Cannabis and Dependence

An extract from Cannabis: A General Survey of its Harmful Effects
Mary Brett updated
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Drug abuse: Individuals cause harm to themselves (physical, mental or social) or to others through use of the drug. There is a degree of control, use is not constant and they can abstain.

Dependence: A compulsive need for the drug. All harm (physical, mental and social) is ignored as are all other everyday interests. Obtaining the drug becomes all-consuming.

Physical dependence: produces tolerance where more of the drug is needed to get the same effect. Changes take place in the brain. Also observed are **withdrawal symptoms** when use of the drug is stopped. (Because of the long-term persistence of THC in brain cells, the withdrawal symptoms are ameliorated unlike the more dramatic symptoms of heroin withdrawal which is metabolised quickly. Heroin users need a "fix" about every 4 hours).

Psychological dependence: A strong desire or craving for the drug. The drugged state is preferred to normality. It is the more difficult to treat.

Almost all addictive drugs stimulate a part of the brain, the mesolymbic **dopamine system** which is the Central nervous System's Reward Pathway. Cannabis receptors are found here. When stimulated, these receptors begin the cycle of reward which can lead people on to take more. This circuit is shared with animals. (Koob GF 1992).

Some early experiments on dependence failed to prove anything as the doses given to experimental subjects were unrealistically low and the timescale was too short (e.g. Hollister 1986).
However in 1983, Jones et al gave higher and more frequent doses for 3 weeks. Their subjects rapidly developed tolerance and showed withdrawal symptoms. And before that, in 1979 Georgotas and Zeidenberg gave daily doses of 210mg THC, equivalent to a single 1g cigarette today. After 4 weeks the subjects found the marijuana "much weaker" In the first week of abstinence they were irritable, unco-operative, resistant and "hostile", suffered from insomnia and were hungry. The symptoms took 3 weeks to disappear.

After 1986, a substantial number of studies and observations have supported these findings, ie that dependence develops in association with long-term use. (e.g. Miller and Gold 1989, Gable 1993 and Stephens et al 1993).

It was also generally agreed that tolerance develops (Compton et al 1990, Oviedo et al 1993, De Fonseca et al 1994).
Haney et al 1999, researching oral cannabis, THC and cigarettes with 1.8-3.1% THC, described in particular the tolerance to the "high" sought by users.
This tolerance results in a rise in dosage or increased use observed in experiments and in studies of users (Swift et al 2001, Coffey et al 2000, Von Sydow et al 2001).
Compton also described the withdrawal symptoms he found: sleeplessness, anxiety, irritability, sweating, trembling, nausea and weight loss. The severity of these symptoms increased with a longer time, a greater frequency and a larger dosage.

Withdrawal symptoms were also found by Duffy and Milin 1996, Hutcheson et al 1998, Haney et al 1999, Kouri et al 1999 and Johns 2001. The prevalence of withdrawal symptoms in chronic cannabis usage was estimated at 16 to 29% (Thomas 1996 and Wiesbeck et al 1996).

More serious withdrawal symptoms, psychiatric problems and aggression, were reported by Teitel 1971, Rohr et al 1989, and Kouri et al 1999.

People using cannabis therapeutically reported uncomfortable feelings on cessation of use (BMA 1997).

Crowley et al in 1997 looked at University-based adolescents in treatment programmes for substance abuse. They involved males and females. 78.6% met the standard criteria for cannabis dependence. Two thirds (over 80% of men and over 60% of women) reported withdrawal symptoms. The progress from first use to regular use was as rapid as tobacco progression and more rapid than alcohol, suggesting cannabis is a reinforcer. All the patients said that cannabis had clearly caused serious trouble in their lives.

Experimental animals had brain changes similar to those resulting from opiate, alcohol and cocaine withdrawal (De Fonseca et al 1997). Laboratory animals (squirrel monkeys) will self-administer doses of THC equivalent to those used by humans. Self-administration by animals has long been considered a model for human drug-seeking behaviour characteristic of virtually all abused and addictive drugs. The drug-seeking behaviour was comparable in intensity to that maintained by cocaine under identical conditions therefore suggesting that marijuana has as much potential for abuse as drugs like heroin and cocaine. (Goldberg et al 2000).

As a result of these findings, cannabis dependence (but not yet "withdrawal conditions following cannabis use" due to continuing disagreement among researchers) was included as a diagnostic unit in the DSM IV (Diagnostic and Statistical Manual of Mental Disorders 1994) and ICD-10, WHO 1992.

The European Description of The ICD-10 Classification of Mental and Behavioural Disorders, WHO, Geneva, 1992 Diagnosis of Cannabinoid Dependence Syndrome, is as follows:

Diagnostic Guidelines

A definite diagnosis of dependence should be made only if three or more of the following have been experienced or exhibited at some time during the previous year.

(a) a strong desire or sense of compulsion to take cannabinoid;
(b) difficulties in controlling cannabinoid-taking behaviour in terms of its onset, termination or levels of use;
(c) a physiological withdrawal state when cannabinoid use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for cannabinoid; or use of the same(or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
(d) evidence of tolerance, such that increased doses of cannabinoid are required in order to achieve effects originally produced by lower doses;
(e) progressive neglect of alternative pleasures or interests because of cannabinoid use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
(f) persisting with cannabinoid use despite clear evidence of overtly harmful consequences, such as depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm.

Narrowing of the personal repertoire of patterns of cannabinoid use has also been described as a characteristic feature.

It is an essential characteristic of the dependence syndrome that either cannabinoid taking or a desire to take cannabinoid should be present, the subjective awareness of compulsion to use drugs is most commonly seen during attempts to stop or control substance use.

Morgenstern et al in 1994 found the DSM concept at least as valid as those for dependence found in opiates, alcohol, stimulants and sedatives.

Jan Ramstrom who wrote "Adverse Health Consequences of cannabis Use", A Survey of Scientific Studies published up to and including the Autumn of 2003 said, "…there is now general agreement on the issue of cannabis and dependence including the importance of withdrawal symptoms".

One recent paper seems to buck the trend of the general acceptance of cannabis addiction and the fact that it is a recognised diagnosable condition. In 2002, NT Smith published a review paper in "Addiction".
"This review highlights the methodological weaknesses in some of the literature on this subject i.e. variable levels of drug dose administration in laboratory conditions, lack of controlled studies and absence of definitions of the withdrawal syndrome. It concludes that more controlled research might uncover a diagnosis of withdrawal symptoms in human users and may be a precedent for the introduction of a cannabis-withdrawal syndrome before the exact route is known".

Coffey et al in 2003 reported that weekly use of cannabis marks the threshold for an increased risk of later cannabis dependency with selection of cannabis in preference to alcohol possibly indicating an early addiction process. She found that 30% of teenagers smoking more than one a week became addicted by their early twenties, those between 14 and 17 were 20 times more likely. Those starting between 14 and 15 progressed to the most harmful use. Almost 66% of teenagers smoke cannabis and about 7% show signs of dependence. The more they smoke, the higher the risk. Interestingly, dependent cannabis users reported compulsive and out-of-control use more frequently than dependent alcohol users, withdrawal to a similar extent and tolerance considerably less often.

Chambers and others in a paper in 2003 on the development of the adolescent brain, warned of their increased vulnerability to addiction compared to adults. He suggested that drug addiction should be thought of as a development disorder in the brains of teenagers, as the changing brain circuitry leaves them especially vulnerable to the effects of drugs and alcohol. This brain circuitry is centred on the chemical (neurotransmitter) dopamine. Parts of the brain changing rapidly during adolescence are stimulated by addictive drugs. The circuitry that releases chemicals that associate novel experiences with motivation to repeat them develops far more quickly in adolescence than the mechanisms that inhibit urges and impulses. Drugs tapping into this neural imbalance may underlie a teenager's affinity for impulsive and risky behaviour. They are more likely to experiment with drugs but the experience will have more profound effects, sometimes permanent, on the brain. "You have a situation where the motivational brain areas are particularly active", he said, "and the part of the brain that is supposed to inhibit impulses is not working well, because it is sort of under construction. The parts of the frontal cortex that are activated by adults when they weigh risks and rewards lag developmentally".

A definitive review of the addictive propensity of cannabis was undertaken in 2003 by Eliot L Gardner. He reviewed 224 scientific papers, 75 of which were published in the 1970s and 80s and the other 149 after 1989. He concluded that "cannabinoids act on the brain reward processes and reward-related behaviours in strikingly similar fashion to other addictive drugs".

And a review of papers (55 references) dealing with withdrawal symptoms was published in 2004 by Budney, Hughes and others. " Converging evidence from basic laboratory and clinical studies indicates that a withdrawal syndrome reliably follows discontinuation of chronic heavy use of cannabis or tetrahydrocannabinol. …..The onset and time course of these symptoms appear similar to those of other substances withdrawal symptoms. The magnitude and severity of these symptoms appear substantial, and these findings suggest that the syndrome has clinical importance".

Continuing their work, Budney and Hughes have just (2006) contributed again to our knowledge of the withdrawal syndrome in cannabis. In their "Purpose of review" they say, "The demand for treatment for cannabis dependence has grown dramatically. The majority of the people who enter treatment have difficulty in achieving and maintaining abstinence from cannabis". Among their findings are, "The neurological basis for cannabis withdrawal has been established via discovery of an endogenous cannabinoid system, identification of cannabinoid receptors, and demonstrations of precipitated withdrawal with cannabinoid receptor antagonists. Laboratory studies have established the reliability, validity and time course of a cannabis withdrawal syndrome and have begun to explore the effect of various medications on such withdrawal. Reports from clinical samples indicate that the syndrome is common among treatment seekers". Another research report by Budney in Addiction 101 (suppl.1) 2006, found that "…cannabis dependence is much more similar to than different from other types of substance dependence, even with regard to withdrawal. The generic DSM-1V dependence criteria can be applied fairly well to cannabis , and yield findings similar to that observed with other substance dependence disorders….whether we can do better by developing more sophisticated generic criteria or using substance specific criteria".

In a paper still in press (2006), Budney et al say, " The demonstration of a dose-dependent suppression of cannabis withdrawal by oral THC provides additional support for validity of the cannabis withdrawal syndrome and its inclusion in the DSM".

Several papers have been written on the extent and prevalence of cannabis dependence.

Young Americans were followed for 13 years from the 7th 8th or 9th grade in school. At 27 to 29 years old just under 24% abused cannabis and just over a quarter of them were addicted, ie 8% of the total population (Newcomb 1992).

A North American population study of 20,000 people reported that, of the 4.4% who abused cannabis roughly 60% were dependent on it. That is about 2.6% of the population (Hall et al 1994) And in a letter to The Lancet in 1998 Hall and Solowij wrote that, of those who ever start using cannabis, 10% will become daily users and 20 to 30% will use it weekly.

In 2003 Fergusson et al, following up 1265 children born in Christchurch, New Zealand for 21 years, concluded that, for the majority of users, cannabis did not lead to problems of dependence. Nonetheless, nearly 10% of the cohort showed clear signs of cannabis dependence by age 21, especially males who were prone to other forms of risk-taking behaviour.

On Sunday June 13th 2004 The Observer carried a story that increasing numbers of people were becoming dependent on the drug. Department of Health figures recorded 9% of attendees at clinics cited cannabis as their problem drug, twice the number ten years before. Research from the United States showed that cannabis is the commonest reason for 12 to 17 year olds to be placed in treatment centres – 60% of all cases. Treatment for cannabis dependence or habitual usage among youngsters had risen 142% in a decade.

Dr Romeo Ashruf, a Dutch addiction specialist and Director of the Parnassia Clinic in The Hague, told Network 2's Bijous Theis TV programme on March 20th 2006 that Dutch children as young as 12 were addicted to cannabis. The powerful home-grown nederwiet they are using is up to 20 times stronger in its THC content than imported varieties. Referrals used to be for young people between 16 and 21, but are now for 14 to 19 year olds. He warned parents of the difference in strength of the drug today.

Cambridge University Press has recently (2006) published a book "Cannabis Dependence: Its Nature, Consequences and Treatment in the series: *International Research Monographs in the Addictions, which*
"Breaks through the controversial politics of cannabis use to give a clear, scientific synthesis of all the Health-related issues relating to cannabis use".
" Reviews and assesses all the interventions applied to both adult and adolescent users".
"Gives the criteria for diagnosis and scope of cannabis dependence".

In 2006 Copersino et al looked at 104 non-treatment seeking adults, primarily cannabis users who had made at least one serious attempt to stop using the drug. "Study findings provide evidence for the clinical significance of a cannabis withdrawal syndrome, based on the high prevalence and co-occurrence of multiple symptoms that follow a consistent time course and that prompt action by the subjects to obtain relief, including serving as negative reinforcement for cannabis use" They said that these findings support the existence of a clinically significant cannabis withdrawal syndrome, which should be considered for inclusion in the DSM-V.

An article in The Ottawa Citizen on 24/11/06 reported that Psychiatrist Kathy Szirtes, speaking at a "Dazed and Confused" forum for teenagers in Rideau High School, said that adults may take 2 years to become addicted to marijuana while children can take only about 6 months as their brains are still not properly developed. Marijuana cravings she said were often mistaken for symptoms of ADHD. The forum was sponsored by the CAMC, Champlain Addiction Coordinating Body and Ottawa Integrated Drugs and Addictions Strategy.

CB1 gene variants may be linked with symptoms of marijuana dependence in adolescents. Hopfer and others found that two CB1 variants (present in 12% of the population) were significantly linked to the likelihood of the development of one or more dependent symptoms and another variant (present in 21% of the population) was linked to a lower risk of dependent symptoms developing. DNA samples were

taken from 541 youths aged 17 or over who had recently used marijuana at least 5 times. 327 had one or more symptoms of dependence, the other 214 became the controls.

Chronic abuse of different drugs cause similar brain changes. Whether long-term users favour cocaine, cannabis or PCP, autopsies of their brains show a number of common gene changes consistent with diminished brain plasticity (ability to learn from new experiences and adapt to new situations). A paper by Lehrmann and others found that the anterior pre-frontal cortex (decision-making region) was dysfunctional in the brains of drug users. The brains of 42 deceased abusers were studied. Nearly 80% of them had similar alterations in genetic output compared to the controls. Genes involved in calcium signalling were turned down and those in lipid and cholesterol-related pathways were turned up. The abuser's ability to make sound decisions could be threatened.

2006: Nocon et al examined prospectively over 4 years, the profile of cannabis dependence and the risk of specific dependence criteria in a community sample of 2,446 young people between 14 and 24. 30% were users of cannabis. 35%met at least one dependence criterion, withdrawal 17%, tolerance 15%, loss of control 14%, and continued use despite a health problem 13%. Even 22% of low frequency users met one criterion, as did 81% of high frequency users. The occurrence of dependence could not be attributed to the concomitant use of other illicit drugs or dependence on alcohol or tobacco.

Over 2500 adult daily cannabis users completed an Internet survey. Fewer than half of daily cannabis users meet the DSM-IV-TR criteria for cannabis dependence. This study aimed to determine whether the negative aspects associated with use of cannabis can be explained by a proxy measure of dependence instead of by frequency of use. Comparing those who were dependent (N=1111) with those who were not (N=1770), the former consumed greater amounts of cannabis, various other drugs and alcohol. They also exhibited higher levels of depression and lower levels of happiness, motivation and satisfaction with life. The study concluded, " Although all of our subjects reported daily use, only those meeting proxy criteria for cannabis dependence reported significant associated problems. Our data suggests that dependence need not arise from daily use, but consuming larger amounts of cannabis and other drugs undoubtedly increases problems" (Looby and Earleywine 2007).

A paper from STASH (Science Threads of Addiction, Substance Use and Health), January 2007, looked at the transition from drug use to dependence. Over 8,000 participants were involved in the study (a report of 3 papers). The probabilities of initiation of drug use peaked at age 18 for alcohol and marijuana. The risk of developing dependence on these drugs also peaked in the teens. Male marijuana users were approximately twice as likely to become dependent in the 2 to 5 years after first use than female users.

A plant extract which may block cannabis addiction has been discovered. MLA (methyllycaconitine) from the seeds of Delphinium brownie, a plant in the buttercup family was given to rats. They lost their craving for a synthetic version of THC and a reward response to THC was blocked in the brain. By analysing fluid from the nucleus acumbens in the reward signalling area of the brain they found that release of dopamine was blocked by MLA. It is not known exactly how MLA works but no side-effects were reported. Dopamine levels were not reduced below the normal. (Goldberg S et al 2007).

A review paper on Marijuana Dependence and its Treatment by Budney and others was published in December 2007. They concluded that the "good news" was the increased recognition that cannabis can cause addiction. Significant negative consequences in a sub-set of users has resulted in specific marijuana-related treatments and interventions similar to those used for other substance disorders. More people are now seeking help as it is now perceived to be acceptable to do so. Rapid advances in the neurobiology associated with marijuana and the cannabinoid system bring hope for increasingly effective treatment options. More severe dependence may be prevented in some users and better contacts made with users who may benefit.

2007 Adult Psychiatric and Morbidity Study: The prevalence of drug dependence was 3.4% (4.5%of men, 2.3%of women). Most dependence was on cannabis only (2.5%), rather than other drugs (0.9%). Symptoms of dependence were most commonly reported by adults aged between 16 and 24 (13.3%)of men, 7.0% of women in this age group).

Vandrey et al compared withdrawal symptoms from cannabis and tobacco in a paper in January 2008. They concluded that, "Overall withdrawal severity associated with cannabis alone and tobacco alone

was of a similar magnitude. Withdrawal during simultaneous cessation of both substances was more severe than for each substance alone, but these differences were of short duration and substantial individual differences were noted. These results are consistent with other evidence suggesting cannabis withdrawal is clinically important and warrants detailed description in the DSM-V and ICD-11".

In 2008 (May) Walden and Earleywine found that the quantity of cannabis used predicts future problems with dependence, social factors and respiratory health. Nearly 6,000 adults using at least once a month reported on levels of intoxication and quantity used. Quantity was found to be an important predictor of these 3 problems.

It should be pointed out that most people in Northern Europe smoke cannabis with tobacco. Addiction to nicotine, according to some experts is one of the most difficult to treat and certainly many smokers seem to find it almost impossible to give up. This "double addiction" would significantly exacerbate the problems of giving up cannabis.

EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) in their annual report in 2010 found that 'Factors specifically associated with progression to dependence include intensive or risky patterns of cannabis use, persistent use and early onset. Individuals who experience positive effects (e.g. laughter, happiness) of their early cannabis use (at age 14-15) had an increased risk of cannabis dependence later in life'.

James Langton smoked cannabis for 30 years. He said, "When I was smoking cannabis it was the most important thing in my life. More important than my family, my friends, my relationships or my job. …. When I was without it, I was irritable, anxious and could concentrate on little else until I was stoned again….if you had asked me at any time over that long period whether I was addicted to the stuff, I would have laughed in your face and denied it. I knew, as everyone knew at the time, that cannabis wasn't addictive. …"….Apart from denial, fear is the other factor that reinforces cannabis addiction…I was terrified of physical withdrawal. ….disrupted sleep, night sweats, cramps, nausea and loss of appetite. Other symptoms are closer to nicotine withdrawal such as mood swings, irritability and depression".

He has now set up "Clearhead", a new privately funded organisation offering support and information to those seeking to make positive changes in their lives regarding their use of cannabis. He has a website and runs weekend workshops.

2011 Lopez-Larson et al looked at prefrontal and insular cortical thickness in adolescent users. 18 heavy users were compared with 18 non-users. 'Our results suggest that the age of regular use may be associated with altered prefrontal cortical gray matter development in adolescents. Furthermore reduced insular cortical thickness may be a biological marker for increased risk of drug dependence'.

2011 Vanderbilt Addiction Center researchers found that exercise can curb marijuana use and cravings. 12 participants, all cannabis-dependent (av 5.9 joints/day) and not willing to have treatment exercised by running on a treadmill. Their cravings for and use of cannabis were cut by more than 50% after exercising on the treadmill for 10 sessions of 30 minutes each over a fortnight. The maximum reduction occurred in the first week, and overall fell to 2.8 joints/day.

2011 Allsop et al looked at the development of a 'Cannabis Withdrawal Scale'. Results showed that the scale had excellent psychometric properties. Nightmares and/or strange dreams was the most valid item but caused relatively little associated distress. Unlike intense angry outbursts which caused much associated distress. Inability to get to sleep caused significant distress. They concluded that 'The Cannabis Withdrawal scale can be used as a diagnostic instrument in clinical and research settings where regular monitoring of withdrawal symptoms is required'.

2013 NIDA researchers suggested that medication to treat marijuana addiction may be on the horizon. Kynurenic acid is a naturally occurring substance in the brain that can lessen the effects of THC in animal models of drug abuse and addiction. If effective in humans, this could lead to a medication for the treatment of marijuana addiction.

2013 Hurd et al provided an overview of the endocannabinoid system in relation to cannabis exposure and provide insights regarding factors such as genetics and behavioural traits that confer risk for

subsequent addiction. Current evidence suggests that the long-term impact of adolescent cannabis exposure on brain and behaviour has a far-reaching influence on adult addictive behaviours particularly for certain subsets of vulnerable individuals.

2014 April NIDA found that marijuana use may promote nicotine consumption.
Most marijuana users smoke cigarettes, and about 1 in 5 individuals who use both substances (1 in 3 among African Americans) used marijuana first. In one recent study, adolescents who used marijuana weekly were more likely than less frequent marijuana users or nonusers to initiate tobacco use. These patterns occur in part because some of the same personal traits and social and environmental exposures that lead people to use marijuana also influence them to try other drugs. The new findings (on rats) suggest that marijuana use itself, independently of these influences, predisposes users to become regular smokers, increasing their odds of becoming addicted to nicotine.

2014 March, Van der Pol and others found that the behaviour of smokers is more important than the potency of their pot (amount of THC) for predicting who will become dependent. Smokers of pot varieties did inhale less smoke and they smoked at a slower pace. They 'titrated' their THC intake but not sufficiently to fully compensate for the THC strength so users of more potent cannabis are generally exposed to more THC. Smoking behaviour appears to be a stronger predictor of cannabis dependence severity than THC content.

2014 September 2nd Greene and Kelly found that cannabis withdrawal symptoms are common in adolescents treated for substance use disorder. A study by Massachusetts general Hospital found that 40% of cannabis-using adolescents receiving outpatient treatment for substance use disordrer experienced withdrawal symptoms. 127 adolescents (14-19) were studied, 90 with cannabis as their most frequently used drug – 84% met the criteria for cannabis dependence. 36(40% of the overall) of them reported withdrawal symptoms, all of whom also met the criteria for dependence.

2015 Freemnan and Winstock looked at high-potency cannabis and its association with severity of cannabis dependence as demand for treatment in addiction services continues to rise. They found that frequent use of high-potency cannabis predicted a greater severity of dependence and this effect became stronger as age decreased. Its profile is strongly defined by negative effects (memory, paranoia), but also positive characteristics – best high, preferred type. It is also the most available.

2016 Gelernter et al looked at genes related to cannabis addiction, depression and schizophrenia. The genes of nearly 15,000 people from 3 different groups. Between 18% and 36% had cannabis addiction. One of the genes was linked to risk for both depression and marijuana addiction. They also found a marijuana-addiction gene related to risk for schizophrenia.

2016 Hindocha et al investigated whether the combination of tobacco and cannabis can increase the likelihood of dependence. 33,687 cannabis users, participants of the 2014 Global Drug Survey, took part anonymously in the research. Tobacco routes for cannabis, joints, blunts or pipes are most popular in Europe (between 77.2% and 90.9%) while only 51.6% of Australians and 20.7% of New Zealanders used them. They are least popular in the Americas. Cannabis users who favour non-tobacco routes had 61.5% higher odds of wanting professional help to use less cannabis and 80.6% higher odds of wanting to use less tobacco than those who used tobacco routes. Cannabis users who prefer non-tobacco routes had 10.7% higher odds of wanting to use lss tobacco and 103.9% higher odds of actively planning to seek help to use less tobacco. These results suggest that people who regularly mix tobacco with cannabis are more at risk of psychological dependence than those who use cannabis and tobacco separately, without mixing them.

2016 Freeman looked at addiction and super-strength cannabis (skunk). More than 400 adolescents and young adults (aged 16-23) in the UK using marijuana were studied. 43% of the participants who smoked skunk were dependent on the drug while 22% who used less potent types were dependent.

2018 Livne et al looked at DSM-5 cannabis withdrawal syndrome Abstract: Cannabis withdrawal syndrome (CWS) was newly added to the Diagnostic and Statistical Manual of Mental Disorders in its most recent edition, DSM-5. With cannabis use increasing among U.S. adults, information is needed about the prevalence and correlates of DSM-5 CWS in the general population. This study presents nationally representative findings on the prevalence, sociodemographic and clinical correlates of DSM-5 CWS among U.S. adults. Participants ≥18 years were interviewed in the National Epidemiologic

Survey on Alcohol and Related Conditions-III (NESARC-III) in 2012-2013. Among the sub-sample of frequent cannabis users in the prior 12 months (≥3 times a week; N = 1527), the prevalence and demographic and clinical correlates of DSM-5 CWS were examined. In frequent cannabis users, the prevalence of CWS was 12.1%. The most common withdrawal symptoms among those with CWS were nervousness/anxiety (76.3%), hostility (71.9%), sleep difficulty (68.2%) and depressed mood (58.9%). CWS was associated with significant disability ($p < 0.001$), and with mood disorders (adjusted odds ratios [aOR] = 1.9–2.6), anxiety disorders (aOR = 2.4–2.5), personality disorders (aOR = 1.7–2.2) and family history of depression (aOR = 2.5) but not personal history of other substance use disorders or family history of substance use problems. CWS is highly comorbid and disabling. Its shared symptoms with depressive and anxiety disorders call for clinician awareness of CWS and the factors associated with it to promote more effective treatment among frequent cannabis users.

2020 Bahji et al investigated the Prevalence of Cannabis Withdrawal Symptoms Among People With Regular or Dependent Use of Cannabinoids

Abstract: Data Extraction and Synthesis All abstracts, full-text articles, and other sources were reviewed, with data extracted in duplicate. Cannabis withdrawal syndrome prevalence was estimated using a random-effects meta-analysis model, alongside stratification and meta-regression to characterize heterogeneity. Main Outcomes and Measures Cannabis withdrawal syndrome prevalence was reported as a percentage with 95% CIs.

Results Of 3848 unique abstracts, 86 were selected for full-text review, and 47 studies, representing 23 518 participants, met all inclusion criteria. Of 23 518 participants included in the analysis, 16 839 were white (72%) and 14 387 were men (69%); median (SD) age was 29.9 (9.0) years. The overall pooled prevalence of CWS was 47% (6469 of 23 518) (95% CI, 41%-52%), with significant heterogeneity between estimates ($I^2 = 99.2\%$). When stratified by source, the prevalence of CWS was 17% (95% CI, 13%-21%) in population-based samples, 54% in outpatient samples (95% CI, 48%-59%), and 87% in inpatient samples (95% CI, 79%-94%), which were significantly different ($P < .001$). Concurrent cannabis ($\beta = 0.005$, $P < .001$), tobacco ($\beta = 0.002$, $P = .02$), and other substance use disorders ($\beta = 0.003$, $P = .05$) were associated with a higher CWS prevalence, as was daily cannabis use ($\beta = 0.004$, $P < .001$). Conclusions and Relevance These findings suggest that cannabis withdrawal syndrome appears to be prevalent among regular users of cannabis. Clinicians should be aware of the prevalence of CWS in order to counsel patients and support individuals who are reducing their use of cannabis.

2020 Leung et al the prevalence and risk of cannabis use disorders among people who use cannabis. We conducted a systematic review of epidemiological cross-sectional and longitudinal studies on the prevalence and risks of CUDs among cannabis users. We identified studies published between 2009 and 2019 through PubMed, the Global Burden Disease (GBD) Database, and supplementary searches up to 2020. The outcomes of interest were CUDs based on DSM or ICD criteria. Estimates were synthesized using random-effects *meta*-analyses, followed by *meta*-regression of study characteristics on effect sizes. Results From 1383 records identified, 21 studies were included. Meta-analyses showed that among people who used cannabis, 22% (18–26%) have CUD, 13% (8–18%) have CA, and 13% (10–15%) have CD. Estimates from cohort studies, showed that the risk of developing CD increased to 33% (22–44%) among young people who engaged in regular (weekly or daily) use of cannabis. There was a lack of data from cohort studies to estimate the risk of CUD or CA among regular cannabis users. Conclusions Cannabis users need to be informed about the risks of developing CUDs and the higher risks among those who initiate early and use frequently during adolescence. Future studies are needed to examine how changes in cannabis policies may affect the risks of CUDs in the population.

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