoking—compared to about 278,000 men (Smoking & Tobacco Use, 2014). Some dangers associated with smoking—such as blood clots, heart attack, or stroke—increase in women using oral contraceptives (Farley et al., 1998).

The number of smokers in the United States declined in the 1970s and 1980s, remained relatively stable throughout the 1990s, and declined further through the early 2000s. Because this decline in smoking was greater among men than women, the prevalence of smoking is only slightly higher for men today than it is for women. Several factors appear to be contributing to this narrowing gender gap, including women being less likely than men to quit and more likely to relapse if they do quit (Piper et al., 2010).

Substance Use While Pregnant and Breastfeeding

Research shows that use of tobacco, alcohol, or illicit drugs or abuse of prescription drugs by pregnant women can have severe health consequences for infants. This is because many substances pass easily through the placenta, so substances that a pregnant woman takes also, to some degree, reach the baby (Neonatal abstinence syndrome, 2014). Recent research shows that smoking tobacco or marijuana, taking prescription pain relievers, or using illegal drugs during pregnancy is associated with double or even triple the risk of stillbirth (Tobacco, drug use in pregnancy, 2013).

Regular drug use can produce dependence in the newborn, and the baby may go through withdrawal upon birth. Most research in this area has focused on the effects of opioid misuse (prescription pain relievers or heroin). However, more recent data has shown that use of alcohol, barbiturates, benzodiazepines, and caffeine during pregnancy may also cause the infant to show withdrawal symptoms at birth (Hudak et al., 2012). The type and severity of an infant's withdrawal symptoms depend on the drug(s) used, how long and how often the birth mother used, how her body breaks the drug down, and whether the infant was born full term or prematurely (Neonatal abstinence syndrome, 2014).

Symptoms of drug withdrawal in a newborn can develop immediately or up to 14 days after birth and can include (Hudak, 2012):

- blotchy skin coloring
- diarrhea
- excessive or high-pitched crying
- abnormal sucking reflex
- fever
- hyperactive reflexes
- increased muscle tone
- irritability
- poor feeding
- rapid breathing
- increased heart rate
- seizures
- sleep problems
- slow weight gain
- stuffy nose and sneezing
- sweating
- trembling
- vomiting

Risks of Stillbirth from Substance Use in Pregnancy

- Tobacco use—1.8 to 2.8 times greater risk of stillbirth, with the highest risk found among the heaviest smokers
- Marijuana use—2.3 times greater risk of stillbirth
- Evidence of any stimulant, marijuana, or prescription pain reliever use—2.2 times greater risk of stillbirth
- Passive exposure to tobacco—2.1 times greater risk of stillbirth

Source: Tobacco, drug use in pregnancy, 2013

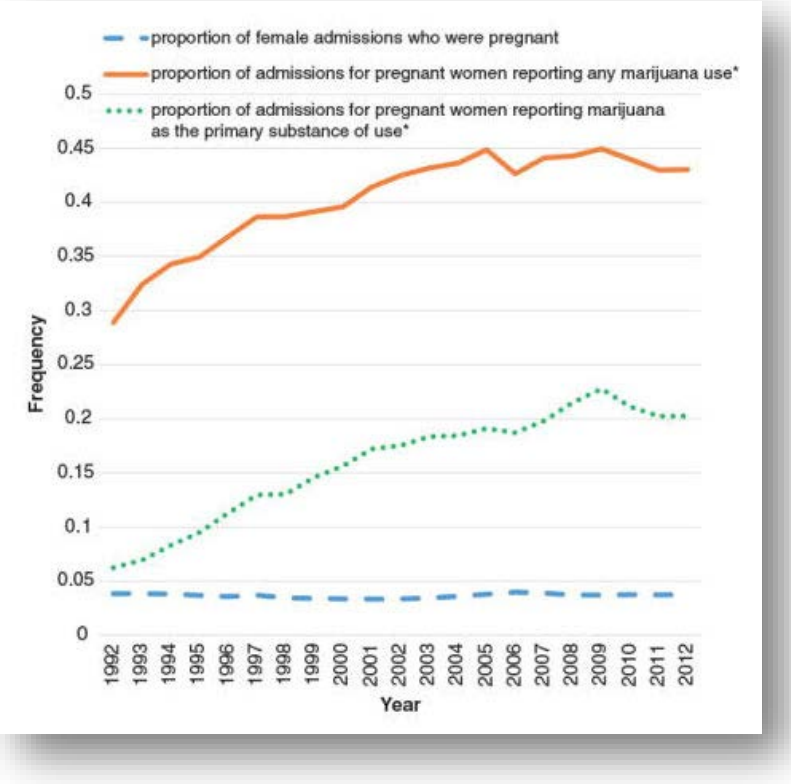
Effects of using some drugs could be long-term and possibly fatal to the baby (Neonatal abstinence syndrome, 2014):

- low birth weight
- birth defects
- small head circumference
- premature birth
- sudden infant death syndrome (SIDS)

Illegal Drugs

Marijuana (Cannabis)

More research needs to be done on how marijuana use during pregnancy could impact the health and development of infants, given changing policies about access to marijuana, as well as significant increases over the last decade in the number of pregnant women seeking substance use disorder treatment for marijuana use (Martin et al., 2015).



Source: Martin et al., 2015

There is no human research connecting marijuana use to the chance of miscarriage (Kline et al., 1991; Wilcox et al., 1990), although animal studies indicate that the risk for miscarriage increases if marijuana is used early in pregnancy (Asch & Smith, 1986). Some associations have been found between marijuana use during pregnancy and future developmental and hyperactivity disorders in children (Campolongo et al., 2011; Fried et al., 1992; Goldschmidt et al., 2000; Fried & Smith, 2001). Evidence is mixed as to whether marijuana use by pregnant women is associated with low birth rate (Janisse et al., 2014; Hayatbakhsh et al., 2012; Shiono et al., 1995; Mark et al., 2015; Schempf & Strobino, 2008) or premature birth (Mark et al., 2015), although long-term use may elevate these risks (Shiono et al., 1995). Given the potential of marijuana to negatively impact the developing brain, the American College of Obstetricians and Gynecologists recommends that obstetrician-gynecologists counsel women against using marijuana while trying to get pregnant, during pregnancy, and while they are breastfeeding (ACOG, 2015).

Some women report using marijuana to treat severe nausea associated with their pregnancy (Roberson et al., 2014; Westfall et al., 2006); however, there is no research confirming that this is a safe practice, and it is generally not recommended. Women considering using medical marijuana while pregnant should not do so without checking with their health care providers. Animal studies have shown that moderate concentrations of *delta-9-tetrahydrocannabinol* (or THC, the main psychoactive ingredient in marijuana), when administered to mothers while pregnant or nursing, could have long-lasting effects on the child, including increasing stress responsivity and abnormal patterns of social interactions (Trezza et al., 2008). Animal studies also show learning deficits in prenatally exposed individuals (Antonelli et al., 2005; Mereu et al., 2003).

Human research has shown that some babies born to women who used marijuana during their pregnancies display altered responses to visual stimuli, increased trembling, and a high-pitched cry (Fried & Makin, 1987), which could indicate problems with neurological development (de Moraes et al., 2008). In school, marijuana-exposed children are more likely to show gaps in problem-solving skills, memory (Richardson et al., 2002), and the ability to remain attentive (Goldschmidt et al., 2000). More research is needed, however, to disentangle marijuana-specific effects from those of other environmental factors that could be associated with a mother's marijuana use, such as an impoverished home environment or the mother's use of other drugs (Schempf & Strobino, 2008). Prenatal marijuana exposure is also associated with an increased likelihood of a person using marijuana as a young adult, even when other factors that influence drug use are considered (Sonon et al., 2015). More information on marijuana use during pregnancy in NIDA's *Marijuana Research Report* at www.drugabuse.gov/publications/research-reports/marijuana/can-marijuana-use-during-pregnancy-harm-baby.

Prenatal marijuana exposure is also associated with an increased likelihood of a person using marijuana as a young adult, even when other factors that influence drug use are considered.

Very little is known about marijuana use and breastfeeding. One study suggests that moderate amounts of THC find their way into breast milk when a nursing mother uses marijuana (Perez-Reyes & Wall, 1982). Some evidence shows that exposure to THC through breast milk in the first month of life could result in decreased motor development at 1 year of age (Astley & Little, 1990). There have been no studies to determine if exposure to THC during nursing is linked to effects later in the child's life. With regular use, THC can accumulate in human breast milk to high concentrations (Perez-Reyes & Wall, 1982). Because a baby's brain is still forming, THC consumed in breast milk could affect brain development. Given all these uncertainties, nursing mothers are discouraged from using marijuana (ACOG, 2015; Djulus et al., 2005). New mothers using medical marijuana should be vigilant about coordinating care between the doctor recommending their marijuana use and the pediatrician caring for their baby.

Stimulants (Cocaine and Methamphetamine)

Some may recall news items about "crack babies," a term coined in the 1980s to describe babies born to mothers who smoked cocaine while pregnant. These babies were initially predicted to suffer from severe, irreversible cognitive and behavioral consequences, including reduced intelligence and social skills. These purported effects turned out to be somewhat exaggerated. However, it is not completely known how a pregnant woman's cocaine use affects her child, since cocaine-using women are more likely to also use other drugs such as alcohol, to have poor nutrition, or to not seek prenatal care. All of these factors can affect a developing fetus, making it difficult to isolate the effects of cocaine (Cain et al., 2013).

Research does show, however, that pregnant women who use cocaine are at higher risk for maternal migraines and seizures, premature membrane rupture, and placental abruption (separation of the placental lining from the uterus) (Wendell, 2013). Pregnancy is accompanied by normal cardiovascular changes, and cocaine abuse exacerbates these changes—sometimes leading to serious problems with high blood pressure (hypertensive crises), spontaneous miscarriage, preterm labor, and difficult delivery (Cain et al., 2013). Babies born to mothers who use cocaine during pregnancy may also have low birth

weight and smaller head circumferences, and are shorter in length than babies born to mothers who do not use cocaine. They also show symptoms of irritability, hyperactivity, tremors, high-pitched cry, and excessive sucking at birth (Bauer et al., 2005). These symptoms may be due to the effects of cocaine itself, rather than withdrawal, since cocaine and its metabolites are still present in the baby's body up to 5 to 7 days after delivery (Chasnoff et al., 1986; Eyler et al., 2001).

Pregnant women who use methamphetamine have a greater risk of preeclampsia (high blood pressure and possible organ damage) (Gorman et al., 2014), premature delivery, and placental abruption. Their babies are more likely to be smaller and to have low birth weight (Smith et al., 2006). In a large, longitudinal study of children prenatally exposed to methamphetamine, exposed children had increased emotional reactivity and anxiety/depression, were more withdrawn, had problems with attention, and showed cognitive problems that could lead to poorer academic outcomes (Diaz et al., 2014; LaGasse et al., 2012).

MDMA (Ecstasy, Molly)

What little research exists on the effects of MDMA use in pregnancy suggests that prenatal MDMA exposure may cause learning, memory (Schaefer et al., 2013), and motor problems in the baby (Singer et al., 2012). More research is needed on this topic.

Heroin

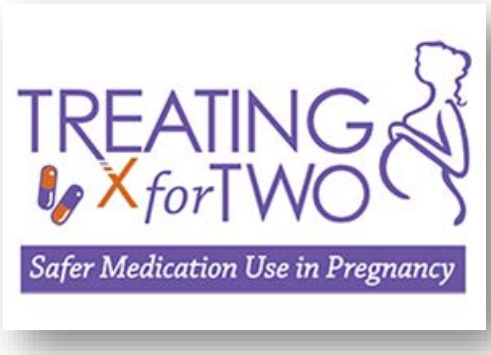
Heroin use during pregnancy can result in neonatal abstinence syndrome (NAS). NAS occurs when heroin passes through the placenta to the fetus during pregnancy, causing the baby to become dependent on opioids. Symptoms include excessive crying, high-pitched cry, irritability, seizures, and gastrointestinal problems, among others (Bandstra et al., 2010). NAS requires hospitalization of the affected infant and possibly treatment with morphine or methadone to relieve symptoms (Hudak et al., 2012); researchers have also studied buprenorphine for this purpose (Kraft et al., 2011). The medication is gradually tapered off until the baby adjusts to being opioid-free.

Medications

Prescription and Over-the-Counter Drugs

Pregnancy can be a confusing time for pregnant women facing many choices about legal drugs, like tobacco and alcohol, as well as prescription and over-the-counter (OTC) drugs that may affect their baby. These are difficult issues for researchers to study because scientists cannot give potentially dangerous drugs to pregnant women. Here are some of the known facts about popular medications and pregnancy:

There are more than 6 million pregnancies in the United States every year, and pregnant women take an average of three to five prescription drugs while pregnant. The U.S. Food and Drug Administration recently issued new rules on drug labeling to provide clearer instructions for pregnant and nursing women, including a summary of the risks of use during pregnancy and breastfeeding, a discussion of the data supporting the summary, and other information to help prescribers make safe decisions (FDA issues final rule, 2014).



See the *CDC Treating for Two* webpage at www.cdc.gov/pregnancy/meds/treatingfortwo/

Even so, we know little about the effects of taking most medications during pregnancy. This is because pregnant women are often not included in studies to determine safety of new medications before they come on the market (Pregnancy: Medications and Pregnancy, 2014). A recent study shows that use of short-acting prescription opioids such as oxycodone during pregnancy, especially when combined with tobacco and/or certain antidepressant medications, is associated with an increased likelihood of neonatal abstinence syndrome (NAS) in the infant (Patrick et al., 2015).

Although some prescription and OTC medications are safe to take during pregnancy, a pregnant woman should tell her doctor about all prescription medications, OTC cold and pain medicines, and herbal or dietary supplements she is taking or planning to take. This will allow her doctor to weigh the risks and benefits of a medication during pregnancy. In some cases, the doctor may recommend the continued use of specific medications, even though they could have some impact on the fetus. Suddenly stopping the use of a medication may be more risky for both the mother and baby than continuing to use the medication while under a doctor's care (Pregnancy: Medications and Pregnancy, 2014). This could also include medications to treat substance use disorders—something that is discussed in further detail in the "Sex and Gender Differences in Substance Use Disorder Treatment" section on page 14.

Some prescription and OTC medications are generally compatible with breastfeeding, and the American Academy of Pediatrics (www.aap.org/en-us/Pages/Default.aspx) maintains a list of such substances. Others, such as some anti-anxiety and antidepressant medications, have unknown effects (AAP Committee on Drugs, 2001), so mothers who are using these medications should consult with their doctor before breastfeeding. Nursing mothers should contact their infant's health care provider if their infants show any of these reactions to the breast milk: diarrhea, excessive crying, vomiting, skin rashes, loss of appetite, or sleepiness (Ages & Stages, 2014).

Other Substances

Alcohol

Alcohol use while pregnant can result in Fetal Alcohol Spectrum Disorders (FASD), a general term that includes Fetal Alcohol Syndrome, partial Fetal Alcohol Syndrome, alcohol-related disorders of brain development, and alcohol-related birth defects. These effects can last throughout life, causing difficulties with motor coordination, emotional control, schoolwork, socialization, and holding a job. More information can be found on the NIAAA Fetal Alcohol Exposure webpage at www.niaaa.nih.gov/alcohol-health/fetal-alcohol-exposure.

Fetal alcohol exposure occurs when a woman drinks while pregnant. Alcohol can disrupt fetal development at any stage during a pregnancy—including at the earliest stages before a woman even knows she is pregnant.

There is currently little research into how a nursing mother's alcohol use might affect her breastfed baby. What science suggests is that, contrary to folklore, alcohol does not increase a nursing mother's milk production, and it may disrupt the breastfed child's sleep cycle (Mennella, n.d.). The American Academy of Pediatrics recommends that alcohol drinking should be minimized during the months a woman nurses and daily intake limited to no more than 2 ounces of liquor, 8 ounces of wine, or two average beers for a 130-pound woman. In this case, nursing should take place at least 2 hours after drinking to allow the alcohol to be reduced or eliminated from the mother's body and milk. This will minimize the amount of alcohol passed to the baby (AAP, 2012).

More information can be found in the NIAAA publication *Alcohol's Effect on Lactation* at http://pubs.niaaa.nih.gov/publications/arh25-3/230-234.htm.

Nicotine (Tobacco Products and e-Cigarettes)

Almost 16 percent of pregnant women in the United States have smoked in the past month (SAMHSA, 2014). Carbon monoxide and nicotine from tobacco smoke may interfere with the oxygen supply to the fetus. Nicotine also readily crosses the placenta, and concentrations of this drug in the blood of the fetus can be as much as 15 percent higher than in the mother (Wickström, 2007). Smoking during pregnancy increases the risk for certain birth defects, premature birth, miscarriage, and low birth weight (Reproductive Health, 2014) and is estimated to have caused 1,015 infant deaths annually from 2005 through 2009 (CDC, 2014). Newborns of smoking mothers also show signs of stress and drug withdrawal consistent with what has been reported in infants exposed to other drugs. In some cases, smoking during pregnancy may be associated with sudden infant death syndrome (SIDS), as well as learning and behavioral problems and an increased risk of obesity in children. In addition, smoking more than one pack a day during pregnancy nearly doubles the risk that the affected child will become addicted to tobacco if that child starts smoking (Rydell et al., 2014). Even a mother's secondhand exposure to cigarette smoke can cause problems; such exposure is associated with premature birth and low birth weight, for example (Khader et al., 2011). The U.S. Department of Health and Human Services provides resources specifically designed to help pregnant women quit smoking at http://women.smokefree.gov/pregnancy-motherhood.aspx.

Recent research provides strong support that nicotine is a gateway drug, making the brain more sensitive to the effects of other drugs such as cocaine (NIH study examines nicotine, 2011). This shows that pregnant women who use nicotine may be affecting their baby's brain in ways they may not anticipate. Because e-cigarettes typically also contain nicotine, those products may also pose a risk to the baby's health. More research is needed.

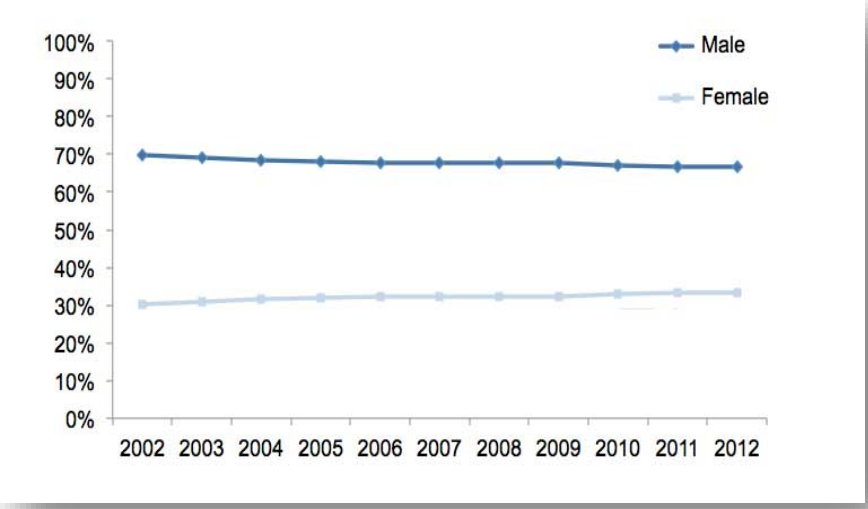
Similar to pregnant women, nursing mothers are also advised against using tobacco. New mothers who smoke should be aware that nicotine is passed through breast milk (Mennella et al., 2007), so tobacco use can impact the infant's brain and body development—even if the mother never smokes near the baby. There is also evidence that the milk of mothers who smoke smells and may taste like cigarettes. It is unclear whether this will make it more likely that exposed children may find tobacco flavors/smells more appealing later in life (Mennella & Beauchamp, 1998).

Secondhand Smoke

Newborns exposed to secondhand smoke are at greater risk for SIDS, respiratory illnesses (asthma, respiratory infections, and bronchitis), ear infections (Smoking & Tobacco Use, 2015), cavities (Aligne et al., 2003), and increased medical visits and hospitalizations (Leung et al., 2004). If a woman smokes and is planning a pregnancy, the ideal time to seek smoking cessation help is before she becomes pregnant.

Sex and Gender Differences in Substance Use Disorder Treatment

There are more men than women in treatment for substance use disorders. However, women are more likely to seek treatment for dependence on sedatives such as anti-anxiety and sleep medications (TEDS, 2012b). In addition, although men have historically been more likely to seek treatment for heroin use, the rate of women seeking treatment has increased in recent decades. By 2010, there were nearly equal numbers of male and female heroin users seeking treatment (Cicero et al., 2014).



Source: 2012 SAMHSA TEDS

Substance use disorders may progress differently for women than for men. Women often have a shorter history of abusing certain substances such as cocaine (Haas & Peters, 2000), opioids(Hernandez-Avila et al., 2004), marijuana (Khan et al., 2013; Hernandez-Avila et al., 2004; Ehlers et al., 2010), or alcohol (Hernandez-Avila et al., 2004; Mann et al., 2005; Randall et al., 1999). However, they typically enter

substance use disorder treatment with more severe medical, behavioral, psychological, and social problems. This is because women show a quicker progression from first using the substance to developing dependence (Greenfield et al., 2010).

Many women who are pregnant or have young children do not seek treatment or drop out of treatment early because they are unable to take care of their children; they may also fear that authorities will remove their children from their care. The combined burdens of work, home care, child care, and other family responsibilities, plus attending treatment frequently, can be overwhelming for many women. Successful treatment may need to provide an increased level of support to address these needs (SAMHSA, 2006).

https://findtreatment.samhsa.gov/

Women and Smoking Cessation Treatment

Research shows that women are less likely to try to quit smoking and more likely to relapse if they do quit (Piper et al., 2010). Nicotine-replacement options, such as the patch or gum, are not as effective for women as for men, and nicotine withdrawal may be more intense for women (Perkins & Scott, 2008; Langdon et al., 2013). Research shows that nicotine craving (Franklin et al., 2004) and withdrawal (Weinberger et al., 2015) vary across the menstrual cycle, which may further complicate a woman's attempts to quit.

Some women continue to smoke because they are afraid they will gain weight. However, research shows only a modest weight gain after quitting. The average smoker gains 6 to 10 pounds after quitting smoking, but certain diet and lifestyle changes can reduce the risk of weight gain. If a person does gain weight, the average person loses much of the extra weight within 6 months (Tobacco Research and Intervention Program, 2000). In fact, long-term quitters gain, on average, only 2 pounds (Quitting Smoking Benefits Health Despite Weight Gain, 2013). Most importantly, the health benefits of quitting smoking far exceed the risks of gaining a few pounds. For example, the stress on the heart due to smoking one pack of cigarettes per day is equivalent to being 90 pounds overweight. Quitting also decreases risks for various types of cancers, heart attack, and lung disease (Tobacco Research and Intervention Program, 2000). The U.S. Department of Health and Human Services has resources to help a woman quit smoking at http://women.smokefree.gov/.

The stress on the heart due to smoking one pack of cigarettes per day is the equivalent of being 90 pounds overweight.

Substance Use Disorder Treatment for Mothers and Their Babies While Pregnant or Breastfeeding

A pregnant woman should ask for medical help to stop her drug use. If she attempts to suddenly withdraw from addictive drugs and alcohol without medical assistance, she could be putting her fetus at risk (Jones et al., 2010). Federal law requires that pregnant women receive priority admission into publicly funded substance use disorder treatment programs, allowing them to bypass waiting lists and gain immediate admission when a bed in a residential program is available. The primary treatment provider must secure prenatal care if a pregnant woman is not already receiving such care (SAMHSA, 2009). State-level contacts for this program are available from www.samhsa.gov/sites/default/files/ssa-directory.pdf.

Intensive outpatient treatment, which provides a higher treatment level than traditional outpatient programs but does not require structured residential living, has produced positive results for pregnant women. Pregnant women are more likely to stay in these treatment programs if they provide services such as child care (Chen et al., 2004), parenting classes, and vocational training (McMurtrie et al., 1999; Volpicelli et al., 2000).

In addition, it is important to monitor newborns of substance-using mothers for symptoms of withdrawal and provide proper treatment if necessary. Treatment of drug dependency in newborns depends on the severity of symptoms and may include hospitalization in order to receive intravenous fluids and medications. These medications are gradually tapered off until the infant adapts to being drug-free.

Treating Opioid Disorders in Pregnant Women

Pregnant women who are addicted to opioid pain relievers or heroin face special problems because the baby can be born dependent (a condition called neonatal abstinence syndrome, or NAS). Currently, the U.S. Food and Drug Administration has not approved medications to treat opioid-dependent pregnant women, but methadone or buprenorphine maintenance combined with prenatal care and a comprehensive drug treatment program can improve many of the adverse outcomes associated with untreated opioid use disorder (Jones et al., 2010; Meyer et al., 2015). In general, it is neither recommended nor necessary for pregnant women to cease methadone or buprenorphine treatment (SAMHSA, 2009; Meyer et al., 2015). However, newborns exposed to methadone during pregnancy still require treatment for withdrawal symptoms.

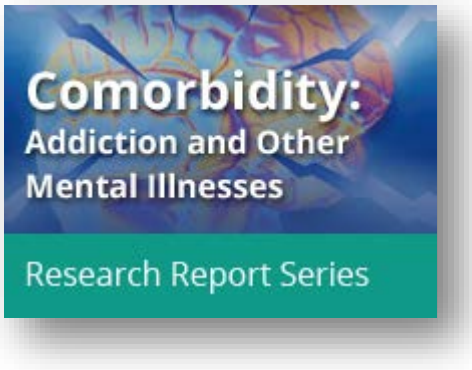
Recent studies suggest that buprenorphine (Suboxone®, Subutex®) has some advantages over methadone as a treatment for opioid addiction in pregnant women. Infants born to mothers treated with buprenorphine had fewer symptoms of dependence and reduced length of hospital stay compared to those treated with methadone (NIDA, 2012).

Pregnant women who take buprenorphine for opioid addiction during pregnancy should be aware that the amount of buprenorphine passed through breast milk may be inadequate to prevent opioid withdrawal in their infant. In some cases, treatment of the infant may be required (LACTMED: Buprenorphine, 2015).

Pregnant women who are addicted to opioids, even if they are in treatment, should monitor their babies for drowsiness, inadequate weight gain, and failure to meet developmental milestones—especially in younger, exclusively breastfed infants. Although unlikely, if a breastfed baby of a woman on buprenorphine therapy shows signs of increased sleepiness, difficulty feeding or breathing, or limpness, a health care provider should be contacted immediately. Infants should be observed for withdrawal signs if breastfeeding is abruptly stopped (LACTMED: Buprenorphine, 2015).

Other Sex and Gender Issues for Women Related to Substance Use

Co-Occurring Mental Health Disorders



More information about comorbidity can be found at www.drugabuse.gov/publications/research-reports/comorbidity-addiction-other-mental-illnesses/letter-director.

Many women with substance use disorders are also diagnosed with other mental disorders. This is important because interactions between illnesses can worsen the course of both. Patients who have both a substance use disorder and another mental health condition often have symptoms that are more persistent, severe, and resistant to treatment compared with patients who have either disorder alone. Both disorders should be treated at the same time to improve the likelihood of success. Although men are more likely than women to report both a mental health and substance use disorder within the past year (SAMHSA, 2013), women are more likely to suffer from certain mental health conditions, such as depression (Depression: What Is Depression?, n.d.), anxiety, post-traumatic stress disorder—or PTSD (NIMH, 2009), and eating disorders (NIMH, 2014). Some women report using substances to relieve stress or negative emotions (Annis & Graham, 1995; Perkins et al., 2012; Shen et al., 2012). In addition, women are more vulnerable to developing substance use or other mental health disorders following divorce, loss of child custody, or the death of a partner or child (SAMHSA, 2011).

Women, Violence, and Substance Abuse

More than one in three women have experienced physical violence at the hands of an intimate partner, including a range of behaviors from slapping, pushing, or shoving to severe acts such as being beaten, burned, raped, or choked (de Boinville, 2013). Victims of violence are at increased risk of chronic health conditions, including obesity, chronic pain, depression, and substance use (2013 Trans-HHS Intimate Partner Violence Screening, 2014). In recognition of the severity of violence against women and the need for a national strategy to address this issue, in 1994 Congress enacted the Violence Against Women Act to hold offenders accountable and to provide services to victims(Factsheet: The Violence Against Women Act, n.d.). In 2013, the President reauthorized the Act to expand programs for reaching especially vulnerable populations (Reauthorizing the Violence Against Women Act, n.d.).

The Institute of Medicine and the U.S. Preventive Services Task Force (USPSTF) have recommended that clinicians screen and counsel for interpersonal violence. To help meet that need, the Affordable Care Act of 2010 (Section 2713) requires that health insurance providers cover all preventive services recommended by the USPSTF without co-pays or deductibles. However, improved prevention and screening guidelines are needed to help clinicians identify those who need help and link them to the care they need (Report: Intimate Partner Violence Screening, n.d.).

The Importance of Including Women in Research

In the past, women were not included in most clinical research. This was often based on two notions: (1) that women are more biologically complicated than men; and (2) as primary caregivers of young children, a woman had too many competing time demands to participate in research studies(National Bioethics Advisory Commission, 2001). More than two decades ago, NIH established the Office of Research on Women's Health, in recognition that excluding specific subgroups from research produces knowledge that only helps a portion of the public. In 1991, the U.S. Department of Health and Human Services established the Office on Women's Health to ensure that broader public health issues related to sex and gender were addressed. Since these offices were established, significant progress has been made in several major areas:

- Policies have been implemented ensuring that women and minorities are included in NIH-funded clinical research (see http://orwh.od.nih.gov/about/mission.asp).
- Research on women's health and sex differences has expanded.
- Career development and mentoring programs have increased the numbers of women's health researchers.
- Research results have been translated into health benefits for women (ORWH, 2014).
- There has been greater communication to a variety of public audiences about sex and gender differences in basic and behavioral science, as well as in public health.

"Remember the famous study, take an aspirin a day to keep the heart attack away? That study was done on 10,000 men. Not one woman was included. In a study of the aging process, they told me women weren't included because there wasn't a ladies room available for study participants. Yet the results of these studies were being applied to men and women. I vowed to fix that."

—The Honorable Barbara Mikulski, U.S. Senator, Maryland
August 16, 2010

Source: *Moving into the Future with New Dimensions and Strategies: A Vision for 2020 Women's Health Research* (http://orwh.od.nih.gov/research/strategicplan/ORWH_StrategicPlan2020_Vol1.pdf)

Although significant strides have been made to include women in clinical research, most animal-based research still tends to over-rely on males. Because these studies are important in guiding clinical studies, NIH announced a new policy in 2014 requiring that both sexes be represented in NIH-funded research involving animal and cell models (see www.nature.com/news/policy-nih-to-balance-sex-in-cell-and-animal-studies-1.15195).

Since its inception, NIDA has sponsored research on issues related to women and substance use. Beginning with an early focus on the effects of drug use on pregnant women and the children they carry, NIDA then expanded its interest to sponsor research into women's specific substance use disorder risk factors and treatment needs. When the HIV/AIDS epidemic emerged in the 1980s, NIDA responded with funding for projects on gender-specific risk factors for infection and on the impact of drug use on HIV transmission between mother and newborn and the subsequent health of both. In 1995, NIDA formally established the Women and Sex/Gender Differences Research Program to understand the underlying causes of substance use disorders and the best ways to prevent and treat them in both men and women (Whitten, 2012). Read more about this research program at www.drugabuse.gov/about-nida/organization/offices/office-nida-director-od/women-sexgender-differences-research-program.

References

2013 Trans-HHS Intimate Partner Violence Screening and Counseling: Research Symposium. Women's Health Resources. Office of Research on Women's Health. http://whr.nlm.nih.gov/ipv-symposium.html#b00. Updated July 17, 2014. Accessed July 7, 2015.

Ages & Stages: Medications and Breastfeeding. HealthyChildren.org. American Academy of Pediatrics. www.healthychildren.org/English/ages-stages/baby/breastfeeding/Pages/Medications-and-Breastfeeding.aspx. Updated November 3, 2014. Accessed July 7, 2015.

Ailes EC, Dawson AL, Lind JN, et al (from Centers for Disease Control and Prevention). Opioid prescription claims among women of reproductive age—United States, 2008-2012. *MMWR Morb and Mortal Wkly Rep*. 2015;64(2);37-41.

Aligne CA, Moss ME, Auinger P, Weitzman M. Association of pediatric dental caries with passive smoking. *JAMA.* 2003;289(10):1258-1264.

American Academy of Pediatrics (AAP) Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics.* 2001;108(3):776-789.

American Academy of Pediatrics (AAP). Policy statement: breastfeeding and the use of human milk. *Pediatrics.* 2012;129(3):e827-e841.

American College of Obstetricians and Gynecologists (ACOG). Marijuana use during pregnancy and lactation. Committee Opinion No. 637. *Obstet Gynecol.* 2015;126:234-238.

Anker JJ, Carroll ME. Females are more vulnerable to drug abuse than males: evidence from preclinical studies and the role of ovarian hormones. *Curr Top Behav Neurosci.* 2011;8:73-96.

Annis HM, Graham JM. Profile types on the Inventory of Drinking Situations: implications for relapse prevention counseling. *Psychol Addict Behav.* 1995;9(3):176-182.

Anthony JC, Warner LA, Kessler RC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: basic findings from the National Comorbidity Survey. *Exp Clin Psychopharmacol.* 1994;2(3):244-268.

Antonelli T, Tomasini MC, Tattoli M, et al. Prenatal exposure to the CB1 receptor agonist WIN 55,212-2 causes learning disruption associated with impaired cortical NMDA receptor function and emotional reactivity changes in rat offspring. *Cereb Cortex.*2005;15(12):2013-2020.

Anxiety Disorders. National Institute of Mental Health. www.nimh.nih.gov/health/topics/anxiety-disorders/index.shtml. Accessed July 7, 2015.

Asch RH, Smith CG. Effects of delta 9-THC, the principal psychoactive component of marijuana, during pregnancy in the rhesus monkey. *J Reprod Med.*1986;31(12):1071-1081.

Astley SJ, Little RE. Maternal marijuana use during lactation and infant development at one year. *Neurotoxicol Teratol.* 1990;12(2):161-168.

Bandstra ES, Morrow CE, Mansoor E, Accornero VH. Prenatal drug exposure: infant and toddler outcomes. *J Addict Dis.* 2010;29(2):245-258.

Bauer CR, Langer JC, Shankaran S, et al. Acute neonatal effects of cocaine exposure during pregnancy. *Arch Pediatr Adolesc Med.* 2005;159(9):824-834.

Brecht M-L, O'Brien A, von Mayrhauser C, Anglin MD. Methamphetamine use behaviors and gender differences. *Addict Behav.* 2004;29(1):89-106.

Bryant J, Brener L, Hull P, Treloar C. Needle sharing in regular sexual relationships: an examination of serodiscordance, drug using practices, and the gendered character of injecting. *Drug Alcohol Depend.*2010;107(2-3):182-187.

Buckner JD, Heimberg RG, Schneier FR, Liu SM, Wang S, Blanco C. The relationship between cannabis use disorders and social anxiety disorder in the National Epidemiological Study of Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend.* 2012;124(1-2):128-134.

Buckner JD, Mallott MA, Schmidt NB, Taylor J. Peer influence and gender differences in problematic cannabis use among individuals with social anxiety. *J Anxiety Disord.* 2006;20(8):1087-1102.

Butters JE. Promoting healthy choices: the importance of differentiating between ordinary and high risk cannabis use among high-school students. *Subst Use Misuse.* 2005;40(6):845-855.

Cain MA, Bornick P, Whiteman V. The maternal, fetal, and neonatal effects of cocaine exposure in pregnancy. *Clin Obstet Gynecol.* 2013;56(1):124-132.

Campbell GA, Rosner MH. The agony of ecstasy: MDMA (3,4-methylenedioxymethamphetamine) and the kidney. *Clin J Am Soc Nephrol.* 2008;3(6):1852-1860.

Campolongo P, Trezza V, Ratano P, Palmery M. Cuomo V. Developmental consequences of perinatal cannabis exposure: behavioral and neuroendocrine effects in adult rodents. *Psychopharmacology (Berl).* 2011;214(1):5-15.

CDC Vital Signs: Prescription Painkiller Overdoses: A growing epidemic, especially among women. Centers for Disease Control and Prevention. www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/index.html. Reviewed July 2, 2013. Accessed July 7, 2015.

Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Substance Abuse Treatment Admissions by Primary Substance of Abuse, According to Sex, Age Group, Race, and Ethnicity, Year = 2012, United States. wwwdasis.samhsa.gov/webt/quicklink/US12.htm. Accessed July 7, 2015.

Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Table 2.1a. Admissions aged 12 and older, by gender and age at admission according to primary substance of abuse: 2012.www.samhsa.gov/data/2K14/TEDS2012NA/TEDS2012NTbl2.1a.htm. Accessed July 7, 2015.

Centers for Disease Control and Prevention (CDC). *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General.* Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

Chasnoff IJ, Bussey ME, Savich R, Stack CM. Perinatal cerebral infarction and maternal cocaine use. *J Pediatr.* 1986;108(3):456-459.

Chen X, Burgdorf K, Dowell K, Roberts T, Porowski A Herrell JM. Factors associated with retention of drug abusing women in long-term residential treatment. *Eval Program Plann.* 2004;27(2):205-212.

Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry.* 2014;71(7):821-826.

Clayton JA, Collins FS. Policy: NIH to balance sex in cell and animal studies. *Nature.* 2014;509:282-283.

Cosgrove KP, Wang S, Kim S-J, et al. Sex differences in the brain's dopamine signature of cigarette smoking. *J Neurosci.* 2014;34(50):16851-16855.

Craft RM, Leitl MD. Gonadal hormone modulation of the behavioral effects of Δ9-tetrahydrocannabinol in male and female rats. *Eur J Pharmacol.* 2008;578(1):37-42.

Craft RM, Marusich JA, Wiley JL. Sex differences in cannabinoid pharmacology: a reflection of differences in the endocannabinoid system? *Life Sci.* 2013;92(8-9):476-481.

Craft RM, Wakley AA, Tsutsui KT, Laggart JD. Sex differences in cannabinoid 1 vs. cannabinoid 2 receptor-selective antagonism of antinociception produced by Δ9-tetrahydrocannabinol and CP55,940 in the rat. *J Pharmacol Exp Ther.* 2012;340(3):787-800.

Cretzmeyer M, Sarrazin MV, Huber DL, Block RI, Hall JA. Treatment of methamphetamine abuse: research findings and clinical directions. *J Subst Abuse Treat.* 2003;24(3):267-277.

Daley M, Argeriou M, McCarty D, Callahan JJ Jr, Shepard DS, Williams CN. The impact of substance abuse treatment modality on birth weight and health care expenditures. *J Psychoactive Drugs*. 2001;33(1):57-66.

de Boinville M. Office of The Assistant Secretary for Planning and Evaluation. *ASPE Policy Brief: Screening for Domestic Violence in Health Care Settings.* Washington, DC: U.S. Department of Health and Human Services; 2013.

de Moraes Barros MC, Guinsburg R, Mitsuhiro S, Chalem E, Laranjeira RR. Neurobehavioral profile of healthy full-term newborn infants of adolescent mothers. *Early Hum Dev.* 2008;84(5):281-287.

Depression: What Is Depression? National Institute of Mental Health. www.nimh.nih.gov/health/topics/depression/index.shtml. Accessed July 7, 2015.

Diaz SD, Smith LM, LaGasse LL, et al. Effects of prenatal methamphetamine exposure on behavioral and cognitive findings at 7.5 years of age. *J Pediatr.*2014;164(6):1333-1338.

Djulus J, Moretti M, Koren G. Marijuana use and breastfeeding. *Can Fam Physician.* 2005;51(3):349-350.

Dluzen DE, Liu B. Gender differences in methamphetamine use and responses: a review. *Gend Med.* 2008;5(1):24-35.

Dwyer R, Richardson D, Ross MW, Wodak A, Miller ME, Gold J. A comparison of HIV risk between women and men who inject drugs. *AIDS Educ Prev.* 1994;6(5):379-389.

Eggert J, Theobald H, Engfeldt P. Effects of alcohol consumption on female fertility during an 18-year period. *Fertil Steril.* 2004;81(2):379-383.

Ehlers CL, Gizer IR, Vieten C, et al. Cannabis dependence in the San Francisco Family Study: age of onset of use, DSM-IV symptoms, withdrawal, and heritability. *Addict Behav.* 2010;35(2):102-110.

Evans SM, Foltin RW. Exogenous progesterone attenuates the subjective effects of smoked cocaine in women, but not in men. *Neuropsychopharmacology.*2006;31(3):659-674.

Eyler FD, Behnke M, Garvan CW, Woods NS, Wobie K, Conlon M. Newborn evaluations of toxicity and withdrawal related to prenatal cocaine exposure. *Neurotoxicol Teratol.* 2001;23(5):399-411.

Factsheet: The Violence Against Women Act. The White House. www.whitehouse.gov/sites/default/files/docs/vawa_factsheet.pdf. Accessed July 7, 2015.

Farley TM, Meirik O, Chang CL, Poulter NR. Combined oral contraceptives, smoking, and cardiovascular risk. *J Epidemiol Community Health.* 1998;52(12):775-785.

Fattore L, Spano MS, Altea S, Angius F, Fadda P, Fratta W. Cannabinoid self-administration in rats: sex differences and the influence of ovarian function. *Br J Pharmacol.* 2007;152(5):795-804.

Fattore L, Spano MS, Altea S, Fadda P, Fratta W. Drug- and cue-induced reinstatement of cannabinoid-seeking behaviour in male and female rats: influence of ovarian hormones. *Br J Pharmacol.* 2010;160(3):724-735.

FDA issues final rule on changes to pregnancy and lactation labeling information for prescription drug and biological products [press release]. Silver Spring, MD: U.S. Food and Drug Administration; December 3, 2014. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm425317.htm. Accessed July 7, 2015.

Fox HC, Morgan PT, Sinha R. Sex differences in guanfacine effects on drug craving and stress arousal in cocaine-dependent individuals. *Neuropsychopharmacology.* 2014;39:1527-1537.

Franklin TR, Napier K, Ehrman R, Gariti P, O'Brien CP, Childress AR. Retrospective study: influence of menstrual cycle on cue-induced cigarette craving. *Nicotine Tob Res.* 2004;6(1):171-175.

Frezza M, di Padova C, Pozzato G, Terpin M, Baraona E, Lieber CS. High blood alcohol levels in women – the role of decreased gastric alcohol dehydrogenase activity and first-pass metabolism. *N Engl J Med.* 1990;322(2):95-99.

Fried PA, Makin JE. Neonatal behavioural correlates of prenatal exposure to marihuana, cigarettes and alcohol in a low risk population. *Neurotoxicol Teratol.*1987;9(1):1-7.

Fried PA, Smith AM. A literature review of the consequences of prenatal marihuana exposure. An emerging theme of a deficiency in aspects of executive function. *Neurotoxicol Teratol.* 2001;23(1):1-11.

Fried PA, Watkinson B, Gray R. A follow-up study of attentional behavior in 6-year-old children exposed prenatally to marihuana, cigarettes, and alcohol. *Neurotoxicol Teratol.* 1992;14(5):299-311.

Gerdle B, Björk J, Cöster L, Henriksson KG, Henriksson C, Bengtsson A. Prevalence of widespread pain and associations with work status: a population study. *BMC Musculoskelet Disord.* 2008;9:102.

Gjersing L, Bretteville-Jensen AL. Gender differences in mortality and risk factors in a 13-year cohort study of street-recruited injecting drug users. *BMC Public Health.*2014;14:440.

Goldschmidt L, Day NL, Richardson GA. Effects of prenatal marijuana exposure on child behavior problems at age 10. *Neurotoxicol Teratol.* 2000;22(3):325-336.

Gorman MC, Orme KS, Nguyen NT, Kent EJ 3rd, Caughey AB. Outcomes in pregnancies complicated by methamphetamine use. *Am J Obstet Gynecol*. 2014;211(4):429.e1-e7.

Greenfield SF, Back SE, Lawson K, Brady KT. Substance abuse in women. *Psychiatr Clin North Am.* 2010;33(2):339-355.

Haas AL, Peters RH. Development of substance abuse problems among drug-involved offenders. Evidence for the telescoping effect. *J Subst Abuse.* 2000;12(3):241-253.

Haney M. Opioid antagonism of cannabinoid effects: differences between marijuana smokers and nonmarijuana smokers. *Neuropsychopharmacology.* 2007;32:1391-1403.

Hayatbakhsh MR, Flenady VJ, Gibbons KS, et al. Birth outcomes associated with cannabis use before and during pregnancy. *Pediatr Res.* 2012;71(2):215-219.

Hernandez-Avila CA, Rounsaville BJ, Kranzler HR. Opioid-, cannabis- and alcohol-dependent women show more rapid progression to substance abuse treatment. *Drug Alcohol Depend.* 2004;74(3):265-272.

Hitschfeld MJ, Schneekloth TD, Ebbert JO, et al. Female smokers have the highest alcohol craving in a residential alcoholism treatment cohort. *Drug Alcohol Depend.* 2015;150:179-182.

Holman CD, English DR, Milne E, Winter MG. Meta-analysis of alcohol and all-cause mortality: a validation of NHMRC recommendations. *Med J Aust.* 1996;164(3):141-145.

Hoshi R, Pratt H, Mehta S, Bond AJ, Curran HV. An investigation into the sub-acute effects of ecstasy on aggressive interpretative bias and aggressive mood – are there gender differences? *J Psychopharmacol.* 2006;20(2):291-301.

Hser YI, Evans E, Huang YC. Treatment outcomes among women and men methamphetamine abusers in California. *J Subst Abuse Treat.* 2005;28(1):77-85.

Hudak ML, Tan RC, The Committee on Drugs, The Committee on Fetus and Newborn. Clinical report: neonatal drug withdrawal. *Pediatrics*. 2012;129(2):e540-e560.

Is your drinking pattern risky? What's "low-risk" drinking? Rethinking Drinking: Alcohol and your health. National Institute on Alcohol Abuse and Alcoholism. www.rethinkingdrinking.niaaa.nih.gov/IsYourDrinkingPatternRisky/WhatsLowRiskDrinking.asp. Accessed July 7, 2015.

Janisse JJ, Bailey BA, Ager J, Sokol RJ. Alcohol, tobacco, cocaine, and marijuana use: relative contributions to preterm delivery and fetal growth restriction. *Subst Abus.* 2014;35(1):60-67.

Joesoef MR, Beral V, Aral SO, Rolfs RT, Cramer DW. Fertility and use of cigarettes, alcohol, marijuana, and cocaine. *Ann Epidemiol.* 1993;3(6):592-594.

Jones HE, Kaltenbach K, Heil SH, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *N Engl J Med.* 2010;363(24):2320-2331.

Justice AJ, de Wit H. Acute effects of *d*-amphetamine during the early and late follicular phases of the menstrual cycle in women. *Pharmacol Biochem Behav.*2000;66(3):509-515.

Justice AJ, de Wit H. Acute effects of *d*-amphetamine during the follicular and luteal phases of the menstrual cycle in women. *Psychopharmacology (Berl).*1999;145(1):67-75.

Kennedy AP, Epstein DH, Phillips KA, Preston KL. Sex differences in cocaine/heroin users: drug-use triggers and craving in daily life. *Drug Alcohol Depend.*2013;132(0):29-37.

Khader YS, Al-Akour N, Alzubi IM, Lataifeh I. The association between second hand smoke and low birth weight and preterm delivery. *Matern Child Health J*. 2011;15(4):453-459.

Khan SS, Secades-Villa R, Okuda M, et al. Gender differences in cannabis use disorders: results from the National Epidemiologic Survey of Alcohol and Related Conditions. *Drug Alcohol Depend.* 2013;130(1-3):101-108.

Kim JY, Fendrich M. Gender differences in juvenile arrestees' drug use, self-reported dependence, and perceived need for treatment. *Psychiatr Serv.*2002;53(1):70-75.

Kippin TE, Fuchs RA, Mehta RH, et al. Potentiation of cocaine-primed reinstatement of drug seeking in female rats during estrus. *Psychopharmacology (Berl).*2005;182(2):245-252.

Kline J, Hutzler M, Levin B, Stein Z, Susser M, Warburton D. Marijuana and spontaneous abortion of known karyotype. *Paediatr Perinat Epidemiol.*1991;5(3):320-332.

Kraft WK, Dysart K, Greenspan JS, Gibson E, Kaltenbach K, Ehrlich ME. Revised dose schema of sublingual buprenorphine in the treatment of the neonatal opioid abstinence syndrome. *Addiction.* 2011;106(3):574-580.

Krebs-Kraft DL, Hill MN, Hillard CJ, McCarthy MM. Sex difference in cell proliferation in developing rat amygdala mediated by endocannabinoids has implications for social behavior. *Proc Natl Acad Sci U S A.* 2010;107(47):20535-20540.

LACTMED: Buprenorphine. TOXNET Toxicology Data Network. Bethesda, MD: U.S. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+lactmed:@term+@DOCNO+338. Revised May 5, 2015. Accessed July 7, 2015.

LaGasse LL, Derauf C, Smith LM, et al. Prenatal methamphetamine exposure and childhood behavior problems at 3 and 5 years of age. *Pediatrics.*2012;129(4):681-688.

Langdon KJ, Leventhal AM, Stewart S, Rosenfield D, Steeves D, Zvolensky MJ. Anhedonia and anxiety sensitivity: prospective relationships to nicotine withdrawal symptoms during smoking cessation. *J Stud Alcohol Drugs.* 2013;74(3):469-478.

Leung GM, Ho LM, Lam TH. Secondhand smoke exposure, smoking hygiene, and hospitalization in the first 18 months of life. *Arch Pediatr Adolesc Med.*2004;158(7):687-693.

Lieber CS. Ethnic and gender differences in ethanol metabolism. *Alcohol Clin Exp Res.* 2000;24(4):417-418.

Liechti ME, Gamma A, Vollenweider FX. Gender differences in the subjective effects of MDMA. *Psychopharmacology (Berl).* 2001;154(2):161-168.

Lin SK, Ball D, Hsiao CC, Chiang YL, Ree SC, Chen CK. Psychiatric comorbidity and gender differences of persons incarcerated for methamphetamine abuse in Taiwan. *Psychiatry Clin Neurosci.* 2004;58(2):206-212.

Lum PJ, Sears C, Guydish J. Injection risk behavior among women syringe exchangers in San Francisco. *Subst Use Misuse.* 2005;40(11):1681-1696.

Mack KA, Jones CM, Paulozzi LJ. Vital Signs: overdoses of prescription opioid pain relievers and other drugs among women – United States, 1999-2010. *Morbidity and Mortality Weekly Report.* 2013;62(26):537-542.

Makela P, Wakeley J, Gijsman H, Robson PJ, Bhagwagar Z, Rogers RD. Low doses of Δ-9-tetrahydrocannabinol (THC) have divergent effects on short-term spatial memory in young, healthy adults. *Neuropsychopharmacology.* 2006;31:462-470.

Mann K, Ackermann K, Croissant B, Mundle G, Nakovics H, Diehl A. Neuroimaging of gender differences in alcohol dependence: are women more vulnerable? *Alcohol Clin Exp Res.* 2005;29(5):896-901.

Mark K, Desai A, Terplan M. Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes [published online ahead of print April 19, 2015]. *Arch Womens Ment Health.*

Martin CE, Longinaker N, Mark K, Chisolm, MS, Terplan M. Recent trends in treatment admissions for marijuana use during pregnancy. *J Addict Med.* 2015;9(2):99-104.

McHugh RK, DeVito EE, Dodd D, et al. Gender differences in a clinical trial for prescription opioid dependence. *J Subst Abuse Treat.* 2013;45(1):38-43.

McMurtrie C, Rosenberg KD, Kerker BD, Kan J, Graham EH. A unique drug treatment program for pregnant and postpartum substance-using women in New York City: results of a pilot project, 1990-1995. *Am J Drug Alcohol Abuse.* 1999;25(4):701-713.

McQueeny T, Padula CB, Price J, Medina KL, Logan P, Tapert SF. Gender effects on amygdala morphometry in adolescent marijuana users. *Behav Brain Res.*2011;224(1):128-134.

MDMA can be fatal in warm environments [news release]. Rockville, MD: National Institute on Drug Abuse; June 3, 2014. www.drugabuse.gov/news-events/news-releases/2014/06/mdma-can-be-fatal-in-warm-environments. Accessed July 7, 2015.

Medina KL, McQueeny T, Nagel BJ, Hanson KL, Yang TT, Tapert SF. Imaging Study: Prefrontal cortex morphometry in abstinent adolescent marijuana users: subtle gender effects. *Addict Biol.* 2009;14(4):457-468.

Melikian AA, Djordevic MV, Hosey J, et al. Gender differences relative to smoking behavior and emissions of toxins from mainstream cigarette smoke. *Nicotine Tob Res*. 2007;9(3):377-387.

Mennella J. Alcohol's Effect on Lactation. National Institute on Alcohol Abuse and Alcoholism. http://pubs.niaaa.nih.gov/publications/arh25-3/230-234.htm. Accessed July 7, 2015.

Mennella JA, Yourshaw LM, Morgan LK. Breastfeeding and smoking: short-term effects on infant feeding and sleep. *Pediatrics.* 2007;120(3):497-502.

Mereu G, Fà M, Ferraro L, et al. Prenatal exposure to a cannabinoid agonist produces memory deficits linked to dysfunction in hippocampal long-term potentiation and glutamate release. *Proc Natl Acad Sci U S A.* 2003;100(8):4915-4920.

Meyer MC, Johnston AM, Crocker AM, Heil SH. Methadone and buprenorphine for opioid dependence during pregnancy: a retrospective cohort study. *J Addict Med.* 2015;9(2):81-86.

Moritz ML, Kalantar-Zadeh K, Ayus JC. Ecstacy-associated hyponatremia: why are women at risk? *Nephrol Dial Transplant.* 2013;28(9):2206-2209.

National Heart, Lung, and Blood Institute (NHLBI). *Problem Sleepiness in Your Patient.* Bethesda, MD: National Institutes of Health; 1997. NIH Publication No. 97-4073.

National Institute of Mental Health (NIMH). *Anxiety Disorders.* Bethesda, MD: National Institutes of Health; 2009. NIH Publication No. 09-3879.

National Institute of Mental Health (NIMH). *Women and Depression: Discovering Hope.* Bethesda, MD: National Institutes of Health; 2009. NIH Publication No. 09-4779.

National Institute on Alcohol Abuse and Alcoholism (NIAAA). *Alcohol: A Women's Health Issue.* Bethesda, MD: National Institutes of Health; 2008. NIH Publication No. 03-4956.

National Institute on Alcohol Abuse and Alcoholism (NIAAA). Are women more vulnerable to alcohol's effects? *Alcohol Alert.* Rockville, MD: National Institute on Alcohol Abuse and Alcoholism; 1999.

National Institute on Drug Abuse (NIDA). *Principles of Drug Addiction Treatment: A Research-Based Guide, Third Edition.* Bethesda, MD: National Institutes of Health; 2012. NIH Publication No. 12-4180.

National Institutes of Health (NIH). Amendment: NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research. http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html. Released October 9, 2001. Accessed July 7, 2015.

Neonatal abstinence syndrome. MedlinePlus. U.S. National Library of Medicine. www.nlm.nih.gov/medlineplus/ency/article/007313.htm. Updated January 31, 2014. Accessed July 7, 2015.

New CDC Vital Signs: Prescription Painkiller Epidemic Among Women [press release]. Atlanta, GA: Centers for Disease Control and Prevention; December 16, 2013.www.cdc.gov/media/dpk/2013/dpk-Prescription%20drug%20overdose.html. Accessed July 7, 2015.

NIDA Notes: Gender Differences in Drug Abuse Risks and Treatment. National Institute on Drug Abuse.http://archives.drugabuse.gov/NIDA_Notes/NNVol15N4/Tearoff.html. Published September 2000. Accessed July 7, 2015.

NIH study examines nicotine as a gateway drug [news release]. Rockville, MD: National Institute on Drug Abuse; November 2, 2011. www.drugabuse.gov/news-events/news-releases/2011/11/nih-study-examines-nicotine-gateway-drug. Accessed July 7, 2015.

Office of Research on Women's Health (ORWH). How sex and gender influence health and disease [infographic]. http://orwh.od.nih.gov/resources/sex-and-gender-infographic/images/SexGenderInfographic_11X17_508.pdf. Accessed July 7, 2015.

Patrick SW, Dudley J, Martin PR, et al. Prescription opioid epidemic and infant outcomes. *Pediatrics.* 2015;135(5):842-850.

Penetar DM, Kouri EM, Gross MM, et al. Transdermal nicotine alters some of marihuana's effects in male and female volunteers. *Drug Alcohol Depend.* 2005;79(2):211-223.

Perez-Reyes M, Wall ME. Presence of Δ9-tetrahydrocannabinol in human milk. *N Engl J Med.* 1982;307(13):819-820.

Perkins KA, Giedgowd GE, Karelitz JL, Conklin CA, Lerman C. Smoking in response to negative mood in men versus women as a function of distress tolerance. *Nicotine Tob Res.* 2012;14(12):1418-1425.

Perkins KA, Scott J. Sex differences in long-term smoking cessation rates due to nicotine patch. *Nicotine Tob Res.* 2008;10(7):1245-1250.

Piazza NJ, Vrbka JL, Yeager RD. Telescoping of alcoholism in women alcoholics. *Int J Addict.* 1989;24(1):19-28.

Piper ME, Cook JW, Schlam TR, et al. Gender, race, and education differences in abstinence rates among participants in two randomized smoking cessation trials.*Nicotine Tob Res.* 2010;12(6):647-657.

Pope HG Jr, Jacobs A, Mialet JP, Yurgelun-Todd D, Gruber S. Evidence for a sex-specific residual effect of cannabis on visuospatial memory. *Psychother Psychosom.* 1997;66(4):179-184.

Powis B, Griffiths P, Gossop M, Strang J. The differences between male and female drug users: community samples of heroin and cocaine users compared. *Subst Use Misuse.* 1996;31(5):529-543.

Pregnancy: Medications and Pregnancy. Centers for Disease Control and Prevention. www.cdc.gov/pregnancy/meds/index.html. Reviewed December 3, 2014. Accessed July 7, 2015.

Quitting Smoking Benefits Health Despite Weight Gain [research update]. Bethesda, MD: National Institutes of Health. www.nih.gov/researchmatters/march2013/03252013smoking.htm. Published March 25, 2013. Accessed July 7, 2015.

Randall CL, Roberts JS, Del Boca FK, Carroll KM, Connors GJ, Mattson ME. Telescoping of landmark events associated with drinking: a gender comparison. *J Stud Alcohol.* 1999;60(2):252-260.

Rawson RA, Gonzales R, Obert JL, McCann MJ, Brethen P. Methamphetamine use among treatment-seeking adolescents in Southern California: participant characteristics and treatment response. *J Subst Abuse Treat.* 2005;29(2):67-74.

Reauthorizing the Violence Against Women Act: Key Provisions in S. 47. The White House. www.whitehouse.gov/sites/default/files/docs/vawa_improvements_1_pager.pdf. Accessed July 7, 2015.

Rehm J, Shield KD, Joharchi N, Shuper PA. Alcohol consumption and the intention to engage in unprotected sex: systematic review and meta-analysis of experimental studies. *Addiction.* 2012;107(1):51-59.

Reproductive Health: Tobacco Use and Pregnancy. Centers for Disease Control and Prevention. www.cdc.gov/Reproductivehealth/TobaccoUsePregnancy/index.htm. Reviewed August 5, 2014. Accessed July 7, 2015.

Report: Intimate Partner Violence Screening and Counseling Research Symposium, December 9, 2013. Women's Health Resources. Office of Research on Women's Health. http://whr.nlm.nih.gov/Report_IPV_Symposium.pdf. Accessed July 7, 2015.

Richardson GA, Ryan C, Willford J, Day NL, Goldschmidt L. Prenatal alcohol and marijuana exposure: effects on neuropsychological outcomes at 10 years. *Neurotoxicol Teratol.* 2002;24(3):309-320.

Riley JL III, Robinson ME, Wise EA, Myers CD, Fillingim RB. Sex differences in the perception of noxious experimental stimuli: a meta-analysis. *Pain.* 1998;74(2-3):181-187.

Roberson EK, Patrick WK, Hurwitz EL. Marijuana use and maternal experiences of severe nausea during pregnancy in Hawai'i. *Hawaii J Med Public Health.* 2014;73(9):283-287.

Robbins SJ, Ehrman RN, Childress AR, O'Brien CP. Comparing levels of cocaine cue reactivity in male and female outpatients. *Drug Alcohol Depend.* 1999;53(3):223-230.

Romero EM, Fernández B, Sagredo O, et al. Antinociceptive, behavioural and neuroendocrine effects of CP 55,940 in young rats. *Brain Res Dev Brain Res.* 2002;136(2):85-92.

Rubonis AV, Colby SM, Monti PM, Rohsenow DJ, Gulliver SB, Sirota AD. Alcohol cue reactivity and mood induction in male and female alcoholics. *J Stud Alcohol.* 1994;55(4):487-494.

Rydell M, Magnusson C, Cnattingius S, Granath F, Svensson AC, Galanti MR. Exposure to maternal smoking during pregnancy as a risk factor for tobacco use in adult offspring. *Am J Epidemiol.* 2014;179(12):1409-1417.

Schaefer TL, Grace CE, Braun AA, et al. Cognitive impairments from developmental exposure to serotonergic drugs: citalopram and MDMA. *Int J Neuropsychopharmacol.* 2013;16(6):1383-1394.

Schempf AH, Strobino DM. Illicit drug use and adverse birth outcomes: is it drugs or context? *J Urban Health.* 2008;85(6):858-873.

Shen W, Liu Y, Longhui L, Zhang Y, Zhou W. Negative moods correlate with craving in female methamphetamine users enrolled in compulsory detoxification. *Subst Abuse Treat Prev Policy.*2012;7:44.

Schoenbaum EE, Hartel D, Lo Y, et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis.* 2005;41(10):1517-1524.

Shiono PH, Klebanoff MA, Nugent RP, et al. The impact of cocaine and marijuana use on low birth weight and preterm birth: a multicenter study. *Am J Obstet Gynecol.* 1995;172(1 Pt 1):19-27.

Singer LT, Moore DG, Min MO, et al. One-year outcomes of prenatal exposure to MDMA and other recreational drugs. *Pediatrics.* 2012;130(3):407-413.

Smith LM, LaGasse LL, Derauf C, et al. The infant development, environment, and lifestyle study: effects of prenatal methamphetamine exposure, polydrug exposure, and poverty on intrauterine growth. *Pediatrics.* 2006;118(3):1149-1156.

Smoking & Tobacco Use: Secondhand Smoke (SHS) Facts. Centers for Disease Control and Prevention. www.cdc.gov/tobacco/data_statistics/fact_sheets/secondhand_smoke/general_facts/index.htm#harm. Reviewed February 6, 2015. Accessed July 7, 2015.

Smoking & Tobacco Use: Tobacco-Related Mortality. Centers for Disease Control and Prevention.www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/tobacco_related_mortality/. Reviewed November 21, 2014. Accessed July 7, 2015.

Sonon KE, Richardson GA, Cornelius JR, Kim KH, Day NL. Prenatal marijuana exposure predicts marijuana use in young adulthood. *Neurotoxicol Teratol.* 2015;47:10-15.

Substance Abuse and Mental Health Services Administration (SAMHSA). *Addressing the Needs of Women and Girls: Developing Core Competencies for Mental Health and Substance Abuse Service Professionals.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2011. HHS Publication No. (SMA) 11-4657.

Substance Abuse and Mental Health Services Administration (SAMHSA). *Results from the 2012 National Survey on Drug Use and Health: Mental Health Findings.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2013. HHS Publication No. (SMA) 13-4805. NSDUH Series H-47.

Substance Abuse and Mental Health Services Administration (SAMHSA). *Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014. HHS Publication No. (SMA) 14-4863. NSDUH Series H-48.

Substance Abuse and Mental Health Services Administration (SAMHSA). *Substance Abuse: Clinical Issues in Intensive Outpatient Treatment.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2006. Publication No. (SMA) 06-4182.

Substance Abuse and Mental Health Services Administration (SAMHSA). *Substance Abuse Treatment: Addressing the Specific Needs of Women*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2009. HHS Publication No. (SMA) 09-4426.

Svikis DS, Golden AS, Huggins GR, et al. Cost-effectiveness of treatment for drug-abusing pregnant women. *Drug Alcohol Depend*. 1997;45(1-2):105-113.

Thomas H. A community survey of adverse effects of cannabis use. *Drug Alcohol Depend.* 1996;42(3):201-207.

Thun MJ, Carter BD, Feskanich D, et al. 50-year trends in smoking-related mortality in the United States. *N Engl J Med.* 2013;368(4):351-364.

Tobacco, drug use in pregnancy can double risk of stillbirth. NIH network study documents elevated risk associated with marijuana, other substances [news release]. Bethesda, MD: *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; December 11, 2013.www.nichd.nih.gov/news/releases/Pages/121113-stillbirth-drug-use.aspx. Accessed July 7, 2015.

Tobacco Research and Intervention Program, H. Lee Moffitt Cancer Center & Research Institute, University of South Florida. *Forever Free: A Guide To Remaining Smoke Free. Booklet 3: Smoking And Weight.* Tampa, FL: H. Lee Moffitt Cancer Center & Research Institute, University of South Florida; 2000.

Tolstrup JS, Kjaer SK, Holst C, et al. Alcohol use as predictor for infertility in a representative population of Danish women. *Acta Obstet Gynecol Scand.* 2003;82(8):744-749.

Torres OV, O'Dell LE. Stress is a principal factor that promotes tobacco use in females [published online ahead of print April 22, 2015]. *Prog Neuropsychopharmacol Biol Psychiatry.*

Trezza V. Campolongo P, Cassano T, et al. Effects of perinatal exposure to delta-9-tetrahydrocannabinol on the emotional reactivity of the offspring: a longitudinal behavioral study in Wistar rats. *Psychopharmacology (Berl).* 2008;198(4):529-537.

Tseng AH, Craft RM. Sex differences in antinociceptive and motoric effects of cannabinoids. *Eur J Pharmacol.* 2001;430(1):41-47.

Verheyden SL, Hadfield J, Calin T, Curran HV. Sub-acute effects of MDMA (+/-3,4-methylenedioxymethamphetamine, "ecstasy") on mood: evidence of gender differences. *Psychopharmacology (Berl).* 2002;161(1):23-31.

Volpicelli JR, Markman I, Monterosso J, Filing J, O'Brien CP. Psychosocially enhanced treatment for cocaine-dependent mothers: evidence of efficacy. *J Subst Abuse Treat.* 2000;18(1):41-49.

Weinberger AH, Smith PH, Allen SS, et al. Systematic and meta-analytic review of research examining the impact of menstrual cycle phase and ovarian hormones on smoking and cessation. *Nicotine Tob Res.* 2015;17(4):407-421.

Wendell AD. Overview and epidemiology of substance abuse in pregnancy. *Clin Obstet Gynecol.* 2013;56(1):91-96.

Westfall RE, Janssen PA, Lucas P, Capler R. Survey of medicinal cannabis use among childbearing women: patterns of its use in pregnancy and retroactive self-assessment of its efficacy against 'morning sickness.' *Complement Ther Clin Pract.* 2006;12(1):27-33.

Wickström R. Effects of nicotine during pregnancy: human and experimental evidence. *Curr Neuropharmacol.* 2007;5(3):213-222.

Wilcox AJ, Weinberg CR, Baird DD. Risk factors for early pregnancy loss. *Epidemiology.* 1990;1(5):382-385.

Wiley JL. Sex-dependent effects of Δ9-tetrahydrocannabinol on locomotor activity in mice. *Neurosci Lett.* 2003;352(2):77-80.

Winsauer PJ, Daniel JM, Filipeanu CM, et al. Long-term behavioral and pharmacodynamics effects of delta-9-tetrahydrocannabinol in female rats depend on ovarian hormone status. *Addict Biol.* 2011;16(1):64-81.

Wizemann TM, Pardue M-L, eds, Committee on Understanding the Biology of Sex and Gender Differences. *Exploring the Biological Contributions to Human Health: Does Sex Matter?* Washington, DC: National Academies Press; 2001.

Zweben JE, Cohen JB, Christian D, et al. Psychiatric symptoms in methamphetamine users. *Am J Addict.* 2004;13(2):181-190.

Where can I get further information about substance use in women?

To learn more about substance use in women, visit the NIDA website at **www.drugabuse.gov** or contact *DrugPubs* Research Dissemination Center at 877-NIDA-NIH (877-643-2644) (TTY/TDD: 240-645-0228).

NATIONAL INSTITUTE ON DRUG ABUSE
NIDA DRUGPUBS
RESEARCH DISSEMINATION CENTER

NIDA's website includes:

- Information on drugs of abuse and related health consequences
- NIDA publications, news, and events
- Resources for health care professionals, educators, and patients and families
- Information on NIDA research studies and clinical trials
- Funding information (including program announcements and deadlines)
- International activities
- Links to related websites (access to websites of many other organizations in the field)
- Information in Spanish (en español)

NIDA Websites and Webpages

www.drugabuse.gov
www.teens.drugabuse.gov
www.easyread.drugabuse.gov
www.drugabuse.gov/related-topics/women-drugs
www.drugabuse.gov/publications/finder/t/160/drugfacts
www.hiv.drugabuse.gov
www.researchstudies.drugabuse.gov
www.irp.drugabuse.gov

For Physician Information

NIDAMED

www.drugabuse.gov/nidamed

Other Websites

Information on substance use in women is also available through:

- Substance Abuse and Mental Health Services Administration: *www.samhsa.gov*
- Drug Enforcement Administration: *www.dea.gov*
- Monitoring the Future: *www.monitoringthefuture.org*
- Partnership for Drug-Free Kids: *www.drugfree.org*

Updated September 2016