

National Institute on Drug Abuse (NIDA) Substance Use in Women

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Summary

People may face unique issues when it comes to substance use, as a result of both sex and gender. *Sex differences* result from biological factors, such as sex chromosomes and hormones, while *gender differences* are based on culturally defined roles for men and women, as well as those who do not identify with either category. Gender roles influence how people perceive themselves and how they interact with others.^{1,2} Sex and gender can also interact with each other to create even more complex differences among people. While the NIH is working to strengthen research on sex/gender differences across domains of health, current evidence is limited; for the purpose of this report, male and female subjects identify as such across both sex and gender.

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 substance use disorder.

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 (e.g. greater sensitivity to visual and olfactory cues as triggers and greater concern about weight gain while quitting).

Sources: ORWH, 2015; NIDA, 2002

For example, women and men sometimes use drugs for different reasons and respond to them differently. Additionally, substance use disorders can manifest differently in women than in men. A substance use disorder occurs when a person continues to use drugs or alcohol even after experiencing negative consequences.

Some of the unique issues women who use drugs face relate to their reproductive cycles. Some substances can increase the likelihood of infertility³⁻⁵ and early onset of menopause.⁶ Substance use is also further complicated during pregnancy and breastfeeding. Pregnant women using drugs, including tobacco and alcohol, can pass those drugs to their developing fetuses and cause them harm. Similarly, new mothers using drugs can pass those to their babies through breast milk and cause them harm. (See [Substance Use While Pregnant and](#)

Breastfeeding)

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,⁷ 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.^{8,9}

Women, pregnant or not, 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.¹⁰ (See [Sex and Gender Differences in Substance Use Disorder Treatment](#))

Despite the many differences between men and women, for many years most animal and human research has traditionally used male participants. To find out more about sex and gender differences to inform better treatment approaches, federal agencies have developed guidelines to promote the inclusion of women and analyses of sex and gender differences in research.^{11,12} (See [The Importance of Including Women in Research](#))

Sex and Gender Differences in Substance Use

Men are more likely than women to use almost all types of illicit drugs,¹³ 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.¹⁴ However, women are just as likely as men to develop a substance use disorder.¹⁵ In addition, women may be more susceptible to craving¹⁶⁻¹⁹ and relapse,^{20,21} 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.

Illegal Drugs

Marijuana (Cannabis)

Similar to other addictive drugs, fewer females than males use marijuana.¹³ 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,^{22,23} while males show a greater marijuana-induced high.^{24,25}

In one study specific to teenagers, male high school students who

smoke marijuana reported poor family relationships and problems at school more often than female students who smoke marijuana.²⁶ However, a few studies have suggested that teenage girls who use marijuana may have a higher risk of brain structural abnormalities associated with regular marijuana exposure than teenage boys.^{27,28}

Animal studies show that female rats are more sensitive to the rewarding,^{29,30} pain-relieving,³¹⁻³³ and activity-altering^{31,33,34} effects of marijuana's main active ingredient, *delta-9-tetrahydrocannabinol* (THC). Many of these differences have been attributed to the effects of sex hormones,^{29,31,35-37} 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.^{30,38}

Marijuana Use Disorder

Men		Women	
Similarities			
<ul style="list-style-type: none"> • At least one other mental health disorder • Low rate of seeking treatment 			
Differences			
<ul style="list-style-type: none"> • Other substance use disorders • Antisocial personality disorder • Severity of disorder 		<ul style="list-style-type: none"> • Panic attacks • Anxiety disorders • Disorder develops more quickly 	

For both sexes, marijuana use disorder is associated with an increased risk of at least one other mental health condition, such

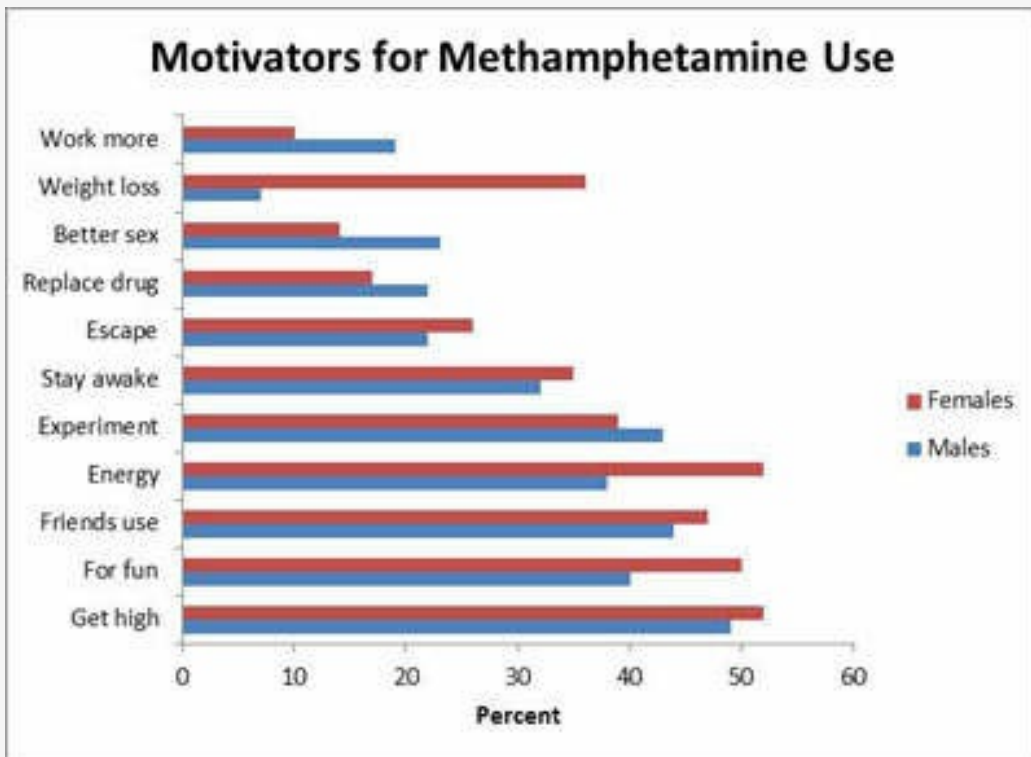
as depression or anxiety. However, men who are addicted to marijuana have higher rates of other substance use problems as well as antisocial personality disorders. By contrast, women who are addicted to marijuana have more panic attacks³⁹ and anxiety disorders.^{40,41} Although the severity of marijuana use disorders is generally higher for men, women tend to develop these disorders more quickly after their first marijuana use.⁴² Rates of seeking treatment for marijuana use disorder are low for both sexes.⁴³

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.⁴⁴⁻⁴⁷ 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, 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 detrimental effects of cocaine on the brain.⁴⁸

As for methamphetamine, women report using the drug because they believe it will increase energy and decrease exhaustion associated with work, home care, child care, and family responsibilities. Weight loss is another incentive women cite for methamphetamine use—and one reported significantly more by women than by men.^{49,50} 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.^{49,50} Women who use methamphetamine also have high rates of co-occurring depression.⁵¹⁻⁵⁴



Source: Brecht et al., 2004

Women tend to begin using methamphetamine at an earlier age than do men,^{50,51} with female users typically more dependent on methamphetamine compared to male users.^{53,55} Women are also less likely to switch to another drug when they lack access to methamphetamine.⁵⁰ In addition, as with other substances, women tend to be more receptive than men to methamphetamine treatment.^{51,54,56}

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.⁵⁷ 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.⁵⁸ Both men and women show similar increases in aggression a few days after they stop using MDMA.^{58,59}

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.^{60,61} MDMA can also interfere with temperature regulation and cause acute hyperthermia, leading to neurotoxic effects and even death.⁶²

Heroin

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

Research suggests that women tend to use smaller amounts of heroin and for less time, and are less likely than men to inject it.⁶³ Most women who inject heroin point to social pressure and sexual partner encouragement as factors.⁶³⁻⁶⁶ One study indicates that women are more at risk than men for overdose death during the first few years of injecting heroin, but 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.⁶⁷

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 drug misuse can be dangerous if mixed together without a physician's guidance, or mixed with other drugs or alcohol.

Prescription Opioids

Some research indicates that women are more sensitive to pain than men⁶⁸ and more likely to have chronic pain,⁶⁹ which could contribute to the high rates of opioid prescriptions among women of reproductive age.⁷⁰ 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.⁷¹

A possible consequence of prescription opioid misuse is fatal overdose, which can occur because opioids suppress breathing. In 2016, 7,109 women and 9,978 men died from prescription opioid overdose (a total of 17,087)* which is about 19 women per day compared to about 27 men dying from overdosing on prescription opioids. However, from 1999 to 2016, deaths from prescription opioid overdoses increased more rapidly for women (596 percent or sevenfold) than for men (312 percent or fourfold). Women between the ages of 45 and 54 are more likely than women of other age groups to die from a prescription opioid overdose.⁷²

*Note that in this instance, “prescription opioids” includes other opioids and methadone (ICD-10 codes T40.2-T40.3).

Anti-Anxiety Medications and Sleeping Aids

Women are more likely to seek treatment for misuse of central nervous system depressants,¹⁴ which include 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 involving medications for mental health conditions, like antidepressants. Antidepressants and benzodiazepines (anti-anxiety or sleep drugs) send more women than men to emergency departments.⁷³ Because women are also more at risk than men for anxiety^{74,75} and insomnia,⁷⁶ 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 substance use disorder or overdose.

Other Substances

Alcohol

In general, men have higher rates of alcohol use, including binge drinking. However, young adults are an exception: girls ages 12 to 20 have slightly higher rates of alcohol misuse and binge drinking than their male counterparts.¹³

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.^{77,78} 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.⁷⁹ 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,⁸⁰ and an increased risk of becoming a victim of violence and sexual assault. In addition, drinking as little as one drink per day is associated with a higher risk of breast cancer in some women, especially those who are postmenopausal or have a family history of breast cancer.⁷⁹

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.^{79,81-83} As a result, women become intoxicated from smaller quantities of alcohol than men.⁸²

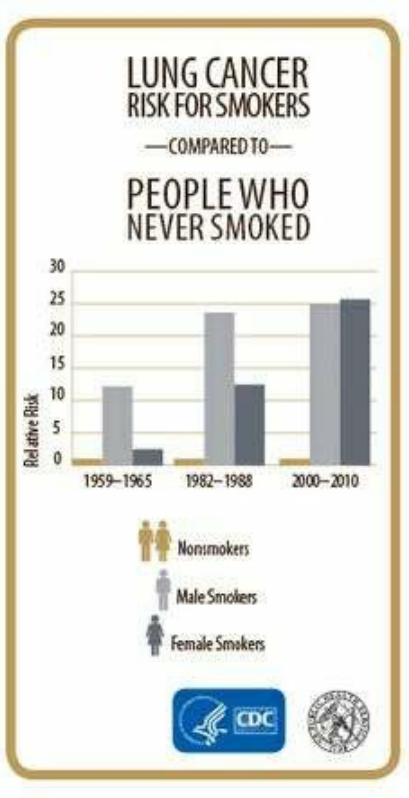
More information on sex and gender differences in alcohol use is available from the [National Institute of Alcohol Abuse and Alcoholism \(NIAAA\)](#).

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.⁸⁴ Women also may smoke for different reasons than men, including regulation of mood and stress.⁸⁵ 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.⁸⁶

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.⁸⁷ 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.⁸⁸ Some dangers associated with smoking—such as blood clots, heart attack, or stroke—increase in women using oral contraceptives.⁸⁹

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.⁹⁰



Source: CDC, 2014

Substance Use While Pregnant and Breastfeeding

Research shows that use of tobacco, alcohol, or illicit drugs or misuse 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 reach the fetus.⁹¹ 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.⁹² Estimates suggest that about 5 percent of pregnant women use one or more addictive substances.⁹³

Regular use of some drugs can cause neonatal abstinence syndrome (NAS), in which the baby goes through withdrawal upon birth. Most research in this area has focused on the effects of opioids (prescription pain relievers or heroin). However, data has shown that use of alcohol, barbiturates, benzodiazepines, and caffeine during pregnancy may also cause the infant to show withdrawal symptoms at birth.⁹⁴ 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.⁹⁵

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

Symptoms of drug withdrawal in a newborn can develop immediately or up to 14 days after birth and can include⁹⁴:

- blotchy skin coloring
- diarrhea
- excessive or high-pitched crying
- abnormal sucking reflex
- fever
- hyperactive reflexes
- increased muscle tone
- irritability
- poor feeding
- rapid breathing
- seizures
- sleep problems

- slow weight gain
- stuffy nose and sneezing
- sweating
- trembling
- vomiting

Effects of using some drugs could be long-term and possibly fatal to the baby:⁹⁵

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

Risks of Sudden Infant Death (SIDS)

Children born to mothers who both drank and smoked beyond the first trimester of pregnancy have a twelvefold increased risk for sudden infant death syndrome (SIDS) compared to those unexposed or only exposed in the first trimester of pregnancy. [New information from the NIH Safe Passage Study](#) calls for stronger public health messaging regarding the dangers of drinking and smoking during pregnancy.

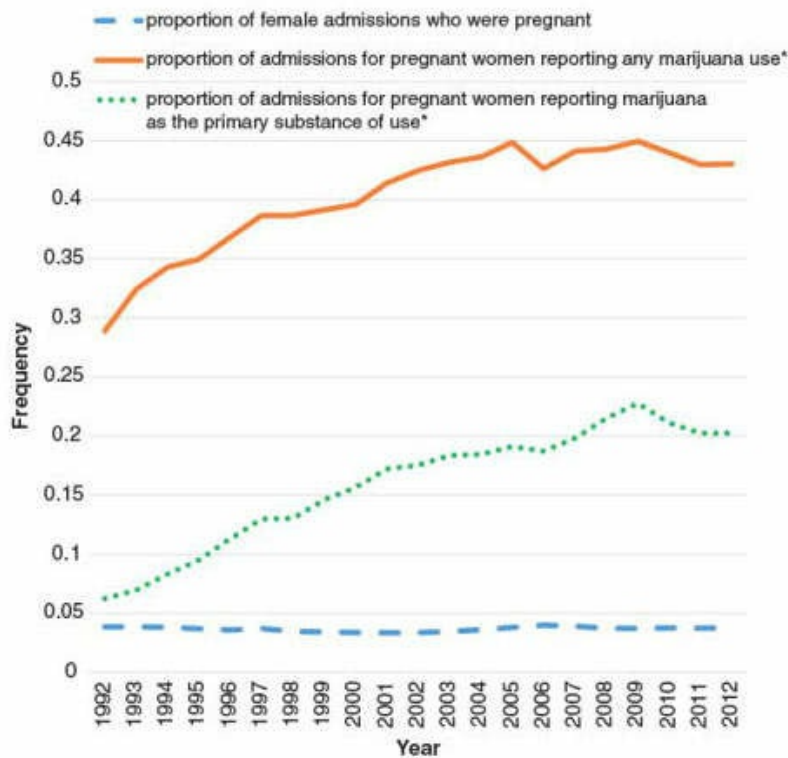
Illegal Drugs

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, significant increases in the number of pregnant women seeking substance use disorder treatment for marijuana use, and confounding effects of polysubstance use.⁹⁶ A 2017 opinion posted by the American College of Obstetrics and Gynecology (ACOG) suggests that cannabis effects on fetal growth (e.g., low birth weight and length) may be more pronounced in women who consume marijuana frequently, especially in the first and second trimesters. ACOG recommends that pregnant women or women contemplating pregnancy should be encouraged to discontinue use of marijuana for medicinal purposes in favor of an alternative therapy for which there are better pregnancy-specific safety data.¹⁹⁰

A recent study suggests that cannabis use more than doubled among pregnant women in the United States from 2010-2017.¹⁹¹ Cannabis use was more common during the first trimester than during the second and third. Between 2002-2003 and 2016-2017, past-month cannabis use increased from 3.4% to 7.0% among pregnant women overall and from 5.7% to 12.1% during the first trimester. The study included information from 467,100 women aged 12-44 who participated in the National Survey on Drug Use and Health (NSDUH). Researchers also concluded that past-month clinician-recommended cannabis use was low among pregnant women, and nonmedical use was lower than among nonpregnant women, possibly reflecting the ACOG recommendations.



Source: Martin et al., 2015

There is no human research connecting marijuana use to the chance of miscarriage,^{98,99} although animal studies indicate that the risk for miscarriage increases if marijuana is used early in pregnancy.¹⁰⁰ Some associations have been found between marijuana use during pregnancy and future developmental and hyperactivity disorders in children.¹⁰¹⁻¹⁰⁴ There is substantial evidence of a statistical association between marijuana smoking among pregnant women and low birth weight.¹⁰⁵ Researchers theorize that elevated levels of carbon dioxide might restrict fetal growth in women who use marijuana during pregnancy.¹⁰⁶ Evidence is mixed related to premature birth,¹⁰⁷ although some evidence suggests long-term use may elevate these risks.¹⁰⁸ 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.¹⁰⁹

Some women report using marijuana to treat severe nausea

associated with their pregnancy;^{110,111} 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 provider. Animal studies have shown that moderate concentrations of THC, 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.¹¹² Animal studies also show learning deficits in prenatally exposed individuals.^{113,114}

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,¹¹⁵ which could indicate problems with neurological development.¹¹⁶ In school, marijuana-exposed children are more likely to show gaps in problem-solving skills, memory,¹¹⁷ and the ability to remain attentive.¹⁰³ 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.¹¹⁸ 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.¹¹⁹ More information on marijuana use during pregnancy in NIDA's [Marijuana Research Report](#).

Despite various surveys, the precise number of women who use marijuana while pregnant is unclear. One study found that women were about twice as likely to screen positive for marijuana use via a drug test than they state in self-reported measures. This suggests that self-reported rates of marijuana use in pregnant females is not an accurate measure of marijuana use and may be an underestimation.⁹⁷

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.¹²⁰ 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.¹²¹ 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.¹²⁰ 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.^{109,122} 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)

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.¹²³

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).⁹³ Pregnancy is accompanied by normal cardiovascular changes, and cocaine use exacerbates these changes—sometimes leading to serious problems with high blood pressure (hypertensive crisis), spontaneous miscarriage, preterm labor, and difficult delivery.¹²³ 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.¹²⁴ 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.^{125,126} Estimates suggest that there are about 750,000 cocaine-exposed pregnancies every year.¹²³

Pregnant women who use methamphetamine have a greater risk of preeclampsia (high blood pressure and possible organ damage),¹²⁷ premature delivery, and placental abruption. Their babies are more likely to be smaller and to have low birth weight.¹²⁸ 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.^{129,130}

MDMA (Ecstasy, Molly)

More research is needed on the effects of MDMA use during pregnancy. What research exists suggests that prenatal MDMA exposure may cause learning, memory,¹³¹ and motor problems in the baby.^{132,133}

Heroin

Heroin use during pregnancy can result in neonatal abstinence syndrome (NAS) specifically associated with opioid use. 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.¹³⁴

Medications

Prescription and Over-the-Counter (OTC) Drugs

Pregnancy can be a confusing time for women facing many choices about legal drugs, like tobacco and alcohol, as well as prescription and over-the-counter (OTC) drugs that may affect the developing fetus. 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,^{[135](#)} and about 9 out of 10 pregnant women take medication.^{[136](#)} The U.S. Food and Drug Administration issued 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.^{[137](#)}



Even so, we know little about the effects of taking most medications during pregnancy. Fewer than 10% of prescriptions have enough information to determine fetal risks.¹³⁸ This is because pregnant women are often not included in studies to determine safety of new medications before they come on the market.¹³⁸ One 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 NAS in the infant.¹³⁹

Although some prescription and OTC medications are safe to take during pregnancy, a pregnant woman should tell her doctor about all prescription and over-the-counter medications, 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 fetus than continuing to use the medication while under a doctor's care.¹⁴⁰ 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](#)."

Some prescription and OTC medications are generally compatible with breastfeeding. Others, such as some anti-anxiety and antidepressant medications, have unknown effects,¹⁴¹ 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.¹⁴²

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](#).

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.¹⁴³ 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.¹⁴⁴

Nicotine (Tobacco Products and e-Cigarettes)

Almost 10 percent of pregnant women in the United States have smoked cigarettes in the past month.¹³ 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.¹⁴⁵ Smoking during pregnancy increases the risk for certain birth defects, premature birth, miscarriage, and low birth weight and is estimated to have caused more than 1,000 infant deaths each year.¹⁴⁶ 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.¹⁴⁷ 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.¹⁴⁸

Research provides strong support that nicotine is a gateway drug, making the brain more sensitive to the effects of other drugs such as cocaine.¹⁴⁹ This shows that pregnant women who use nicotine may be affecting their fetus's brain in ways they may not anticipate. Additionally, e-cigarettes (or e-vaporizers) sometimes contain nicotine. Therefore, those products may also pose a risk to the fetus'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,¹⁵⁰ 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.¹⁵¹

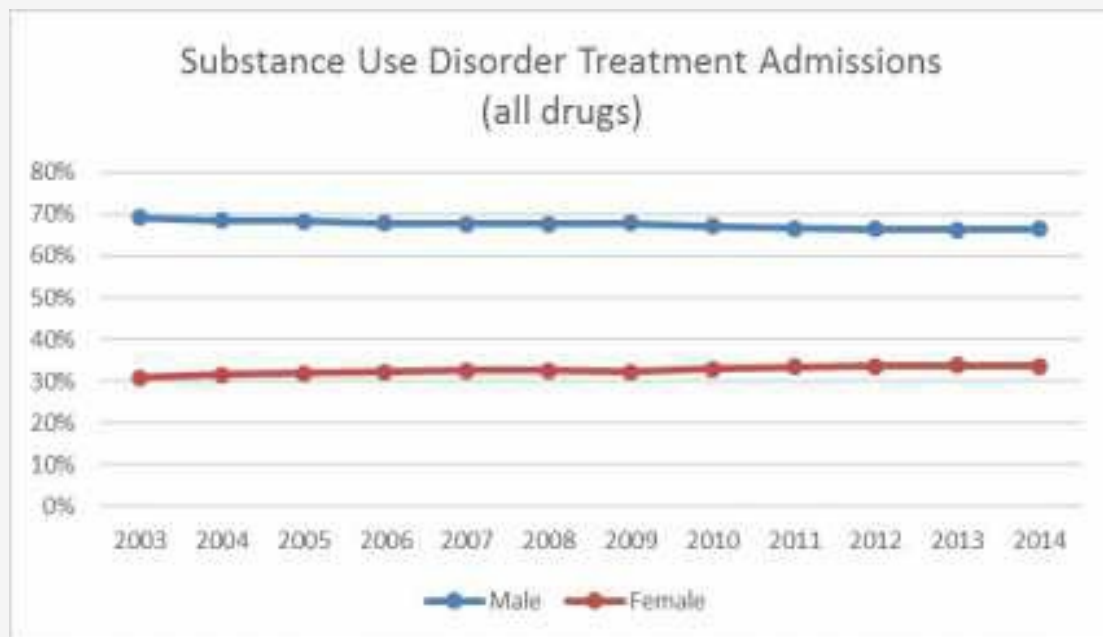
Secondhand Smoke

Newborns exposed to secondhand smoke are at greater risk for SIDS, respiratory illnesses (asthma, respiratory infections, and bronchitis), ear infections,⁸⁸ cavities,¹⁵² and increased medical visits and hospitalizations.¹⁵³ 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.¹⁴ 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.¹⁵⁴

Substance Use Disorder Treatment Admissions (all drugs)

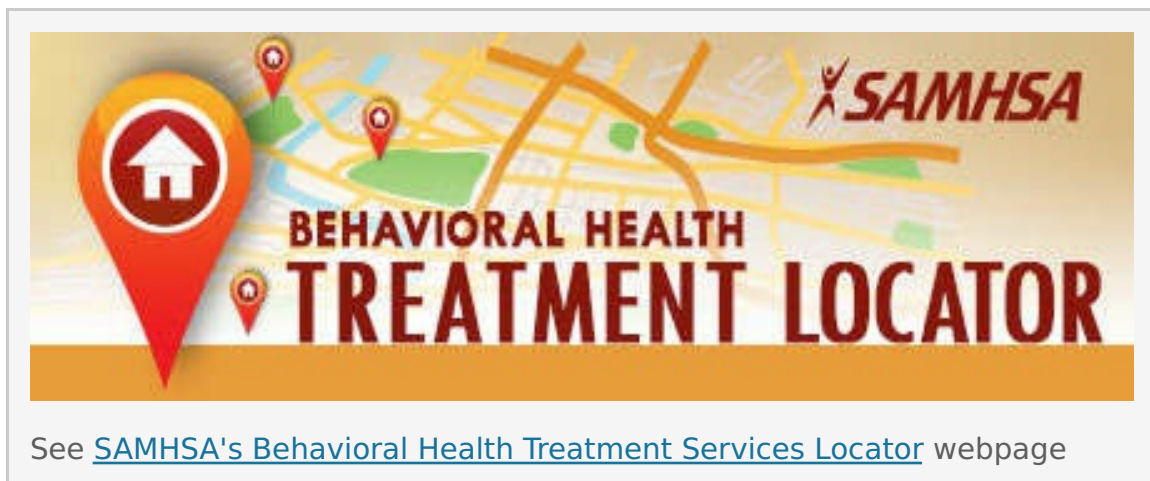


Source: 2014 SAMHSA TEDS

Substance use disorders may progress differently for women than for men. Women often have a shorter history of using certain substances such as cocaine,¹⁵⁵ opioids,⁴² marijuana,^{42,43,156} or alcohol.^{42,157,158}

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.¹⁵⁹

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.⁷



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.⁹⁰ 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.^{160,161} Nicotine craving¹⁶² and withdrawal¹⁶³ vary across the menstrual cycle, which may further complicate a woman's attempts to quit.

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

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.¹⁶⁴ In fact, long-term quitters gain, on average, only 2 pounds.¹⁶⁵ Most importantly, the health benefits of quitting smoking far exceed the risks of gaining a few pounds. Quitting also decreases risks for various types of cancers, heart attack, and lung disease.¹⁶⁴

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.¹⁶⁶

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,¹⁶⁸ parenting classes, and vocational training.^{169,170}

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.¹⁶⁷ State-level contacts for this program are available from <https://www.samhsa.gov/sites/default/files/ssadirectory.pdf>

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, while nonpharmacological treatments are preferred, it sometimes 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 Use 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. 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.^{166,171} In general, it is neither recommended nor necessary for pregnant women to cease methadone or buprenorphine treatment.^{167,171} However, newborns exposed to methadone during pregnancy can require treatment for withdrawal symptoms.

Some studies suggest that buprenorphine (Suboxone[®], Subutex[®]) has some advantages over single-dose methadone as a treatment for opioid use disorder 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.¹⁷²

Pregnant women who take buprenorphine for opioid use disorder 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.¹⁷³

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.¹⁷³

As for infants born with NAS due to opioids, recovery can require hospitalization and possibly treatment with morphine or methadone to relieve symptoms;⁹⁴ researchers have also studied buprenorphine for this purpose.¹⁷⁴ There is some evidence that buprenorphine is superior to morphine in treating infants with opioid-related NAS. A NIDA-funded study published found that treating NAS babies with sublingual buprenorphine resulted in a shorter duration of treatment than oral morphine. It also resulted in a shorter length of hospital stay, with similar rates of adverse events.¹⁷⁵

Other Sex and Gender Issues for Women Related to Substance Use

Co-Occuring Mental Health Disorders



More information about comorbidity can be found in [NIDA's Research Report](#).

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,¹³ women are more likely to suffer from certain mental health conditions, such as depression,¹⁷⁶ anxiety, post-traumatic stress disorder (PTSD),¹⁷⁷ and eating disorders.¹⁷⁸ Some women report using substances to relieve stress or negative emotions.¹⁷⁹⁻¹⁸¹ 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.¹⁰

Women, Violence, and Substance Abuse

More than 1 in 3 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.¹⁸² Victims of violence are at increased risk of chronic health conditions, including obesity, chronic pain, depression, and substance use.¹⁸³ 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.¹⁸⁴ In 2013, President Obama reauthorized the Act to expand programs for reaching especially vulnerable populations.¹⁸⁵

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 copays 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.¹⁸⁶

Race and Ethnicity

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. As discussed above, these issues are risk factors for substance use and should be addressed during treatment. More information can be found in [Women of Color: Health Data Book](#).

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.¹⁸⁷ 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
- 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.¹⁸⁸
- 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*

[More information about comorbidity can be found in NIDA's research report on comorbidity.](#)

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.¹²

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.¹⁸⁹

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).

NIDA's website includes:

- Information on drugs that people use and misuse 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.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
- NIDA's Substance Use in Women DrugFacts: <https://www.drugabuse.gov/publications/drugfacts/substance-use-in-women>
- NIDA's Easy to Read Drug Use Hurts Unborn Babies: <https://easyread.drugabuse.gov/content/drug-use-hurts-unborn-babies>
- CDC's Fact Sheet on Substance Use During Pregnancy: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/substance-abuse/substance-abuse-during-pregnancy.htm?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Freproductivehealth%2Fr

Treatment Resources

- Find behavioral health treatment:
<https://findtreatment.samhsa.gov>
- Find Smoking cessation programs. The U.S. Department of Health and Human Services has resources to help a woman quit smoking at <http://women.smokefree.gov/>

References

1. Office of Research on Women's Health (ORWH). How Sex and Gender Influence Health and Disease [*Infographic*].; n.d. https://orwh.od.nih.gov/resources/pdf/SexGenderInfographic_11x17_508.pdf
2. Institute of Medicine (US) Committee on Understanding the Biology of Sex and Gender Differences. *Exploring the Biological Contributions to Human Health: Does Sex Matter?* (Wizemann TM, Pardue M-L, eds.). Washington (DC): National Academies Press (US); 2001. <http://www.ncbi.nlm.nih.gov/books/NBK222288/>. Accessed January 3, 2018.
3. 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. doi:10.1016/j.fertnstert.2003.06.018
4. 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.
5. 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.
6. Schoenbaum EE, Hartel D, Lo Y, et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2005;41(10):1517-1524. doi:10.1086/497270
7. Center for Substance Abuse Treatment. *Substance Abuse: Clinical Issues in Intensive Outpatient Treatment*. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2006. <http://www.ncbi.nlm.nih.gov/books/NBK64093/>. Accessed January 19, 2018.
8. Daley M, Argeriou M, McCarty D, Callahan JJ, 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. doi:10.1080/02791072.2001.10400469

9. 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.
10. Substance Abuse and Mental Health Services Administration (SAMHSA). Addressing the Needs of Women and Girls: Core Competencies for Mental Health and Substance Abuse Service Professionals. Published October 1, 2011. Accessed January 3, 2018.
11. National Institutes of Health (NIH). *Amendment: NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research.*; 2001.
<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html>.
12. Clayton JA, Collins FS. Policy: NIH to balance sex in cell and animal studies. *Nature.* 2014;509(7500):282-283.
13. Center for Behavioral Health Statistics and Quality. *Results from the 2016 National Survey on Drug Use and Health: Detailed Tables.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2017.
<https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>. Accessed November 7, 2017.
14. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Treatment Episode Data Set (TEDS): 2004-2014. *National Admissions to Substance Abuse Treatment Services.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016.
https://www.dasis.samhsa.gov/dasis2/teds_pubs/2014_teds_rpt_natl.pdf.
15. 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. doi:10.1037/1064-1297.2.3.244
16. 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.

17. 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. doi:10.1016/j.drugalcdep.2015.02.016
18. Fox HC, Morgan PT, Sinha R. Sex differences in guanfacine effects on drug craving and stress arousal in cocaine-dependent individuals. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol.* 2014;39(6):1527-1537. doi:10.1038/npp.2014.1
19. 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(1-2):29-37. doi:10.1016/j.drugalcdep.2012.12.025
20. 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. doi:10.1007/s00213-005-0071-y
21. 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.
22. Makela P, Wakeley J, Gijsman H, Robson PJ, Bhagwagar Z, Rogers RD. Low doses of delta-9 tetrahydrocannabinol (THC) have divergent effects on short-term spatial memory in young, healthy adults. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol.* 2006;31(2):462-470. doi:10.1038/sj.npp.1300871
23. Pope HG, 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.
24. Haney M. Opioid antagonism of cannabinoid effects: differences between marijuana smokers and nonmarijuana smokers. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol.* 2007;32(6):1391-1403. doi:10.1038/sj.npp.1301243

25. Penetar DM, Kouri EM, McCarthy EM, et al. Nicotine Pretreatment Increases Dysphoric Effects of Alcohol in Luteal-Phase Female Volunteers. *Int J Environ Res Public Health*. 2009;6(2):526-546. doi:10.3390/ijerph6020526
26. 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. doi:10.1081/JA-200030803
27. Medina KL, McQueeney T, Nagel BJ, Hanson KL, Yang TT, Tapert SF. Prefrontal cortex morphometry in abstinent adolescent marijuana users: subtle gender effects. *Addict Biol*. 2009;14(4):457-468. doi:10.1111/j.1369-1600.2009.00166.x
28. McQueeney 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. doi:10.1016/j.bbr.2011.05.031
29. 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. doi:10.1038/sj.bjp.0707465
30. 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. doi:10.1016/j.lfs.2012.06.009
31. Craft RM, Wakley AA, Tsutsui KT, Laggart JD. Sex differences in cannabinoid 1 vs. cannabinoid 2 receptor-selective antagonism of antinociception produced by delta9-tetrahydrocannabinol and CP55,940 in the rat. *J Pharmacol Exp Ther*. 2012;340(3):787-800. doi:10.1124/jpet.111.188540
32. 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.
33. Tseng AH, Craft RM. Sex differences in antinociceptive and motoric

- effects of cannabinoids. *Eur J Pharmacol*. 2001;430(1):41-47.
34. Wiley JL. Sex-dependent effects of Δ 9-tetrahydrocannabinol on locomotor activity in mice. *Neurosci Lett*. 2003;352(2):77-80. doi:10.1016/j.neulet.2003.08.050
 35. Craft R, Leiti M. Gonadal hormone modulation of the behavioral effects of Δ 9-tetrahydrocannabinol in male and female rats. *Eur J Pharmacol*. 2008;578:37-42. doi:10.1016/j.ejphar.2007.09.004
 36. Fattore L, Spano M, 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. doi:10.1111/j.1476-5381.2010.00734.x
 37. Winsauer PJ, Daniel JM, Filipeanu CM, et al. Long-term behavioral and pharmacodynamic effects of delta-9-tetrahydrocannabinol in female rats depend on ovarian hormone status. *Addict Biol*. 2011;16(1):64-81.
 38. 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. doi:10.1073/pnas.1005003107
 39. Thomas H. A community survey of adverse effects of cannabis use. *Drug Alcohol Depend*. 1996;42(3):201-207.
 40. Buckner JD, Heimberg RG, Schneier FR, Liu S-M, 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. doi:10.1016/j.drugalcdep.2011.12.023
 41. 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. doi:10.1016/j.janxdis.2006.03.002
 42. 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. doi:10.1016/j.drugalcdep.2004.02.001
43. 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. doi:10.1016/j.drugalcdep.2012.10.015
 44. Evans SM, Foltin RW. Exogenous progesterone attenuates the subjective effects of smoked cocaine in women, but not in men. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol.* 2006;31(3):659-674. doi:10.1038/sj.npp.1300887
 45. 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.
 46. 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.
 47. 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. doi:10.1007/7854_2010_93
 48. NIDA Notes: Gender Differences in Drug Abuse Risks and Treatment. <https://archives.drugabuse.gov/news-events/nida-notes/2000/09/gender-differences-in-drug-abuse-risks-treatment>. Published September 1, 2000. Accessed January 26, 2018.
 49. 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.
 50. Brecht M-L, O'Brien A, von Mayrhauser C, Anglin MD. Methamphetamine use behaviors and gender differences. *Addict Behav.* 2004;29(1):89-106.
 51. Hser Y-I, Evans E, Huang Y-C. Treatment outcomes among women and men methamphetamine abusers in California. *J Subst Abuse Treat.* 2005;28(1):77-85. doi:10.1016/j.jsat.2004.10.009

52. Zweben JE, Cohen JB, Christian D, et al. Psychiatric symptoms in methamphetamine users. *Am J Addict.* 2004;13(2):181-190. doi:10.1080/10550490490436055
53. 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. doi:10.1016/j.jsat.2005.04.001
54. Dluzen DE, Liu B. Gender differences in methamphetamine use and responses: a review. *Gend Med.* 2008;5(1):24-35.
55. Kim JYS, Fendrich M. Gender differences in juvenile arrestees' drug use, self-reported dependence, and perceived need for treatment. *Psychiatr Serv Wash DC.* 2002;53(1):70-75. doi:10.1176/appi.ps.53.1.70
56. Lin S-K, Ball D, Hsiao C-C, Chiang Y-L, Ree S-C, Chen C-K. Psychiatric comorbidity and gender differences of persons incarcerated for methamphetamine abuse in Taiwan. *Psychiatry Clin Neurosci.* 2004;58(2):206-212.
57. Liechti ME, Gamma A, Vollenweider FX. Gender differences in the subjective effects of MDMA. *Psychopharmacology (Berl).* 2001;154(2):161-168.
58. 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. doi:10.1007/s00213-001-0995-9
59. 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 Oxf Engl.* 2006;20(2):291-301. doi:10.1177/0269881106060505
60. Campbell GA, Rosner MH. The agony of ecstasy: MDMA (3,4-methylenedioxymethamphetamine) and the kidney. *Clin J Am Soc Nephrol CJASN.* 2008;3(6):1852-1860. doi:10.2215/CJN.02080508

61. Moritz ML, Kalantar-Zadeh K, Ayus JC. Ecstasy-associated hyponatremia: why are women at risk? *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc*. 2013;28(9):2206-2209. doi:10.1093/ndt/gft192
62. MDMA can be fatal in warm environments [news release]. *National Institute on Drug Abuse*. <https://www.drugabuse.gov/news-events/news-releases/2014/06/mdma-can-be-fatal-in-warm-environments>. Published June 3, 2014. Accessed January 4, 2018.
63. 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.
64. 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. doi:10.1016/j.drugalcdep.2009.10.007
65. Lum PJ, Sears C, Guydish J. Injection risk behavior among women syringe exchangers in San Francisco. *Subst Use Misuse*. 2005;40(11):1681-1696. doi:10.1080/10826080500222834
66. 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 Off Publ Int Soc AIDS Educ*. 1994;6(5):379-389.
67. 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. doi:10.1186/1471-2458-14-440
68. Riley JL, 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.
69. Gerdle B, Björk J, Cöster L, Henriksson K, Henriksson C, Bengtsson A. Prevalence of widespread pain and associations with work status: a population study. *BMC Musculoskelet Disord*. 2008;9:102. doi:10.1186/1471-2474-9-102

70. Ailes EC, Dawson AL, Lind JN, et al. Opioid prescription claims among women of reproductive age--United States, 2008-2012. *MMWR Morb Mortal Wkly Rep.* 2015;64(2):37-41.
71. 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. doi:10.1016/j.jsat.2012.12.007
72. Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. Multiple Cause of Death, 1999-2016 on CDC WONDER Online Database, released 2017. Data are from the Multiple Cause of Death Files, 1999-2016, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. <https://wonder.cdc.gov/mcd-icd10.html>. Published 2017. Accessed February 14, 2018.
73. CDC Vital Signs: Prescription Painkiller Overdoses infographic. <https://www.cdc.gov/vitalsigns/prescriptionpainkilleroverdoses/infographic.h> Published November 8, 2017. Accessed January 31, 2018.
74. National Institute of Mental Health (NIMH). Anxiety Disorders. <https://www.nimh.nih.gov/health/topics/anxiety-disorders/index.shtml>. Published 2016. Accessed January 5, 2018.
75. National Institute of Mental Health (NIMH). *Women and Depression: Discovering Hope*. Bethesda, MD: National Institutes of Health http://www.nj.gov/humanservices/dmhas/publications/misc/MH_Fact_Sheets
76. National Heart, Lung, and Blood Institute (NHLBI). *Problem Sleepiness in Your Patient*. NIH Publication No. 97-4073. Bethesda, MD: National Institutes of Health; 2017. https://www.nhlbi.nih.gov/files/docs/resources/sleep/pslp_pat.pdf.
77. 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.
78. Piazza NJ, Vrbka JL, Yeager RD. Telescoping of alcoholism in women alcoholics. *Int J Addict.* 1989;24(1):19-28.
79. National Institute on Alcohol Abuse and Alcoholism. *Alcohol: A*

Women's Health Issue. Bethesda, MD: National Institutes of Health;
2003.<https://pubs.niaaa.nih.gov/publications/brochurewomen/women.htm>.

80. 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. *Addict Abingdon Engl*. 2012;107(1):51-59. doi:10.1111/j.1360-0443.2011.03621.x
81. 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. doi:10.1056/NEJM199001113220205
82. National Institute on Alcohol Abuse and Alcoholism (NIAAA). *Alcohol Alert: Are Women More Vulnerable to Alcohol's Effects?* Rockville, MD; 1999.
<https://pubs.niaaa.nih.gov/publications/aa46.htm>. Accessed January 5, 2018.
83. Lieber CS. Ethnic and gender differences in ethanol metabolism. *Alcohol Clin Exp Res*. 2000;24(4):417-418.
84. Melikian AA, Djordjevic MV, Hosey J, et al. Gender differences relative to smoking behavior and emissions of toxins from mainstream cigarette smoke. *Nicotine Tob Res Off J Soc Res Nicotine Tob*. 2007;9(3):377-387.
doi:10.1080/14622200701188836
85. Cosgrove KP, Wang S, Kim S-J, et al. Sex differences in the brain's dopamine signature of cigarette smoking. *J Neurosci Off J Soc Neurosci*. 2014;34(50):16851-16855.
doi:10.1523/JNEUROSCI.3661-14.2014
86. Torres OV, O'Dell LE. Stress is a principal factor that promotes tobacco use in females. *Prog Neuropsychopharmacol Biol Psychiatry*. 2016;65:260-268. doi:10.1016/j.pnpbp.2015.04.005
87. 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. doi:10.1056/NEJMsa1211127

88. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. Atlanta (GA): Centers for Disease Control and Prevention (US); 2014.
<http://www.ncbi.nlm.nih.gov/books/NBK179276/>.
89. Farley TM, Meirik O, Chang CL, Poulter NR. Combined oral contraceptives, smoking, and cardiovascular risk. *J Epidemiol Community Health*. 1998;52(12):775-785.
90. 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 Off J Soc Res Nicotine Tob*. 2010;12(6):647-657. doi:10.1093/ntr/ntq067
91. Jones HE, Fielder A. Neonatal abstinence syndrome: Historical perspective, current focus, future directions. *Prev Med*. 2015;80:12-17. doi:10.1016/j.ypmed.2015.07.017
92. Tobacco, drug use in pregnancy can double risk of stillbirth. *Eunice Kennedy Shriver National Institute of Child Health and Human Development*.
<https://www.nichd.nih.gov/news/releases/Pages/121113-stillbirth-drug-use.aspx>. Published December 11, 2013. Accessed January 31, 2018.
93. Wendell AD. Overview and epidemiology of substance abuse in pregnancy. *Clin Obstet Gynecol*. 2013;56(1):91-96.
doi:10.1097/GRF.0b013e31827feeb9
94. Hudak ML, Tan RC, COMMITTEE ON DRUGS, COMMITTEE ON FETUS AND NEWBORN, American Academy of Pediatrics. Neonatal drug withdrawal. *Pediatrics*. 2012;129(2):e540-560.
doi:10.1542/peds.2011-3212
95. MedlinePlus, U.S. National Library of Medicine. Neonatal abstinence syndrome: MedlinePlus Medical Encyclopedia.
<https://medlineplus.gov/ency/article/007313.htm>. Published December 21, 2017. Accessed January 12, 2018.
96. 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.
doi:10.1097/ADM.0000000000000095

97. Young-Wolff KC, Tucker L-Y, Alexeeff S, et al. Trends in Self-reported and Biochemically Tested Marijuana Use Among Pregnant Females in California From 2009-2016. *JAMA.* 2017;318(24):2490.
doi:10.1001/jama.2017.17225
98. 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.
99. Wilcox AJ, Weinberg CR, Baird DD. Risk factors for early pregnancy loss. *Epidemiol Camb Mass.* 1990;1(5):382-385.
100. 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.
101. 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.
doi:10.1007/s00213-010-1892-x
102. 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.
103. 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.
104. 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.
105. National Academies of Sciences, Engineering, and Medicine. *The Health Effects of Cannabis and Cannabinoids: Current State of Evidence and Recommendations for Research.* Washington, DC:

The National Academies Press; 2017.

106. Frank DA, Bauchner H, Parker S, et al. Neonatal body proportionality and body composition after in utero exposure to cocaine and marijuana. *J Pediatr*. 1990;117(4):622-626.
107. Mark K, Desai A, Terplan M. Marijuana use and pregnancy: prevalence, associated characteristics, and birth outcomes. *Arch Womens Ment Health*. 2016;19(1):105-111. doi:10.1007/s00737-015-0529-9
108. 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.
109. American College of Obstetricians and Gynecologists Committee on Obstetric Practice. Committee Opinion No. 637: Marijuana Use During Pregnancy and Lactation. *Obstet Gynecol*. 2015;126(1):234-238. doi:10.1097/01.AOG.0000467192.89321.a6
110. Roberson EK, Patrick WK, Hurwitz EL. Marijuana use and maternal experiences of severe nausea during pregnancy in Hawai'i. *Hawaii J Med Public Health J Asia Pac Med Public Health*. 2014;73(9):283-287.
111. 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. doi:10.1016/j.ctcp.2005.09.006
112. 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. doi:10.1007/s00213-008-1162-3
113. 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 N Y N 1991*. 2005;15(12):2013-2020. doi:10.1093/cercor/bhi076

114. 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. doi:10.1073/pnas.0537849100
115. Fried PA, Makin JE. Neonatal behavioural correlates of prenatal exposure to marijuana, cigarettes and alcohol in a low risk population. *Neurotoxicol Teratol*. 1987;9(1):1-7.
116. 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. doi:10.1016/j.earlhumdev.2007.07.001
117. 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.
118. Schempf AH, Strobino DM. Illicit Drug Use and Adverse Birth Outcomes: Is It Drugs or Context? *J Urban Health Bull N Y Acad Med*. 2008;85(6):858-873. doi:10.1007/s11524-008-9315-6
119. 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. doi:10.1016/j.ntt.2014.11.003
120. Perez-Reyes M, Wall ME. Presence of delta9-tetrahydrocannabinol in human milk. *N Engl J Med*. 1982;307(13):819-820. doi:10.1056/NEJM198209233071311
121. Astley SJ, Little RE. Maternal marijuana use during lactation and infant development at one year. *Neurotoxicol Teratol*. 1990;12(2):161-168.
122. Djulus J, Moretti M, Koren G. Marijuana use and breastfeeding. *Can Fam Physician Médecin Fam Can*. 2005;51:349-350.
123. 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. doi:10.1097/GRF.0b013e31827ae167

124. 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. doi:10.1001/archpedi.159.9.824
125. Chasnoff IJ, Bussey ME, Savich R, Stack CM. Perinatal cerebral infarction and maternal cocaine use. *J Pediatr*. 1986;108(3):456-459.
126. 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.
127. Gorman MC, Orme KS, Nguyen NT, Kent EJ, Caughey AB. Outcomes in pregnancies complicated by methamphetamine use. *Am J Obstet Gynecol*. 2014;211(4):429.e1-7. doi:10.1016/j.ajog.2014.06.005
128. 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. doi:10.1542/peds.2005-2564
129. 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. doi:10.1016/j.jpeds.2014.01.053
130. 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. doi:10.1542/peds.2011-2209
131. Schaefer TL, Grace CE, Braun AA, et al. Cognitive impairments from developmental exposure to serotonergic drugs: citalopram and MDMA. *Int J Neuropsychopharmacol Off Sci J Coll Int Neuropsychopharmacol CINP*. 2013;16(6):1383-1394. doi:10.1017/S1461145712001447
132. 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. doi:10.1542/peds.2012-0666
133. Singer LT, Moore DG, Min MO, et al. Motor delays in MDMA (ecstasy) exposed infants persist to 2 years. *Neurotoxicol Teratol*. 2016;54:22-28. doi:10.1016/j.ntt.2016.01.003
 134. Bandstra ES, Morrow CE, Mansoor E, Accornero VH. Prenatal drug exposure: infant and toddler outcomes. *J Addict Dis*. 2010;29(2):245-258. doi:10.1080/10550881003684871
 135. Centers for Disease Control and Prevention (CDC). Reproductive Health: Pregnancy Complications. <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregcomplica> Published June 17, 2016. Accessed February 5, 2018.
 136. Mitchell AA, Gilboa SM, Werler MM, et al. Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. *Am J Obstet Gynecol*. 2011;205(1):51.e1-8. doi:10.1016/j.ajog.2011.02.029
 137. Food and Drug Administration (FDA). Labeling - Pregnancy and Lactation Labeling (Drugs) Final Rule. <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentReso> Published December 3, 2014. Accessed January 16, 2018.
 138. Adam MP, Polifka JE, Friedman JM. Evolving knowledge of the teratogenicity of medications in human pregnancy. *Am J Med Genet C Semin Med Genet*. 2011;157C(3):175-182. doi:10.1002/ajmg.c.30313
 139. Patrick SW, Dudley J, Martin PR, et al. Prescription opioid epidemic and infant outcomes. *Pediatrics*. 2015;135(5):842-850. doi:10.1542/peds.2014-3299
 140. Centers for Disease Control and Prevention (CDC). Medications and Pregnancy. Centers for Disease Control and Prevention. <https://www.cdc.gov/pregnancy/meds/index.html>. Published September 14, 2017. Accessed January 16, 2018.
 141. American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics*.

- 2001;108(3):776-789.
142. American Academy of Pediatrics. Ages and Stages: Medication Safety Tips for the Breastfeeding Mom. HealthyChildren.org. <http://www.healthychildren.org/English/ages-stages/baby/breastfeeding/Pages/Medications-and-Breastfeeding.aspx>. Accessed January 17, 2018.
 143. Julie Mennella. *Alcohol's Effect on Lactation*. National Institute on Alcohol Abuse and Alcoholism (NIAAA) <https://pubs.niaaa.nih.gov/publications/arh25-3/230-234.htm>. Accessed January 17, 2018.
 144. American Academy of Pediatrics. Breastfeeding and the use of human milk. *Pediatrics*. 2012;129(3):e827-841. doi:10.1542/peds.2011-3552
 145. Wickström R. Effects of nicotine during pregnancy: human and experimental evidence. *Curr Neuropharmacol*. 2007;5(3):213-222. doi:10.2174/157015907781695955
 146. Centers for Disease Control and Prevention (CDC). Reproductive Health: Tobacco Use and Pregnancy. <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/tobaccousepr> Published September 29, 2017. Accessed January 17, 2018.
 147. 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. doi:10.1093/aje/kwu074
 148. 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. doi:10.1007/s10995-010-0599-2
 149. National Institute on Drug Abuse (NIDA). NIH study examines nicotine as a gateway drug [news release]. <https://www.drugabuse.gov/news-events/news-releases/2011/11/nih-study-examines-nicotine-gateway-drug>. Published November 2, 2011. Accessed January 17, 2018.

150. Mennella JA, Yourshaw LM, Morgan LK. Breastfeeding and smoking: short-term effects on infant feeding and sleep. *Pediatrics*. 2007;120(3):497-502. doi:10.1542/peds.2007-0488
151. Mennella JA, Beauchamp GK. Understanding the Origin of Flavor Preferences. *Chem Senses*. 2005;30(Suppl 1):i242-i243. doi:10.1093/chemse/bjh204
152. Aligne CA, Moss ME, Auinger P, Weitzman M. Association of pediatric dental caries with passive smoking. *JAMA*. 2003;289(10):1258-1264.
153. Leung GM, Ho L-M, Lam T-H. Secondhand smoke exposure, smoking hygiene, and hospitalization in the first 18 months of life. *Arch Pediatr Adolesc Med*. 2004;158(7):687-693. doi:10.1001/archpedi.158.7.687
154. 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. doi:10.1001/jamapsychiatry.2014.366
155. 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.
156. 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. doi:10.1016/j.addbeh.2009.09.009
157. 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.
158. 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.
159. Greenfield SF, Back SE, Lawson K, Brady KT. Substance abuse in

- women. *Psychiatr Clin North Am.* 2010;33(2):339-355.
doi:10.1016/j.psc.2010.01.004
160. Perkins KA, Scott J. Sex differences in long-term smoking cessation rates due to nicotine patch. *Nicotine Tob Res Off J Soc Res Nicotine Tob.* 2008;10(7):1245-1250. doi:10.1080/14622200802097506
 161. 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.
 162. 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 Off J Soc Res Nicotine Tob.* 2004;6(1):171-175. doi:10.1080/14622200310001656984
 163. 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 Off J Soc Res Nicotine Tob.* 2015;17(4):407-421. doi:10.1093/ntr/ntu249
 164. Tobacco Research and Intervention Program. *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.
 165. National Institutes of Health (NIH). Quitting Smoking Benefits Health Despite Weight Gain. *National Institutes of Health (NIH).* <https://www.nih.gov/news-events/nih-research-matters/quitting-smoking-benefits-health-despite-weight-gain>. Published March 25, 2013. Accessed January 19, 2018.
 166. 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. doi:10.1056/NEJMoa1005359
 167. Center for Substance Abuse Treatment. *Substance Abuse Treatment: Addressing the Specific Needs of Women.* Rockville, MD: Substance Abuse and Mental Health Services Administration (US); 2009. <http://www.ncbi.nlm.nih.gov/books/NBK83252/>.

Accessed January 3, 2018.

168. 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. doi:10.1016/j.evalprogplan.2004.01.010
169. 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.
170. 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.
171. 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. doi:10.1097/ADM.0000000000000092
172. National Institute on Drug Abuse. *Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition)*. Bethesda, MD: National Institutes of Health; 2012. <https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/principles-effective-treatment>. Accessed January 31, 2018.
173. *LACTMED: Buprenorphine. TOXNET Toxicology Data Network*. Bethesda, MD: U.S. National Library of Medicine; 2018.
174. 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. *Addict Abingdon Engl.* 2011;106(3):574-580. doi:10.1111/j.1360-0443.2010.03170.x
175. Kraft WK, Adeniyi-Jones SC, Chervoneva I, et al. Buprenorphine for the Treatment of the Neonatal Abstinence Syndrome. *N Engl J Med.* 2017;376(24):2341-2348. doi:10.1056/NEJMoa1614835

176. National Institute on Mental Health (NIMH). Depression. <https://www.nimh.nih.gov/health/topics/depression/index.shtml>. Published 2016. Accessed January 4, 2018.
177. National Institute of Mental Health (NIMH). *Anxiety Disorders*. Bethesda, MD: National Institutes of Health; 2009.
178. National Institute of Mental Health (NIMH). *Eating Disorders: About More Than Food*. Bethesda, MD: National Institutes of Health; 2018. https://www.nimh.nih.gov/health/publications/eating-disorders/eatingdisorders_148810.pdf. Accessed January 31, 2018.
179. 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.
180. 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. doi:10.1093/ntr/nts075
181. Shen W, Liu Y, Li 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. doi:10.1186/1747-597X-7-44
182. 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.
183. U.S. Department of Health and Human Services (HHS). 2013 Trans-HHS Intimate Partner Violence Screening and Counseling: Research Symposium. <https://sis.nlm.nih.gov/outreach/2013IPVsymposium.html>. Published October 5, 2015. Accessed January 24, 2018.
184. *Factsheet: The Violence Against Women Act*. The White House https://obamawhitehouse.archives.gov/sites/default/files/docs/vawa_factshe Accessed January 24, 2018.
185. *Reauthorizing the Violence Against Women Act: Key Provisions in*

- S. 47. The White House
https://obamawhitehouse.archives.gov/sites/default/files/docs/vawa_improv
Accessed January 24, 2018.
186. National Institutes of Health (NIH). *Report: Intimate Partner Violence Screening and Counseling Research Symposium.*; 2013.
https://sis.nlm.nih.gov/outreach/2013ipv/Report_IPV_Symposium.pdf.
Accessed January 24, 2018.
187. National Bioethics Advisory Commission -- Publications.
<https://bioethicsarchive.georgetown.edu/nbac/pubs.html>.
Published 2001. Accessed January 24, 2018.
188. ORWH. Office of Research on Women's Health.
<https://orwh.od.nih.gov/about/>. Accessed February 1, 2018.
189. Whitten L. NIDA Notes: Women and Sex/Gender Differences Research Program. <https://www.drugabuse.gov/news-events/nida-notes/2012/04/women-sexgender-differences-research-program>.
Published April 19, 2012. Accessed January 24, 2018.
190. Committee on Obstetric Practice. Committee Opinion No. 722: Marijuana use during 118 pregnancy and lactation. *Obstet Gynecol.* 2017;130 (4):e205-e209. <https://www.ncbi.nlm.nih.gov/pubmed/28937574>
191. [Study finds increased cannabis use during pregnancy](#) - Self-reported medical and nonmedical cannabis use among pregnant women in the United States, *JAMA* Published online June 18, 2019.