

# Gender-related differences in addiction: a review of human studies

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Men typically report greater substance use and gambling than women, but the gender gap has been closing in recent years. Men and women engage in drug and gambling behaviors for different reasons and respond differently to drugs and gambling. Telescoping — a phenomenon in which women engage in drug use and/or gambling behaviors at a later age but progress faster to disordered engagement — was initially observed in alcohol and later in opioid, cannabinoid, cocaine, and gambling disorders. Biological and sociocultural gender-related factors may impact withdrawal symptoms and treatment responses among men and women. Further investigation of the neurobiological underpinnings of gender-related differences among addiction populations is required.

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## Introduction

Sex/gender differences (hereafter referred to as 'gender-related differences,' with the understanding of the American Psychiatric Association's [1] definitions of sex as a person's biological status such as male or female, and gender as the attitudes, feelings and behaviors associated with biological sex) in addiction have been widely

described. Addiction is defined here as chronic, compulsive use of a drug or engagement in a behavior despite negative consequences. Generally, men report greater substance use and gambling than women, but the gender gap has been closing in recent years [2]. Drug use/gambling prevalence rates from the Substance Abuse and Mental Health Services Administration (SAMHSA) 2016 National Survey on Drug Use and Health (NSDUH) [3\*\*] and selected gender-related difference findings are highlighted in [Table 1](#). According to the NSDUH, 7.5% of the population meet Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for alcohol or any illicit substance and 0.4% meet DSM criteria for gambling disorder (GD) [4]; however, reports of clinically addicted individuals in this national survey (among others) did not stratify by gender. Some studies have shown that women engage in drug use or gambling behaviors later than men but progress to addiction more rapidly than men, a gender-related phenomenon known as telescoping. Telescoping was initially observed in alcohol [5] and later in opioids [6], cannabinoids [6], cocaine [7], and gambling [8] disorders. Studies have provided mixed support for this phenomenon. Men are more likely to use drugs recreationally, whereas women are more likely to be prescribed drugs as medication. Nonetheless, women with addictions often experience a greater stigma and less social support than men [9\*\*]. Examination of gender-related differences (and similarities) is crucial for informing effective policy, prevention and treatment efforts. This review focuses on the current state of biological, psychological and behavioral gender-related differences (and similarities) ranging from prevalence rates to treatment outcomes in clinical populations for the following drug and behavioral addiction subtypes: alcohol, psychostimulants (mainly cocaine and amphetamine), cannabinoids, gambling, nicotine, and opioids.

## Alcohol

Men generally drink more than women but the gender gap is closing as shown by analyses of recent birth cohorts [10]. While several studies have shown alcohol addiction in women compared to men is 'telescoped,' these women were already enrolled in treatment, and some studies also reported no evidence of the telescoping effect [11]. In addition to potentially more rapid progression to addiction, data have also shown that women progress more rapidly than men to alcohol-related diseases such as liver disease, neurotoxicity, cardiomyopathy and peripheral neuropathy; see [12\*\*] for review. This may in part be due to differences in alcohol metabolism as alcohol dehydrogenase, the enzyme that catabolizes alcohol, is found

Table 1

Percent of individuals in the US reporting drug use/gambling in 2016 (ages 12 years and older) (Substance Abuse and Mental Health Service Administration's National Survey on Drug Use and Health (SAMHSA's NSDUH) [3\*\*]) and selected gender-related difference findings

	Lifetime prevalence		Selected gender-related differences
	Male	Female	
Alcohol	82.4	78.2	Women compared to men demonstrate a 'telescoped' progression to addiction and alcohol-related physiological diseases.
Cigarettes	61.9	53.2	Women have poorer responses to nicotine replacement therapies than men.
Cocaine	17.9	11.2	Subjective effects of cocaine vary by menstrual cycle phase in cocaine-dependent women.
Gambling <sup>b</sup>	82.4	76.5	Men wager on strategic forms of gambling while women wager on nonstrategic forms.
Heroin	2.5	1.2	Men report more use than women, but withdrawal, severity and treatment outcomes are similar.
Cannabis	48.0	40.2	Females are more sensitive to the behavioral and physiological effects of cannabis than males.
Methamphetamine	6.5	4.3	Methamphetamine withdrawal symptoms, relapse rates and treatment outcomes do not vary by sex.
All Illicit Drugs <sup>a</sup>	52.3	44.9	

<sup>a</sup> All Illicit Drug Use includes the misuse of prescription medications or the use of cannabis, cocaine (including crack), heroin, hallucinogens, inhalants, or methamphetamine.

<sup>b</sup> Percent of individuals in the US reporting drug any gambling in the past year in 2013 (age 18 and older) [29].

in much higher concentrations in the stomach of males compared to females [13], although other factors (e.g. distribution volumes) warrant consideration.

There are mixed findings in gender-related differences reported on ratings of craving among alcohol-dependent individuals. With respect to alcohol withdrawal, men are more likely to experience more severe symptoms such as anxiety, insomnia and delirium tremens [14]; however, this study and other studies have not consistently controlled for amounts of alcohol consumed. In alcohol-dependent individuals, men and women show similar abstinence durations and relapse rates [12\*\*].

### Psychostimulants

Generally, men report greater use of psychostimulants (cocaine, amphetamine, methamphetamine) than women [3\*\*]. Cocaine laboratory self-administration in humans has demonstrated gender-related differences; men compared to women report experiencing more euphoric and dysphoric experiences and assign high monetary values to a second dose of the cocaine [15]. Subjective mental and physical 'good drug' effects of cocaine have been reported to be higher in women as compared to men, and menstrual-cycle-phase-dependent have been observed, with greater effects during the follicular phase than the luteal phase [16]. Men also report higher reinforcing effects of amphetamine compared to women; however, the doses of amphetamine have not been consistently weight-adjusted [17]. With regard to craving, women show greater cue-induced cocaine craving as compared to men while stress-induced cocaine craving was similar across genders; however, these responses vary with menstrual cycle phases [18]. Currently, there is little or no evidence of gender-related differences in withdrawal symptoms, relapse rates and treatment outcomes with respect to psychostimulants [12\*\*].

### Cannabinoids

Sex differences have been consistently documented among individuals who use cannabis; see [19\*] for review. According to the NSDUH, males are more likely to use cannabis than females and begin using at earlier ages [3\*\*]. Similar to alcohol, studies have shown the progression to cannabis-use disorder is 'telescoped' in women [20]. Mixed findings describe gender-related differences in subjective reports of 'high' due to cannabis and  $\Delta$ 9-tetrahydrocannabinol (THC) alone [21,22], which may be partially due to differences in tobacco-smoking comorbidity and/or dosing strategies. Data suggest that men experience greater cannabis-induced analgesia relative to women [23].

Females, compared to males, are more sensitive to the behavioral and physiological effects of cannabis and cannabis-like substances [24], such as fatigue, drowsiness and psychomotor suppression; however, the amount of cannabis per bodyweight was not been consistently controlled. It is possible that cannabinoid metabolism is responsible for some gender-related differences. For example, one preclinical study showed that female rats compared to male rats had higher brain levels of a THC metabolite [25]. However, in humans, metabolite levels in plasma following THC exposure has been shown to be both higher [26] and lower [27] in females compared to males. Treatment-seeking women endorse more severe cannabis withdrawal symptoms than treatment-seeking men [28]. While gender-related differences have been reported in the use, subjective effects and metabolism of cannabis, the neural and molecular bases for these differences remain poorly understood.

### Gambling

Gambling occurs in 82.4% of men and 76.5% of women [29], and lifetime prevalence rates for GD are 0.6% for

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