

# Gender Differences in Cannabis Use

Subjects: Health Care Sciences & Services | Neurosciences

Contributor: M.Carmen Arenas

Gender differences in psychiatric disorders and drug use are well known. Cannabis is the most widely used illegal drug among young people. In recent years, its use has been related to the development of psychiatric pathologies; however, few studies have incorporated the gender perspective as of yet. Men have a higher prevalence using cannabis; however, women show a faster transition from recreational use to compulsive use, higher levels of craving with more relapses, and higher prevalence of dual pathology. Clinical studies clearly show the existence of gender differences in psychiatric symptoms associated with cannabis use. Although these results are not conclusive, they seem to indicate a higher vulnerability of women in the development of psychosis and anxiety, while men seem to be more vulnerable to developing depressive symptoms with long-term cannabis misuses.

Keywords: cannabis ; gender differences ; psychotic disorders

---

## 1. Introduction

Men and women differ in the prevalence and manifestation of many psychiatric disorders <sup>[1][2]</sup>. At present, the higher prevalence of psychosis in men is well established <sup>[3][4][5]</sup>, whereas women manifest depressive and anxiety disorders to a greater extent <sup>[6][7][8][9][10]</sup>. Similarly, there are many differences between men and women in addictive disorders <sup>[11][12][13][14][15]</sup>.

Men have long been the subject of research on drug use, given that men typically have a higher prevalence of drug use. However, this fact differs from the current reality. The latest statistics show that women are catching up with men in drug use, especially in the younger population <sup>[16][17]</sup>. Broadly speaking, it can be observed that women have a higher prevalence in the use of legal drugs such as tobacco and alcohol, as well as in the use of prescription and non-prescription hypnotosedatives. In contrast, men continue to be the more prevalent users of illegal drugs such as cannabis, psychostimulants, hallucinogens and opiates. Although women do not consume as much cannabis as men, an increase can be observed in the latest reports with respect to the statistics from previous years <sup>[16][17]</sup>. Hence, the gender gap in the prevalence of drug use is already starting to narrow.

Women are not only increasing their consumption of addictive substances <sup>[18]</sup>, but also present clinical profiles of prolonged cannabis use that are different from those of men <sup>[4][19]</sup>. Women show a faster transition from recreational use to compulsive use, i.e., to dependence, which has been called the "telescoping effect". Additionally, they show higher levels of craving with more relapses and more frequent and severe withdrawal symptoms. They also show different patterns of use than men and higher prevalence of dual pathology, which means a worse prognosis, especially because they ask for less help and they have less social support during treatment, leading to higher abandonment rates <sup>[14]</sup>. Gender differences in the pattern and reasons for cannabis use have also been reported. A 10-year follow-up cohort study showed that adolescent males consumed mostly in groups and in sport-related situations, while females were more prone to be alone and with the aim of reducing stress <sup>[20]</sup>. The most repeated reasons for cannabis use in both sexes were "to relax" and "to sleep better", with women referring most often to the former <sup>[21][20]</sup>.

Cannabis has been the most widely consumed illegal drug in recent years, with an upward trend mainly among young people <sup>[18]</sup>. The legalization of this drug in some countries, as well as the development of its therapeutic use, has led to an underestimation of the possible consequences of its recreational use <sup>[17]</sup>. Nevertheless, numerous reviews highlight the relationship between cannabis use and the development of psychiatric disorders such as psychosis, affective disorders and anxiety disorders <sup>[22][23][24][25]</sup>.

The comorbidity of an addictive disorder with another psychiatric disorder causes a worse prognosis and greater difficulty in treatment <sup>[26][27]</sup>. This fact has led in recent years to the development of research in the field of dual pathology (DP). DP can be defined as the coexistence of a substance use disorder (SUD) and a mental disorder in the same individual in a specific period of time <sup>[28]</sup>. There is evidence of a greater development of DP in women; however, women are less likely to

go to specialized centers for help and, overall, have less social support, which leads them to show less adherence to treatment.

## **2. Dual Diagnoses in Cannabis Users**

Numerous studies have linked cannabis use and psychiatric pathology not only to psychosis and schizophrenia, but also to an amotivational state, depression, anxiety, bipolar disorder and personality disorders [24][29][30][31][32][33][34][35][36][37][38][39]. However, given the complexity of controlling variables in human studies, such as dose or composition of cannabis and the consumption of other drugs, among others, it is very difficult to establish causality between cannabinoid use and psychiatric disorders. Thus, it is still under debate whether comorbid disorders are prior to or a consequence of cannabis abuse [30][40]. For this reason, despite the strong evidence in the association between psychopathology and cannabis abuse, the causal relation of this association is still not understood [24].

The coexistence in an individual of an addictive disorder and a mental disorder in a specific period of time is frequent, and is called dual pathology (DP) [28]. Thus, DP occurs in patients with symptoms that fit the criteria for two different psychiatric disorders, one of them being an addiction. DP is underdiagnosed and poorly treated [41]; in fact, it is not officially recognized in the DSM or CIE nomenclature. However, the term dual pathology is similar to other more commonly used terms, such as dual diagnosis, comorbid or co-occurring disorder or psychiatric comorbidity [41]. The prevalence of DP is high, with 65–85% of addicts in treatment that report having another psychiatric disorder [42] and about 45% of psychiatric patients that report having an addiction [43]. Scientific evidence supports the link between disorders present in DP; therefore, access to a single multidisciplinary care model that integrates and coordinates the mental health network and the addiction network is advocated, enabling personalized bio-psycho-social treatments that do not leave any addict unassisted [26][27].

Patients with DP often present a pattern of polydrug use, and cannabis is one of the most commonly used drugs by these patients [44]. The presence of DP in cannabis addicts under treatment is very high too [24][40]. Firstly, review studies have shown a high comorbidity between cannabis use disorder (CUD) and other SUDs, mainly with those induced by legal drugs such as alcohol and tobacco, but also with illegal drugs such as cocaine. It is interesting to note that in those studies, cannabis use was prior to that of other substances [24].

Among all the psychiatric pathologies related to cannabis use, psychosis has been the most widely studied. In an international study with volunteers from 11 locations in Europe and Brazil, it was observed that the probability of developing a psychotic syndrome among daily cannabis users was two to three times higher than in non-users, while in those who used high-potency cannabis, it was one to six times higher than in non-users. Researchers also highlights the positive relationship between the use of cannabis with higher than 10% THC levels and the development of certain types of psychosis [45]. Not all studies are so categorical in their conclusions, as there are other predisposing factors, such as genetics or childhood trauma [46]. However, increasing evidence indicates a high risk of developing psychosis after frequent cannabis use, especially with high THC levels [24][40]. Both natural and synthetic cannabinoid use in young people has been associated with the occurrence of transient and dose-dependent positive and negative schizophrenic symptoms in healthy individuals not at risk for schizophrenia. However, in adolescents who do present such risk factors, they would cause an earlier onset (between 2 and 6 years of age) and a worse prognosis in the development of schizophrenia [23].

In addition, the percentage of subjects with schizophrenia who use cannabis, even with a CUD, is very high; indeed, it is known that this type of consumption use has been related to the recurrence or worsening of symptoms, both positive and negative, which increases severity and relapses, and hinders adherence to therapeutic and pharmacological treatments [40]. Several studies suggest that cannabis abuse affects antipsychotic treatment, specifically by decreasing adherence to such treatments or worsening abidance, which is consistent with clinical studies indicating that cannabis users in antipsychotic treatment have a higher relapse rate and a worse response to treatment [47]. However, there are no studies as of yet that take into account other determinants, such as THC concentration.

The most repeated reasons to justify cannabis misuse are the enhancement of positive feelings, habit and coping with negative feelings [48]. However, continued cannabis use is associated with the long-term development of depressive and anxious symptoms, the very symptoms that the subject is trying to alleviate during initial use. Thus, it seems that cannabis produces a bidirectional effect, since it can alleviate certain anxious symptoms and reinforce positive mood states when consumed less frequently and with low doses, but depressive and anxious symptoms become more relevant when the frequency of consumption and doses are increased [49]. These dose-dependent effects would be produced mainly by the neurochemical brain changes described in chronic users [30][50].

Cannabis use during adolescence has also been associated with an increased risk of developing depression and suicidal behavior in later years, in this case, without the need for prior risk factors [51]. However, it is not only adolescents who are more vulnerable to pathological cannabis use. Studies in users over 50 years of age, a population that begins to show cognitive deficits due to changes in brain plasticity, have shown that cannabis use has a negative impact. Compared to non-users, this population experiences greater psychological distress and suicidal thoughts, as well as a higher rate of opioid use disorder [52].

The results of longitudinal studies that have evaluated the association between depression and cannabis use are mixed [24][40]. It appears that when the onset of use is early and regular, the risk of depression is higher among cannabis users than among non-users. However, the overlap of the symptoms used to diagnose major depressive disorder with symptoms for cannabis withdrawal syndrome makes it difficult to establish the relationship between cannabis use and depression [24]. Recently, the relationship between the endocannabinoid system and major depressive disorder has been highlighted. Studies have revealed that the endocannabinoid system strongly influences the neurotransmission, neuroendocrine and neuroimmune systems, which have been identified to be dysfunctional in depressive patients [38]. Knowing the involvement of the endocannabinoid system in the etiology of a major depressive disorder can help to understand how cannabis use is associated with the development of depression and suicidal behavior.

Similarly, a relationship between cannabis and anxiety has been observed [24][40]. However, while some studies show that cannabis use, especially during adolescence, increases anxiety levels throughout life, other studies find that anxiety increases when cannabis use ceases [40]. It is known that high doses of THC can cause anxiety symptoms, including panic attacks, and so it has been suggested that continued use may exacerbate anxiety disorders [24]. Overall, the role of cannabis in the etiology, prognosis and treatment of anxiety disorders remains unclear and needs further research [24].

### 3. Gender Differences in the Development of Psychotic, Depressive and Anxious Symptoms Associated with Cannabis Use

The interest in incorporating the gender perspective in dual pathology is quite recent [27]. Some reviews have examined the roles that the interaction between gender and cannabis use have on the development of psychosis [4][53]; however, recently, Prieto-Arenas and Díaz [54] have performed a systematic review on clinically based research evidence of gender differences in the development of psychotic, depressive and anxious symptoms associated with cannabis use. That systematic review was performed on the main databases (PubMed and Web of Science) following PRISMA guidelines on clinical studies published until December 2020. The most important findings to date from the reviewed studies on gender differences in the association between cannabis use and the psychiatric symptomatology described below are summarized in **Table 1**.

**Table 1.** The most important findings to date from the human literature on gender differences in the association between cannabis use and the development of psychotic, depressive and anxious symptoms. M: male; F: female; CUD: cannabis use disorder.

Symptom	Population Profile	Results	References	
Psychosis	nonclinical	Cannabis use increases the risk of first-episode psychosis and the development of psychosis more in men than in women (M > F)	[4,84,91]	
		Synthetic cannabis use increases the risk of the development of psychosis both in men and in women (M = F)	[92]	
		Cannabis use is related with an early start of first-episode psychosis both in men and in women (M = F)	[5,84,93,94]	
		Cannabis use reduces the age of onset of psychosis more in women than in men (F > M)	[4,81,91,95]	
		Greater intensity of psychotic experiences are associated with cannabis use in women than men (F > M)	[96]	
	with risk factors for psychosis	Cannabis use is related with a greater severity of general psychiatric pathology in women than men (F > M) and with a greater severity of negative psychotic symptoms in men than women (M > F)	[97]	
	with CUD	Women present more psychotic symptoms than men (F > M)	[89]	
		Women present worse responses to treatment with more relapses than men (F > M)	[86]	
	with first-episode psychosis	Cannabis use is related with worsening psychological, social and work activity in men than women (M > F)	[83]	
		Cannabis use is related with a severity of clinical symptoms and length of hospitalization period similar in both sexes (M = F)	[3,83,92]	
	with a cannabis-induced psychotic disorder	Men present a greater intensity and prevalence of positive symptoms than women (M > F)	[4,91,98]	
		Women present a greater intensity and prevalence of negative symptoms than men (F > M)	[86]	
	Depression	nonclinical	Cannabis use is predictive of depressive symptoms both in men and women (F = M)	[95,96]
			Cannabis use is predictive of depressive symptoms more in women than men (F > M)	[99,100,101,102,103]
			Cannabis use is predictive of depressive symptoms with a great severity in men (M > F)	[52,104,105]
Cannabis use increases the development of major depression in men (M > F)			[106]	
Cannabis use is related with suicidal ideation both men and women (M = F)			[109]	
with a cannabis misuse		Women show more depressive and somatization symptoms than men (F > M)	[85,88,102,107,108]	
		Men show more depressive symptoms at younger ages (M > F), while women do so at later ages (F > M)	[89]	
		Women show a higher probability of suicide than men in late adolescent (F > M)	[85]	
		Men with a high frequency of consumption manifest a greater probability of suicidal ideation than women (M > F)	[95,109]	
		Women cannabis users present greater dysphoria and depression than men (F > M)	[86,97,98]	
Anxiety	general	Positive relationship between cannabis abuse and generalized anxiety disorder in women and negative relationship between cannabis abuse and panic disorder in men	[111]	
	with CUD	Women present greater anxiety than men during abstinence (F > M)	[95,113]	

Reviewing the human literature that evaluates the association between cannabis use and the development of psychopathologies, some studies show that cannabis use increases the risk of first-episode psychosis and the

development of psychosis more in men than in women [4][53][55], a fact that could be attributed to the greater polyconsumption that men perform [56]. However, when the substance consumed is a synthetic cannabinoid, the risk increases in both sexes [57]. These designed drugs have higher levels of THC, which has been related to the appearance of psychiatric comorbidity [24][29]. However, gender differences are not so conclusive when it comes to the effects of cannabis on the age of onset of psychosis. While some studies relate the use of cannabis with an earlier start of first-episode psychosis in both sexes, without finding gender differences [5][53][58][59], other studies find that the use of this drug reduces the age of onset of psychosis more in women than in men [4][60][55][61], eliminating the gender differences observed in general in the age of onset of psychotic disorders [58].

Thus, cannabis use, whether recreational or compulsive, has been related to the appearance of symptoms of psychosis in both the adolescent [62][20] and young population [63], and in subjects with risk factors for the development of psychosis [64]. In a nonclinical population of university students, women reported greater intensity of psychotic experiences associated with cannabis use than men [63]. Women with risk factors for the development of psychosis also presented a greater severity of general psychiatric pathology related to the consumption of this drug [64]. However, in this same population, male users exhibited a greater severity of negative psychotic symptoms [64].

On the other hand, women diagnosed with a CUD also showed more psychotic and depressive symptoms than men of the same age range (23–25 years), although there was no relationship between the frequency of cannabis use and the age of onset of symptoms [20]. In addition, it should be noted that after one year of treatment, men with CUD significantly reduced their use of cannabis, while women did not [65].

Among patients with first-episode psychosis, cannabis use has been observed to worsen psychological, social and work activity in men, while the opposite result was surprisingly found in women [21]. This finding could be due to the lower number of women being evaluated in the study; therefore, more in-depth research is needed to fully understand this fact [54].

In contrast, in patients with a cannabis-induced psychotic disorder, it is men who have a greater severity of general psychopathology, in addition to a greater intensity and prevalence of positive symptoms [66], while women show more negative symptoms [65]. This coincides with two reviews in which it is concluded that cannabis use in men increases the manifestation of psychotic symptoms and hospitalizations [4][55]. However, other studies do not find these gender differences in first-episode psychosis patients, finding a similar severity of clinical symptoms and length of hospitalization period in both sexes [3][21]. It should be noted that with the use of synthetic cannabis, the levels of agitation in women with psychotic pathology increase compared to those of men [57].

In summary, all the studies demonstrate the existence of an association between the use of cannabis and the appearance of psychotic symptoms. However, despite gender differences being observed, they are not always confirmed by all studies, depending mainly on the population studied [54]. It seems that female cannabis users would manifest a greater intensity of psychotic symptoms and general psychiatric pathology in both the previously asymptomatic population and people with a problematic use of cannabis [62][63][64]. Therefore, cannabis use appears to be a higher risk factor for women than men, and is associated with a worse prognosis of schizophrenia [53] and CUD [65] in women. On the other hand, although male cannabis users with first-episode psychosis showed a worse quality of life [21], there were no gender differences in the severity of clinical symptoms [3][21]. Nonetheless, when cannabis has already induced a psychotic disorder, it is men who show a greater severity of general psychopathology [66].

Cannabis use has generally been associated with depressive symptoms [51]. However, while some studies have shown that women present this cannabis-related symptomatology to a greater extent than men [67], others do not find such differences [61][63]. Therefore, this association should be specified, since some studies focus on gender differences found in the development of depressive symptoms, others in major depression and others in suicidal ideation [54].

The increase in the frequency of cannabis use is predictive of depressive symptoms in adolescents of both sexes [68][69], although more significantly in women [68][69][70], who show greater psychological distress than men [71]. These results coincide with the fact that women present more depression in the general population [7][8]. On the other hand, other studies indicate that cannabis use is a predictor of depressive symptoms with a greater severity only in men [72][73], which is maintained over the years [74]. This would explain why cannabis use has been seen to increase the probability of developing episodes of major depression in males [75]. This notwithstanding, gender differences between cannabis abuse and major depression have not yet been found [71].

Among subjects with cannabis misuse, men show more depressive symptoms at younger ages (19–20 years), while women show higher depressive and somatization symptoms [76][70][77][78] at later ages (23–25 years) [20]. Probably, these

gender differences in the age of onset of depressive symptoms are due to the fact that men start consumption earlier in life [56].

It has also been described that women with risky cannabis use show a higher possibility of suicide than men in late adolescence [76]. However, men manifest a greater probability of suicidal ideation when increasing the frequency of consumption [61][79], and the gender differences disappear when the sample is extended to the general population [79]. On the other hand, although no relationship has been found between the risk of suicide and the age of onset in the development of CUD in any sex [76], a relationship has been observed between the suicidal history and the onset of cannabis use in women [61]. This is in keeping with the fact that the main reason for consumption reported by women is to relax and reduce stress, probably using cannabis as self-medication [21][20].

Additionally, female cannabis users with first-episode psychosis or diagnosed psychosis have shown greater dysphoria and depression than men [65][64][66]. However, among psychotic males who use cannabis daily, two trends have been found according to age. While it is observed that the increase in the frequency of consumption reduces the probability of suicide attempts in the youngest, when the age range increases (35–64 years), there is a relationship between daily consumption and a greater number of suicide attempts compared to non-users [80]. This change in the direction of the relationship between use and suicide in men could be the result of differences between the acute and chronic effects produced by cannabis [31].

Finally, there are few studies that relate cannabis use to the development of anxious symptomatology, as most studies focus on assessing anxiety as a risk factor for its use. In general, women have the highest levels of anxiety and related disorders among adolescents [20][70], the general population [20][81], and psychiatric patients [76][78], with the biggest gender differences found in late adolescents [20]. Specifically, it has been described that the men and women with low stress tolerance are those who show the most problems related to cannabis use, and in particular women who use the drug as a stress-coping mechanism [82], in a manner similar to that previously commented upon [21][20]. Hence, a positive relationship has been found between cannabis abuse and generalized anxiety disorder in women in the general population, while men showed a negative relationship with panic disorder [81]. In addition, women manifest greater anxiety than men in the periods of abstinence [61][83]. As observed with depression, Foster et al. [76] found no relationship between the age of onset of CUD and anxiety problems.

In conclusion, the scientific evidence reveals the existence of gender differences in psychiatric symptoms associated with cannabis use, although the direction of such differences is not always clear [54]. A lack of information in studies about variables such as the THC level in the cannabis used, the frequency of use or the age of onset of cannabis use makes it difficult to know the causes for the conflicting results. Besides, few studies consider the specific characteristics of women diagnosed with dual pathology, although all the data indicate a higher prevalence of drug-associated pathologies and a worse prognosis in women [27]. For this reason, it is necessary to delve deeper into this issue and address gender differences to create more individualized prevention strategies and more effective treatment for dual disorders related with cannabis abuse.

This entry is adapted from [10.3390/brainsci12030388](https://doi.org/10.3390/brainsci12030388)

---

## References

1. Hartung, C.M.; Lefler, E.K. Sex and gender in psychopathology: DSM–5 and beyond. *Psychol. Bull.* **2019**, *145*, 390–409.
2. Riecher-Rössler, A. Sex and gender differences in mental disorders. *Lancet Psychiatry* **2016**, *4*, 8–9.
3. González-Rodríguez, A.; Studerus, E.; Spitz, A.; Bugra, H.; Aston, J.; Borgwardt, S.; Rapp, C.; Riecher-Rössler, A. Gender differences in the psychopathology of emerging psychosis. *Isr. J. Psychiatry Relat. Sci.* **2014**, *51*, 85–93.
4. Mendrek, A.; Fattore, L. Sex differences in drug-induced psychosis. *Curr. Opin. Behav. Sci.* **2017**, *13*, 152–157.
5. Riecher-Rössler, A.; Butler, S.; Kulkarni, J. Sex and gender differences in schizophrenic psychoses—A critical review. *Arch. Women's Ment. Health* **2018**, *21*, 627–648.
6. Bangasser, D.A.; Cuarenta, A. Sex differences in anxiety and depression: Circuits and mechanisms. *Nat. Rev. Neurosci.* **2021**, *22*, 674–684.
7. Eid, R.S.; Gobinath, A.R.; Galea, L.A. Sex differences in depression: Insights from clinical and preclinical studies. *Prog. Neurobiol.* **2019**, *176*, 86–102.

8. Kuehner, C. Why is depression more common among women than among men? *Lancet Psychiatry* 2016, 4, 146–158.
9. Li, S.H.; Graham, B.M. Why are women so vulnerable to anxiety, trauma-related and stress-related disorders? The potential role of sex hormones. *Lancet Psychiatry* 2016, 4, 73–82.
10. Songtachalert, T.; Roomruangwong, C.; Carvalho, A.F.; Bourin, M.; Maes, M. Anxiety Disorders: Sex Differences in Serotonin and Tryptophan Metabolism. *Curr. Top. Med. Chem.* 2018, 18, 1704–1715.
11. Ait-Daoud, N.; Blevins, D.; Khanna, S.; Sharma, S.; Holstege, C.P.; Amin, P. Women and Addiction: An Update. *Med. Clin. N. Am.* 2019, 103, 699–711.
12. McHugh, R.K.; Votaw, V.R.; Sugarman, D.E.; Greenfield, S.F. Sex and gender differences in substance use disorders. *Clin. Psychol. Rev.* 2018, 66, 12–23.
13. Quigley, J.A.; Logsdon, M.K.; Turner, C.A.; Gonzalez, I.L.; Leonardo, N.; Becker, J.B. Sex differences in vulnerability to addiction. *Neuropharmacology* 2021, 187, 108491.
14. Riley, A.L.; Hempel, B.J.; Clasen, M.M. Sex as a biological variable: Drug use and abuse. *Physiol. Behav.* 2018, 187, 79–96.
15. Teixidó-Compañó, E.; Espelt, A.; Sordo, L.; Bravo, M.J.; Sarasa-Renedo, A.; Indave, B.I.; Bosque-Prous, M.; Brugal, M.T. Differences between men and women in substance use: The role of educational level and employment status. *Gac. Sanit.* 2018, 32, 41–47.
16. Observatorio Español de las Drogas y las Adicciones. Informe 2021. Alcohol, Tabaco y Drogas Ilegales en España. Madrid: Ministerio de Sanidad. Delegación del Gobierno Para el Plan Nacional Sobre Drogas, 2021, 243p. Available online: <https://pnsd.sanidad.gob.es/profesionales/sistemasInformacion/informesEstadisticas/pdf/2021OEDA-INFORME.pdf> (accessed on 24 January 2022).
17. World Drug Report 2021 (United Nations Publication, Sales No. E.21.XI.8). Available online: [https://www.unodc.org/res/wdr2021/field/WDR21\\_Booklet\\_3.pdf](https://www.unodc.org/res/wdr2021/field/WDR21_Booklet_3.pdf) (accessed on 24 January 2022).
18. European Monitoring Centre for Drugs and Drug Addiction. European Drug Report 2021: Trends and Developments; Publications Office of the European Union: Luxembourg. 2021. Available online: <https://www.emcdda.europa.eu/system/files/publications/13838/TDAT21001ENN.pdf> (accessed on 24 January 2022).
19. Kerridge BT, Pickering R, Chou P, Saha TD, Hasin DS. DSM-5 cannabis use disorder in the National Epidemiologic Survey on Alcohol and Related Conditions-III: Gender-specific profiles. *Addict Behav.* 2018, 76(April 2017), 52–60. doi: 10.1016/j.addbeh.2017.07.012
20. Leadbeater, B.; Ames, M.E.; Linden-Carmichael, A.N. Age-varying effects of cannabis use frequency and disorder on symptoms of psychosis, depression and anxiety in adolescents and adults. *Addiction* 2018, 114, 278–293.
21. Arranz, S.; Mané, A.; Bergé, D.; Monserrat, C.; Cabezas, A.; Vilella, E.; Sanchez-Gistau, V. The impact of sex and cannabis on clinical features in first-admitted patients with psychosis. *Eur. Neuropsychopharmacol.* 2020, 36, 235–243.
22. Compton, M.T.; Broussard, B.; Ramsay, C.E.; Stewart, T. Pre-illness cannabis use and the early course of nonaffective psychotic disorders: Associations with premorbid functioning, the prodrome, and mode of onset of psychosis. *Schizophr. Res.* 2011, 126, 71–76.
23. Di Forti, M.; Sallis, H.; Allegri, F.; Trotta, A.; Ferraro, L.; Stilo, S.A.; Marconi, A.; La Cascia, C.; Reis Marques, T.; Pariante, C.; et al. Daily Use, Especially of High-Potency Cannabis, Drives the Earlier Onset of Psychosis in Cannabis Users. *Schizophr. Bull.* 2014, 40, 1509–1517.
24. Hasin, D.; Walsh, C. Cannabis Use, Cannabis Use Disorder, and Comorbid Psychiatric Illness: A Narrative Review. *J. Clin. Med.* 2020, 10, 15.
25. Krebs, M.; Kebir, O.; Jay, T.M. Exposure to cannabinoids can lead to persistent cognitive and psychiatric disorders. *Eur. J. Pain* 2019, 23, 1225–1233.
26. Szerman, N.; Martinez-Raga, J. Dual disorders: Two different mental disorders? *Adv. Dual. Diagn.* 2015, 8, 2.
27. Torrens-Melich, M.; Orengo, T.; de Fonseca, F.R.; Almodóvar, I.; Baquero, A.; Benito, A. Gender Perspective in Dual Diagnosis. *Brain Sci.* 2021, 11, 1101.
28. NIDA. Addiction and Co-Occurring Mental Disorders. National Institute on Drug Abuse Website. 1 February 2007. Available online: <https://archives.drugabuse.gov/news-events/nida-notes/2007/02/addiction-co-occurring-mental-disorders> (accessed on 18 January 2022).
29. Araos, P.; Vergara-moragues, E.; Pedraz, M.; Javier, F.; Rodríguez, F. Adicción a cannabis: Bases neurobiológicas y consecuencias médicas. *Rev. Española Drogodepend* 2014, 39, 9–30.
30. Ferland, J.-M.; Hurd, Y.L. Deconstructing the neurobiology of cannabis use disorder. *Nat. Neurosci.* 2020, 23, 600–610.

31. Cohen, K.; Weizman, A.; Weinstein, A. Positive and Negative Effects of Cannabis and Cannabinoids on Health. *Clin. Pharmacol. Ther.* 2019, 105, 1139–1147.
32. De Aquino, J.; Sherif, M.; Radhakrishnan, R.; Cahill, J.D.; Ranganathan, M.; D'Souza, D.C. The Psychiatric Consequences of Cannabinoids. *Clin. Ther.* 2018, 40, 1448–1456.
33. Fonseca-Pedrero, E.; Lucas-Molina, B.; Pérez-Albéniz, A.; Inchausti, F.; Ortuño-Sierra, J. Experiencias psicóticas atenuadas y consumo de cannabis en adolescentes de la población general. *Adicciones* 2019, 32, 41.
34. Moore, T.H.; Zammit, S.; Lingford-Hughes, A.; Barnes, T.R.; Jones, P.B.; Burke, M.; Lewis, G. Cannabis use and risk of psychotic or affective mental health outcomes: A systematic review. *Lancet* 2007, 370, 319–328.
35. Zammit, S.; Moore, T.H.M.; Lingford-Hughes, A.; Barnes, T.R.E.; Jones, P.B.; Burke, M.; Lewis, G. Effects of cannabis use on outcomes of psychotic disorders: Systematic review. *Br. J. Psychiatry* 2008, 193, 357–363.
36. Blanco, C.; Hasin, D.S.; Wall, M.M.; Flórez-Salamanca, L.; Hoertel, N.; Wang, S.; Kerridge, B.T.; Olfson, M. Cannabis Use and Risk of Psychiatric Disorders: Prospective evidence from a US national longitudinal study. *JAMA Psychiatry* 2016, 73, 388–395.
37. Feingold, D.; Weiser, M.; Rehm, J.; Lev-Ran, S. The association between cannabis use and mood disorders: A longitudinal study. *J. Affect. Disord.* 2015, 172, 211–218.
38. Gallego-Landin, I.; García-Baos, A.; Castro-Zavala, A.; Valverde, O. Reviewing the Role of the Endocannabinoid System in the Pathophysiology of Depression. *Front. Pharmacol.* 2021, 12, 762738.
39. Lowe, D.J.E.; Sasiadek, J.D.; Coles, A.S.; George, T.P. Cannabis and mental illness: A review. *Eur. Arch. Psychiatry Clin. Neurosci.* 2019, 176, 107–120.
40. Hanna, R.C.; Perez, J.M.; Ghose, S. Cannabis and development of dual diagnoses: A literature review. *Am. J. Drug Alcohol Abus.* 2016, 43, 442–455.
41. Fantuzzi, C.; Mezzina, R. Dual diagnosis: A systematic review of the organization of community health services. *Int. J. Soc. Psychiatry* 2020, 66, 300–310.
42. Chan, Y.-F.; Dennis, M.L.; Funk, R.R. Prevalence and comorbidity of major internalizing and externalizing problems among adolescents and adults presenting to substance abuse treatment. *J. Subst. Abuse. Treat.* 2008, 34, 14–24.
43. Arias, F.; Szerman, N.; Vega, P.; Mesias, B.; Basurte, I.; Morant, C.; Ochoa, E.; Poyo, F.; Babín, F. Madrid study on the prevalence and characteristics of outpatients with dual pathology in community mental health and substance misuse services. *Adicciones* 2013, 25, 118–127.
44. Serrano-Serrano, A.B.; Marquez-Arrico, J.E.; Navarro, J.F.; Martinez-Nicolas, A.; Adan, A. Circadian Characteristics in Patients under Treatment for Substance Use Disorders and Severe Mental Illness (Schizophrenia, Major Depression and Bipolar Disorder). *J. Clin. Med.* 2021, 10, 4388.
45. Di Forti, M.; Quattrone, D.; Freeman, T.P.; Tripoli, G.; Gayer-Anderson, C.; Quigley, H.; Rodriguez, V.; Jongsma, H.E.; Ferraro, L.; La Cascia, C.; et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): A multicentre case-control study. *Lancet Psychiatry* 2019, 6, 427–436.
46. Hamilton, I.; Monaghan, M. Cannabis and Psychosis: Are We any Closer to Understanding the Relationship? *Curr. Psychiatry Rep.* 2019, 21, 48.
47. Reid, S.; Bhattacharyya, S. Antipsychotic treatment failure in patients with psychosis and co-morbid cannabis use: A systematic review. *Psychiatry Res.* 2019, 280, 112523.
48. Casajuana Kögel, C.; López-pelayo, H.; Oliveras, C.; Colom, J.; Gual, A.; Balcells-oliveró, M.M. The relationship between motivations for cannabis consumption and problematic use. *Adicciones* 2021, 33, 31–42.
49. Leweke, F.M.; Koethe, D. Cannabis and psychiatric disorders: It is not only addiction. *Addict. Biol.* 2008, 13, 264–275.
50. Koob, G.F.; Volkow, N.D. Neurobiology of addiction: A neurocircuitry analysis. *Lancet Psychiatry* 2016, 3, 760–773.
51. Gobbi, G.; Atkin, T.; Zytynski, T.; Wang, S.; Askari, S.; Boruff, J.; Ware, M.; Marmorstein, N.; Cipriani, A.; Dendukuri, N.; et al. Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood. *JAMA Psychiatry* 2019, 76, 426–434.
52. Satre, D.D.; Bahorik, A.; Zaman, T.; Ramo, D. Psychiatric Disorders and Comorbid Cannabis Use. *J. Clin. Psychiatry* 2018, 79, 79–81.
53. Crocker, C.E.; Tibbo, P.G. The interaction of gender and cannabis in early phase psychosis. *Schizophr. Res.* 2017, 194, 18–25.
54. Prieto-Arenas, L.; Díaz Fernando-Alonso, I. Diferencias de género en el desarrollo de sintomatología psicótica, depresiva y ansiosa asociada al consumo de cannabis. Bachelor's Thesis, Universidad Católica de Valencia, Valencia,



55. Hamilton, I.; Galdas, P.; Essex, H. Cannabis psychosis, gender matters. *Adv. Dual. Diagn.* 2015, 8, 153–162.
56. Arranz, B.; Safont, G.; Corripio, I.; Ramirez, N.; Dueñas, R.M.; Pérez, V.; Álvarez, E.; San, L.; San, L. Substance Use in Patients with First-Episode Psychosis: Is Gender Relevant? *J. Dual Diagn.* 2015, 11, 153–160.
57. Nia, A.B.; Mann, C.L.; Spriggs, S.; DeFrancisco, D.R.; Carbonaro, S.; Parvez, L.; Galynker, I.I.; Perkel, C.A.; Hurd, Y.L. The Relevance of Sex in the Association of Synthetic Cannabinoid Use with Psychosis and Agitation in an Inpatient Population. *J. Clin. Psychiatry* 2019, 80, 19424.
58. Dekker, N.; Meijer, J.; Koeter, M.; van den Brink, W.; van Beveren, N.; GROUP Investigators; Kahn, R.S.; Linszen, D.H.; van Os, J.; Wiersma, D.; et al. Age at onset of non-affective psychosis in relation to cannabis use, other drug use and gender. *Psychol. Med.* 2012, 42, 1903–1911.
59. Donoghue, K.; Doody, G.; Murray, R.; Jones, P.; Morgan, C.; Dazzan, P.; Hart, J.; Mazzoncini, R.; MacCabe, J.H. Cannabis use, gender and age of onset of schizophrenia: Data from the AESOP study. *Psychiatry Res.* 2014, 215, 528–532.
60. Allegri, F.; Murri, M.B.; Paparelli, A.; Marcacci, T.; Braca, M.; Menchetti, M.; Michetti, R.; Berardi, D.; Tarricone, I. Current cannabis use and age of psychosis onset: A gender-mediated relationship? Results from an 8-year FEP incidence study in Bologna. *Psychiatry Res.* 2013, 210, 368–370.
61. Calakos, K.C.; Bhatt, S.; Foster, D.W.; Cosgrove, K.P. Mechanisms Underlying Sex Differences in Cannabis Use. *Curr. Addict. Rep.* 2017, 4, 439–453.
62. Fernández-Artamendi, S.; Martínez-Loredo, V.; López-Núñez, C. Sex Differences in Comorbidity Between Substance Use and Mental Health in Adolescents: Two Sides of the Same Coin. *Psicothema* 2021, 33, 36–43.
63. Verdoux, H.; Sorbara, F.; Gindre, C.; Swendsen, J.D.; van Os, J. Cannabis use and dimensions of psychosis in a nonclinical population of female subjects. *Schizophr. Res.* 2001, 59, 77–84.
64. Menghini-Müller, S.; Studerus, E.; Ittig, S.; Heitz, U.; Egloff, L.; Andreou, C.; Valmaggia, L.R.; Kempton, M.J.; van der Gaag, M.; De Haan, L.; et al. Gender differences of patients at-risk for psychosis regarding symptomatology, drug use, comorbidity and functioning—Results from the EU-GEI study. *Eur. Psychiatry* 2019, 59, 52–59.
65. Lange, E.H.; Nesvåg, R.; Ringen, P.A.; Hartberg, C.B.; Haukvik, U.K.; Andreassen, O.A.; Melle, I.; Agartz, I. One year follow-up of alcohol and illicit substance use in first-episode psychosis: Does gender matter? *Compr. Psychiatry* 2014, 55, 274–282.
66. Bachetti, M.C.; Lanzi, R.; Menculini, G.; Scopetta, F.; Tortorella, A.; Moretti, P. Cannabinoid-induced psychosis: A cross-sectional gender study. *Psychiatr. Danub.* 2020, 32, 200–206.
67. Fattore, L.; Fratta, W. How important are sex differences in cannabinoid action? *J. Cereb. Blood Flow Metab.* 2010, 160, 544–548.
68. Poulin, C.; Hand, D.; Boudreau, B.; Santor, D. Gender differences in the association between substance use and elevated depressive symptoms in a general adolescent population. *Addiction* 2005, 100, 525–535.
69. Schuler, M.S.; Vasilenko, S.A.; Lanza, S.T. Age-varying associations between substance use behaviors and depressive symptoms during adolescence and young adulthood. *Drug Alcohol Depend.* 2015, 157, 75–82.
70. Patton, G.C.; Coffey, C.; Carlin, J.; Degenhardt, L.; Lynskey, M.; Hall, W. Cannabis use and mental health in young people: Cohort study. *BMJ* 2002, 325, 1195–1198.
71. Halladay, J.E.; Boyle, M.H.; Munn, C.; Jack, S.M.; Georgiades, K. Sex Differences in the Association Between Cannabis Use and Suicidal Ideation and Attempts, Depression, and Psychological Distress Among Canadians. *Can. J. Psychiatry* 2018, 64, 345–350.
72. Crane, N.A.; Langenecker, S.; Mermelstein, R.J. Gender differences in the associations among marijuana use, cigarette use, and symptoms of depression during adolescence and young adulthood. *Addict. Behav.* 2015, 49, 33–39.
73. Assari, S.; Mistry, R.; Caldwell, C.H.; Zimmerman, M.A. Marijuana Use and Depressive Symptoms; Gender Differences in African American Adolescents. *Front. Psychol.* 2018, 9, 2135.
74. Crane, N.; Schuster, R.M.; Fusar-Poli, P.; Gonzalez, R. Effects of Cannabis on Neurocognitive Functioning: Recent Advances, Neurodevelopmental Influences, and Sex Differences. *Neuropsychol. Rev.* 2012, 23, 117–137.
75. Park, J.-Y.; Wu, L.-T. Differences in behavioral health disorders and unmet treatment needs between medical marijuana users and recreational marijuana users: Results from a national adult sample. *Drug Alcohol Depend.* 2017, 180, 311–318.
76. Foster, K.T.; Li, N.; McClure, E.A.; Sonne, S.C.; Gray, K.M. Gender Differences in Internalizing Symptoms and Suicide Risk Among Men and Women Seeking Treatment for Cannabis Use Disorder from Late Adolescence to Middle

77. Khan, S.S.; Secades-Villa, R.; Okuda, M.; Wang, S.; Pérez-Fuentes, G.; Kerridge, B.; Blanco, C. Gender differences in cannabis use disorders: Results from the National Epidemiologic Survey of Alcohol and Related Conditions. *Drug Alcohol Depend.* 2012, 130, 101–108.
78. Sherman, B.J.; McRae-Clark, A.L.; Ms, N.L.B.; Sonne, S.C.; Killeen, T.K.; Cloud, K.; Gray, K.M. Gender differences among treatment-seeking adults with cannabis use disorder: Clinical profiles of women and men enrolled in the achieving cannabis cessation-evaluating N-acetylcysteine treatment (ACCENT) study HHS Public Access. *Am. J. Addict.* 2017, 26, 136–144.
79. Naji, L.; Rosic, T.; Dennis, B.; Bhatt, M.; Sanger, N.; Hudson, J.; Mouravska, N.; Thabane, L.; Samaan, Z. The association between cannabis use and suicidal behavior in patients with psychiatric disorders: An analysis of sex differences. *Biol. Sex Differ.* 2018, 9, 22.
80. Waterreus A, Di Prinzio P, Badcock JC, Martin-Iverson M, Jablensky A, Morgan VA. Is cannabis a risk factor for suicide attempts in men and women with psychotic illness? *Psychopharmacology (Berl)*, 2018, 235, 2275–85. doi: 10.1007/s00213-018-4924-6
81. Goldstein RB, Dawson DA, Patricia Chou S, Grant BF. Sex differences in prevalence and comorbidity of alcohol and drug use disorders: Results from wave 2 of the national epidemiologic survey on alcohol and related conditions. *J Stud Alcohol Drugs*, 2012, 73(6), 938–50. doi: 10.15288/jsad.2012.73.938
82. Bujarski SJ, Norberg MM, Copeland J. The association between distress tolerance and cannabis use-related problems: the mediating and moderating roles of coping motives and gender. *Addict Behav*, 2012, 37, 1181–4. doi: 10.1016/j.addbeh.2012.05.014
83. Cuttler C, Mischley LK, Sexton M. Sex Differences in Cannabis Use and Effects: A Cross-Sectional Survey of Cannabis Users. *Cannabis Cannabinoid Res*, 2016, 1(1), 166–75. doi: 10.1089/can.2016.0010