Published in final edited form as:
Drug Alcohol Depend. 2012 June 1; 123(1-3): 141–147. doi:10.1016/j.drugalcdep.2011.11.007.

Diagnostic Criteria for Cannabis Withdrawal Syndrome

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Abstract

Objective—Cannabis withdrawal occurs in frequent users who quit, but there are no accepted diagnostic criteria for a cannabis withdrawal syndrome (CWS). This study evaluated diagnostic criteria for CWS proposed in DSM-V and two earlier proposals.

Method—A convenience sample of 384 adult, non-treatment-seeking lifetime cannabis smokers provided retrospective self-report data on their "most difficult" quit attempt without formal treatment, which was used in this secondary analysis. Prevalence, time of onset, and peak intensity (5-point Likert scale) for 39 withdrawal symptoms (drawn from the literature) were assessed via computer-administered questionnaire. Subject groups were compared using chi-square or ANOVA. Symptom clustering was evaluated with principal components analysis.

Results—40.9% of subjects met the DSM-V criterion of ≥ 3 symptoms from a list of 7. There were no associations with sex, race, or type of cannabis preparation used. There were significant positive associations between duration or frequency of cannabis use prior to the quit attempt and experiencing CWS. Subjects with CWS had a significantly shorter duration of abstinence. Alternative syndromal criteria (dropping physical symptoms from DSM-V list; requiring ≥ 2or ≥ 4 symptoms from a list of 11) yielded a similar prevalence of CWS and similar associations with prior cannabis use and relapse. The PCA yielded 12 factors, including some symptom clusters not included in DSM-V.

Conclusions—Findings support the concurrent and predictive validity of the proposed DSM-V CWS, but suggest that the list of withdrawal symptoms and number required for diagnosis warrant further evaluation.

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Contributors
Authors Gorelick, Levin, Copersino, and Heishman designed the study and wrote the protocol. Author Levin was responsible for data collection oversight and data base management. Author Liu performed the statistical analyses. Author Gorelick wrote the first draft of the manuscript. Authors Copersino, Kelly, and Boggs reviewed the manuscript for substantive intellectual content. All authors reviewed and approved the final manuscript.

Conflict of interest
No conflict declared.

Keywords

cannabis; diagnostic criteria; DSM-V; withdrawal

1. Introduction

Cannabis is the most widely used illegal drug, with up to 190 million current users worldwide (United Nations Office on Drugs and Crime, 2009) and an estimated 15.2 million current users in the US (Substance Abuse and Mental Health Services Administration, 2009). A high proportion of frequent cannabis users report experiencing a withdrawal syndrome after stopping use, ranging from 15.6%–40.9% in studies of non-treatment-seeking adults (Cottler et al., 1995; Schuckit et al., 1999; Swift et al., 1998; Swift et al., 2000; Wiesbeck et al., 1996) to 95.5% and 88.8% in two Australian studies of cannabis-dependent adults (Copeland et al., 2001; Swift et al., 2001). A cannabis withdrawal syndrome (CWS) is not formally recognized in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000). One is listed, albeit without diagnostic criteria, in the International Statistical Classification of Diseases and Related Health Problems, tenth revision (ICD-10; World Health Organization, 1993).

The initial draft proposal for DSM-V does include CWS (www.dsm5.org, accessed March 19, 2010). The specific diagnostic criteria proposed are:

> Criterion A: Cessation of cannabis use that has been heavy and prolonged
>
> Criterion B: 3 or more of the following seven symptoms develop within several days after Criterion A: 1) Irritability, anger or aggression, 2) Nervousness or anxiety, 3) Sleep difficulty (insomnia), 4) Decreased appetite or weight loss, 5) Restlessness, 6) Depressed mood, 7) Physical symptoms causing significant discomfort from at least one of the following: stomach pain, shakiness/tremors, sweating, fever, chills, headache
>
> Criterion C: The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
>
> D. The symptoms are not due to a general medical condition and are not better accounted for by another disorder

These proposed diagnostic criteria are based on two literature reviews (Budney et al., 2004; Budney and Hughes 2006) and subsequent published studies of cannabis withdrawal (Agrawal et al., 2008; Arendt et al., 2007; Chung et al., 2008; Copersino et al., 2006; Cornelius et al., 2008; Hasin et al., 2008; Milin et al., 2008). The justification posted with the proposal acknowledges that specific data are not available to address many of the relevant diagnostic issues.

The DSM-V proposal differs somewhat from several prior proposed diagnostic criteria for CWS (Budney et al., 2004; Budney and Hughes 2006; Chung et al., 2008). These proposals varied in the content and length of the symptom list and the required number of symptoms (Table 1). By comparison, DSM-IV criteria for a substance withdrawal syndrome require experiencing at least two (alcohol, sedative/hypnotics/anxiolytics), three (opiates), or four (nicotine) symptoms from a list of substance-specific withdrawal symptoms (American Psychiatric Association, 2000).

Chung and colleagues (Chung et al., 2008) evaluated the prevalence and concurrent and predictive validity of their proposed CWS criteria in their sample of 214 adolescent cannabis users (most with other substance abuse and/or psychiatric comorbidity) participating in intensive outpatient addictions treatment. 37.4% had past-year CWS using the two-symptom

criterion; 17.8% using the four-symptom criterion. Patients meeting either the 2-symptom or 4-symptom CWS criterion had more frequent past year cannabis use and greater number of DSM-IV cannabis dependence criteria than did patients without withdrawal, but did not differ in duration of lifetime regular cannabis use at baseline, suggesting good concurrent validity. The 4-symptom criterion was significantly positively associated with number of DSM-IV dependence criteria met over one year of follow-up, but not with frequency of cannabis use or number or duration of abstinent periods during follow-up. The 2-symptom criterion was not significantly associated with any of these variables, suggesting poor predictive validity. We are not aware of any other studies evaluating the validity of specific diagnostic criteria for CWS.

We have previously reported data from adult cannabis smokers, without significant current medical or psychiatric co-morbidity, who provided retrospective self-report data on 40 individual withdrawal symptoms experienced during their “most difficult” cannabis quit attempt (Levin et al., 2010). We conducted a secondary analysis of these data to evaluate the prevalence and concurrent and predictive validity of the proposed DSM-V criteria for CWS. These data also provide empirical evidence to address some diagnostic issues raised in the DSM-V proposal.

2. Methods

2.1. Subjects

Subjects were a convenience sample of 500 non-treatment-seeking lifetime cannabis smokers recruited from the Baltimore, MD area by the National Institute on Drug Abuse (NIDA) Intramural Research Program (IRP) Central Recruiting Unit using advertising (print, television, radio, internet), word-of-mouth, and referral from other agencies (Levin et al., 2010). Eligible subjects were 18 years or older, able to read English at an 8th grade level, and had made at least one attempt to stop all cannabis use without formal treatment while not in a controlled environment. All subjects were primarily cannabis users with no other current major medical, psychiatric, or substance use disorder except nicotine dependence (based on telephone screening questions).

This study was approved by the Institutional Review Board of the NIDA IRP. After complete description of the study was provided, subjects gave written informed consent while not acutely intoxicated or in withdrawal. All subjects were paid for their study participation.

2.2. Procedures

Data were collected using the Marijuana Quit Questionnaire (MJQQ), a 176-item self-report questionnaire that collects information in three domains: sociodemographic characteristics, history of cannabis use (including any associated problems), and characteristics of subjects’ “most difficult” (self-defined) quit attempt outside a controlled environment, including reasons for quitting, coping strategies to help quit, withdrawal symptoms, and substance use before and during the quit attempt (Levin et al., 2010). The MJQQ was presented on a computer monitor and took 30–45 minutes to complete.

The data on lifetime cannabis-related problems allowed generation of proxy diagnoses for lifetime cannabis abuse or dependence. Subjects who endorsed lifetime experience of at least three problems from among the dependence criteria in DSM-IV were considered to have cannabis dependence. These must be considered proxy or tentative diagnoses because the DSM-IV criterion that the criteria occur within a 12-month interval was not assessed.

Subjects received a list of 40 possible cannabis withdrawal symptoms drawn from the published literature (Levin et al., 2010). If the symptom had been experienced during the index quit attempt, subjects indicated the number of days after last using cannabis that the symptom first appeared (time of onset), its maximum intensity (on a 5-point Likert scale from "very little" to "very high"), and what, if anything, they did to relieve that symptom.

2.3. Statistical analyses

To minimize inclusion of symptoms not actually due to withdrawal, only withdrawal symptoms with onset within one month of the start of the quit attempt were included in the analyses. To mirror the diagnostic requirement that a withdrawal symptom cause clinically significant distress or impairment (DSM-V criterion C), only symptoms for which subjects reported taking action to relieve it (including use of cannabis) were included in the analyses (whereas all symptoms were included in the previous analyses; Levin et al., 2010). In addition, the item "improved memory" (endorsed by 28% of subjects, with mean onset almost two weeks after quitting) was not included in analyses because it probably reflects a rebound from cannabis-associated memory impairment, rather than a true withdrawal symptom.

The MJQQ contained items reflecting all seven withdrawal symptoms in the DSM-V proposal and all 11 core symptoms in the two Budney proposals. However, 7 of the 22 items in the Chung et al. proposal (Table 1) were not contained in the MJQQ: trouble concentrating, tired/sleepy/weak, fast heartbeat, teary/runny nose, muscle pains, hallucinations, and seizures. Therefore, the Chung CWS criterion was not included in further analyses. Some individual MJQQ items had to be combined to reflect the symptoms included in proposed symptom lists (Table 1). Subjects were considered to have a "combined" symptom if they reported at least one of the individual MJQQ items contributing to that combination. Onset of a combined symptom was the earliest onset of any of its component items. The peak intensity of a combined symptom was the greatest intensity of any of its component items.

Comparisons among subject groups used the chi-square test for categorical variables and the t-test or ANOVA for continuous variables. Duration of abstinence during the quit attempt was not normally distributed, so this continuous variable was analyzed by Kruskal-Wallis test. The associations between the three CWS criteria and duration of the quit attempt were compared using a generalized estimating equation model (SAS GENMOD procedure) to implement an algorithm that simultaneously performed each univariate analysis (Pepe et al., 1999).

The internal consistency of the DSM-5 and Budney CWS symptom lists was evaluated using Cronbach's standardized alpha coefficient (SAS CORR procedure).

Principal components analysis (PCA) with varimax rotation and Kaiser normalization (SAS Proc factor) was used to evaluate associations among the individual withdrawal symptoms. Factors were considered significant only if they had eigenvalues ≥1 and individual item (symptom) loadings ≥0.5.

All statistical analyses were performed with SAS statistical software version 9.1 (SAS Institute, Cary, NC). The two-tailed alpha level was set at 0.05.

3. Results

3.1. Subjects

Of the 500 subjects consented to the original study (Levin et al., 2010), 469 provided usable data (2 did not complete the questionnaire, 14 had never made a quit attempt and 15 had quit in a controlled environment such as jail or hospital). To reduce the potential influence of recall problems, the data presented here are limited to the 384 subjects (82% of original sample) who were interviewed within 5 years of the start of their index quit attempt. In brief, they were largely young adult (mean [SD] age 29.2 [9.3] years, range 18 to 65 years), non-Hispanic (94.3%), African-Americans (82.3%) of low socio-economic status. More than half (58.3%) were male. Almost three-quarters (71.1%) reported at least 1000 lifetime uses of cannabis. Almost all subjects (99%) met at least one lifetime criterion for DSM-IV cannabis dependence; 92.4% met at least 3 criteria, suggesting a likely lifetime diagnosis of cannabis dependence.

3.2. Characteristics of index quit attempt

The index ("most difficult") quit attempt started 14.9 [16.2] months (median 9.6 months, range 2 days to 5 years) before the interview, and lasted 6.4 [21.2] months (median 1.4 months, range 1 day to 5 years). At the start of the quit attempt, subjects were 27.9 (9.3) years old (range 16–64 years) and had been using cannabis regularly (i.e., at least weekly) for 11.3 (9.0) years (range <1–42 years). Over the 6 months prior to the index quit attempt, almost two-thirds of subjects (65.6%) averaged daily smoking; another 31.0% smoked at least weekly. Almost two-thirds (64.1%) were generally smoking blunts and more than one-third (35.4%) marijuana (joints). Subjects used cannabis on 22.6 [10.4] days (median 30, range 1–31) in the month prior to the quit attempt, averaging 9.2 [10.9] (median, range 1–120) joints per day and a total of 233.4 [327.2] (median 127.8, range 0–3600) joints over the entire month.

Many subjects used legal psychoactive substances at least weekly over the 6 months prior to their index quit attempt: 53.3% caffeine, 35.4% alcohol, and 67.5% tobacco. Illegal drugs or psychoactive prescription medication were each used at least weekly by less than 10% of subjects: opiates--5.5%, stimulants—6.5%, sedative/hypnotics—3.7%, phencyclidine—0.5%, and hallucinogens—0.8%. Decreases in psychoactive substance use were uncommon during the quit attempt. Among subjects using a drug class at least weekly prior to the quit attempt, only a minority within each class decreased their use during the quit attempt: 10.1% for caffeine (5.2% of all subjects), 15.4% for alcohol (5.5%), 12.4% for tobacco (8.3%), 44.0% for stimulants (2.9%), 19.1% for opiates (1.0%), 14.3% for sedative/hypnotics (0.5%), 33.3% for hallucinogens (0.3%), and 50% for phencyclidine (0.3%).

3.4. Individual withdrawal symptoms

The prevalence, time of onset, and peak intensity of 26 withdrawal symptoms (or combinations of symptoms) relevant to proposed diagnostic criteria for CWS are presented in Table 2.

Some withdrawal symptoms are comprised of two or more items (Table 1). Among subjects experiencing DSM-V "physical symptoms," almost two-thirds (64.9%) reported only one of the five possible items comprising this symptom; another 21.6% reported two items. A minority (13.4%) of subjects reported three or more physical symptom items. Women were significantly more likely than men to report a DSM-V physical symptom (30.6% vs. 21.4%, chi-square = 4.2, p = 0.04).

3.5. PCA of withdrawal symptoms

The PCA of 39 MJQQ withdrawal items generated an 12-factor solution, with non-overlapping item loadings, that accounted for 62.3% of the total variance (Table 3).

3.6. Comparison of cannabis withdrawal syndrome criteria

40.9% of subjects met the DSM-V CWS criterion (at least 3 of 7 symptoms); 30.0% met the Budney and Hughes (2006) 4-symptom criterion (at least 4 of 11 symptoms); and 57.3% met the Budney et al. (2004) 2-symptom criterion (at least 2 of 11 symptoms). Requiring only 2 of 7 symptoms for DSM-V CWS increased the proportion of subjects with CWS to 57.3%, while requiring 4 of 7 symptoms reduced the proportion to 28.1%. Reducing the DSM-V symptom list to six by dropping physical symptoms (reported by 24.7% of subjects) reduced the proportion of subjects meeting the CWS criterion only slightly, from 40.9% to 38.0%.

There was substantial overlap in subjects meeting the various CWS criteria sets. All subjects with DSM-V CWS also met the Budney-2 symptom criterion for CWS; almost three-quarters (73.2%) also met the Budney-4 symptom criterion. More than half (52.3%) of subjects who met any of the 3 CWS criteria met all 3 criteria. The Budney-2 symptom criterion identified 63 subjects (16.4% of total subject pool) who did not meet either of the other 2 CWS criteria. No subject had only Budney-4 symptom CWS.

Subjects meeting the DSM-V or Budney-4 CWS criteria were significantly older at the start of their index quit attempt (2.1 years [$F = 6.93$, $p = 0.008$] or 2.9 years [$F = 8.38$, $p = 0.004$], respectively) than those who did not. There were no significant associations between subjects' sex, race, or ethnicity at the time of the index quit attempt for any CWS criterion.

The two CWS symptom lists had acceptable internal consistency, with Cronbach's standardized alpha coefficients of 0.75 for DSM-V and 0.77 for Budney. Dropping any one of the individual symptoms did not shift the alpha coefficient by more than 0.04 or 0.02, respectively.

PCA of the 7 symptoms in the DSM-V criterion list generated a single factor solution (eigenvalue = 2.85) onto which all 7 symptoms loaded. This was also true of the DSM-V list with physical symptoms deleted (eigenvalue = 2.53). In contrast, the Budney list of 11 symptoms generated a two-factor solution. Factor 1 (eigenvalue = 2.82) included anger/aggression, irritability, anxiety, restlessness, sleep difficulties, and depression. Factor 2 (eigenvalue = 1.93) included tremor/shakiness, chills, stomach pains, and sweating.

3.7. Validity of withdrawal syndrome criteria

3.7.1. Concurrent validity—There was a significant positive association between some measures of cannabis use prior to the index quit attempt and total number of withdrawal symptoms or diagnosis of CWS. Total number of joints smoked in the month prior to the quit attempt was significantly correlated with total number of withdrawal symptoms experienced by a subject ($r = 0.13$, $p = 0.01$). Subjects with DSM-V CWS had a longer duration of lifetime regular (at least weekly) cannabis use at the start of their index quit attempt than did subjects without CWS (12.6 [9.7] years vs. 10.4 [8.4] years; $F = 5.48$, $p = 0.02$). Among subjects averaging less than weekly cannabis use over the six months before quitting, 30.1% had DSM-V CWS, compared with 31.9% who used at least weekly and 45.6% who used at least daily (chi-square = 4.3, $p = 0.04$). Subjects with DSM-V CWS used cannabis on more days during the month before quitting than did those without CWS (24.0 [9.8] days vs. 21.7 [10.8] days, $F = 4.21$, $p = 0.04$. There were similar significant positive associations between prior cannabis use and other CWS criteria (greater than two, three, or four symptoms from among the Budney et al. core 11 symptoms) (data not shown).

There were no significant associations between type of cannabis preparation used or number of joints smoked per day prior to the quit attempt and meeting any CWS criterion (data not shown).

There were no significant associations between reductions in use of caffeine, alcohol, or tobacco by regular users during the quit attempt and meeting criteria for DSM-V CWS (data not shown).

3.7.2. Predictive validity—Subjects with DSM-V CWS had a significantly shorter duration of abstinence during their index quit attempt than those without CWS (median 30.8 days vs. 60.4 days, chi-square = 7.7, p = 0.006). This was also the case for subjects with Budney-2 symptoms CWS (60.8 days vs. 34.0 days, chi-square = 4.3, p = 0.04) or Budney-4 symptoms CWS (60.8 days vs. 30.4 days, chi-square = 9.6, p = 0.002). There was no significant difference among the three CWS criteria in their association with duration of abstinence (chi-square = 2.89, p = 0.24).

There was no significant association between presence of CWS by any definition and outcome (relapse vs. continued abstinence) of the quit attempt (91.1% relapse with CWS vs. 85.9% relapse without CWS, chi-square = 2.36, p = 0.12 for DSM-V; 90.0% vs. 85.4%, chi-square = 1.91, p = 0.17 for Budney—2 symptoms; 89.6% vs. 87.4%, chi-square = 0.37, p = 0.54 for Budney—4 symptoms).

4. Discussion

In our convenience sample of 384 adult cannabis smokers who made a quit attempt without formal treatment outside a controlled environment, two-fifths (40.9%) met proposed DSM-V criteria for CWS during their index (“most difficult”) quit attempt. This prevalence of CWS during a single quit attempt lies at the upper end of the range of lifetime withdrawal prevalence (15.6%–40.9%) reported in studies of non-treatment-seeking adults (Cottler et al., 1995; Schuckit et al., 1999; Swift et al., 1998; Swift et al., 2000; Wiesbeck et al., 1996), although substantially less than the 88.8% reported in an Australian study (Copeland et al., 2001; Swift et al., 2001). The proposed DSM-V CWS had evidence of concurrent and predictive validity and was not significantly associated with any particular type of cannabis preparation or subjects’ sex or race at quit attempt. A recent study of 49 Australian dependent cannabis users also found no significant association between subjects’ sex and the intensity of their cannabis withdrawal, but, unlike this study, found no significant association with age or amount of weekly cannabis use (Allsop et al., in press). Overall, our findings support the inclusion of CWS in DSM-V.

There was substantial overlap in identifying subjects with CWS between the DSM-V draft proposal and the two other proposed criteria sets most commonly cited in the literature: Budney-4 symptoms (Budney and Hughes, 2006) and Budney-2 symptoms (Budney et al., 2004). Concurrent and predictive validity of the CWS criteria sets were similar, including the DSM-V proposal without physical symptoms. The Budney-2 symptom criterion was the most sensitive, identifying an additional 16.4% of subjects with CWS who were not diagnosed by the other two criteria. These findings, while supportive of the DSM-V draft, suggest that the proposed symptom list (seven) and required number of symptoms (three) are somewhat arbitrary, and should be further evaluated empirically.

We are aware of only two other studies that performed factor analysis of cannabis withdrawal symptoms. An earlier PCA from a clinical interview study of 104 non-treatment-seeking adults generated a 4-factor solution accounting for 51.8% of the total variance (Copersino et al., 2006): physical symptoms; mood and sleep difficulty; cannabis craving,

increased appetite, and decreased sex drive; and improved memory. An exploratory factor analysis of the large NESARC sample (1,119 cannabis-only frequent users) generated a two-factor solution (Hasin et al., 2008): “Weakness” (eigenvalue = 7.08), comprising hypersomnia, feeling weak or tired, yawning, and psychomotor retardation; and “Depression/Anxiety” (eigenvalue = 1.57), comprising dysphoric mood (depression, anxiety, restlessness), insomnia, and non-GI physical symptoms (tremors, muscle aches, sweating). Our PCA results confirm these earlier analyses in finding high factor loadings for items comprising physical symptoms, insomnia, and dysphoric mood. Our PCA differs from both earlier analyses in generating a larger number of factors, including separate factors for GI and non-GI physical symptoms. These differences may be due to our use of a larger, more detailed symptom list (39 items) focused on cannabis withdrawal. Both prior studies used 18 items; NESARC included items not necessarily relevant to cannabis withdrawal (and therefore not included in the MJQQ used in our study). Neither prior study included items related to aggression, explaining the absence of aggression factors.

This study has several limitations. Data were obtained by retrospective self-report with no external corroboration, which is true of most studies of cannabis withdrawal. Some subjects reported some withdrawal symptoms lasting up to two years (Levin et al., 2010), suggesting that they might have been reporting other conditions as if they were due to cannabis withdrawal. However, cannabis users not in treatment have been found to give reliable retrospective self-report about their cannabis use histories (Fendrich and Mackesy-Amiti 1995; Ensminger et al., 2007) and withdrawal symptoms (Mennes et al., 2009). Very few subjects endorsed both items in pairs of opposite withdrawal symptoms (3.1% reported both increased and decreased sleep, 1.8% both increased and decreased appetite, 0.5% both increased and decreased sex drive, 0.3% both weight gain and weight loss), suggesting that subjects were accurately reporting their withdrawal experience. Subjects were living in the community, with access to psychoactive substances other than cannabis. However, there were low rates (less than 10% for each drug class) of regular (at least weekly) use of other illegal drugs or psychoactive prescription medication prior to the quit attempt and even lower rates of decreasing use of substances by regular users during the quit attempt. Furthermore, there were no significant associations between decreased use of caffeine, alcohol, or tobacco during the quit attempt and meeting DSM-V criteria for CWS. Thus, we consider it unlikely that our results were due to subjects mistaking other substance withdrawal for cannabis withdrawal. The significant positive associations between some measures of pre-quitting cannabis use and withdrawal symptoms and occurrence of CWS, consistent with the expected pharmacological relationship between substance use and withdrawal, further suggest that subjects were reporting cannabis withdrawal symptoms.

External validity may be limited because subjects were a convenience sample of cannabis users from one research site. Subjects in this study were of similar age and gender distribution, but more likely to be African-American (82.3% vs. 12.4%) and of lower socioeconomic status than the 2000 US national household population of current (past 12 months) cannabis users without other current drug dependence (except tobacco) and no more than minimal use of other illegal drugs (Substance Abuse and Mental Health Services Administration, 2001).

In summary, we found that CWS is a common, clinically significant phenomenon among adult users who quit use without seeking treatment. The proposed DSM-V diagnostic criterion for CWS had good concurrent and predictive validity in our sample, but some aspects of the criterion (items in symptom list, number of required symptoms, handling of physical symptoms) warrant further study.

Acknowledgments

Role of funding sources

This study was supported by the Intramural Research Program, NIH, National Institute on Drug Abuse and NIDA Residential Research Support Services Contract HHSN271200599091CADB (PI: DL Kelly). Dr. Copersino was supported by NIH grant 1K23DA027045-01A1. The funding sources played no further role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

The authors thank Ms. Janeen Nichels for testing participants, Mr. John Etter for testing participants and data management, Dr. Robert McMahon for advice on the statistical analyses, and Dr. Susan Boyd for epidemiological comparison with the 2000 US national household population.

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Table 1

Withdrawal symptoms included in several proposed diagnostic criteria for cannabis withdrawal syndrome

Symptom in MJQQ	Chung et al.	Budney et al.	DSM-V
Irritability	√	√	√
Anger	√	√	
Aggression			
Increased appetite	√ (combined as "change in appetite")		
Decreased appetite		√	√
Weight loss			
Trouble sleeping (insomnia)	√	√ (combined as "sleep difficulties")	√
Vivid, unpleasant dreams	√		
Trouble concentrating *	√		
Restlessness	√	√	√
Anxiety	√	√	√
Depressed mood	√	√	√
Fast heartbeat *	√		
Tired/sleepy/weak *	√		
Yawn a lot *	√		
Tremble, twitch	√		
Tremor/shakiness		√	√ (combined as "physical symptoms")
Headache	√		
Sweating	√ (combined)	√	
Fever *			
Chills		√	
Stomach ache, pain	√ (combined)	√	
Diarrhea			
Teary, runny nose *	√		
Nauseous/vomiting	√		
Muscle pains *	√		
Hallucinations *	√		
Seizures *	√		
Drug craving	√		

* Not included in Marijuana Quit Questionnaire (Levin et al., 2010)

Proposed syndromal criteria are ≥ 2 or ≥ 4 symptoms from among a list of 22 symptoms (Chung et al., 2008); ≥ 2 (Budney et al., 2004) or ≥ 4 (Budney and Hughes 2006) symptoms from among a list of 11 symptoms; or ≥ 3 symptoms from among a list of 7 symptoms (www.dsm5.org)

Table 2

Characteristics of cannabis withdrawal symptoms reported by 384 adult, non-treatment-seeking cannabis smokers

Withdrawal symptom*	% (n) subjects reporting	Onset after quitting (days) (mean [SD])	Peak intensity# (mean [median])
Craving for cannabis (1)	59.4 % (228)	4.4 (0.9)	4.4 (5.0)
Insomnia[a] (1)(3)	48.7% (187)	2.7 (5.0)	3.8 (4.0)
Strange and/or vivid dreams (1)	10.4% (40)	3.7 (5.5)	3.7 (4.0)
Sleep difficulties[b] (2)	50.5% (194)	2.6 (4.9)	3.8 (4.0)
Increased appetite	20.8% (80)	3.3 (6.1)	4.0 (4.0)
Decreased appetite	17.4% (67)	4.0 (7.3)	3.6 (4.0)
Change in appetite[c] (1)	36.4% (140)	3.7 (5.9)	3.9 (4.0)
Weight loss	7.3% (28)	10.3 (10.2)	2.9 (3.0)
Weight loss and/or decreased appetite (2)(3)	20.8% (80)	4.9 (8.1)	3.5 (4.0)
Feeling sad, depressed (1)(2)(3)	34.4% (132)	4.0 (6.7)	3.7 (4.0)
Feeling irritable, “jumpy” (1)(2)	29.4% (113)	3.3 (6.1)	3.7 (4.0)
Feeling anxious, “nervous” (1)(2)(3)	38.5% (148)	3.4 (6.5)	3.6 (3.0)
Feeling restless (1)(2)(3)	21.9% (84)	2.8 (4.4)	3.7 (4.0)
Feeling angry	28.9% (111)	3.1 (5.7)	3.9 (4.0)
Feeling aggressive	20.1% (77)	3.6 (5.6)	3.8 (4.0)
Feeling angry and/or aggressive (1)(2)	33.9% (130)	2.8 (5.4)	3.9 (4.0)
Feeling angry and/or aggressive and/or irritable (3)	45.6% (175)	3.0 (5.5)	3.9 (4.0)
Physical discomfort	8.9% (34)	4.4 (8.4)	3.9 (4.0)
Physical symptom[d] (3)	25.3% (97)	3.1 (5.0)	3.6 (4.0)
Tremor/shakiness (2)	4.9% (19)	1.6 (1.4)	3.2 (3.0)
Nausea and/or vomiting (1)	5.2% (22)	3.2 (6.4)	3.4 (3.0)
Diarrhea and/or stomach pains and/or upset stomach (1)	14.1% (54)	2.5 (4.4)	3.3 (3.0)
Stomach pains (2)	8.3% (32)	1.9 (2.1)	3.4 (3.5)
Chills (2)	3.4% (13)	2.2 (3.9)	3.0 (3.0)
Headaches (1)	16.9% (65)	3.7 (5.9)	3.4 (3.0)
Sweating (2)	5.5% (21)	2.2 (2.2)	3.8 (4.0)

Data represent symptoms reported within one month of the start of subjects’ “most difficult” (self-defined) quit attempt without formal treatment while not in a controlled environment, and for which some action was taken to relieve.

*Symptoms are items from Marijuana Quit Questionnaire (MJQQ) or combinations of MJQQ items. Number shows that symptom was included on indicated proposed withdrawal symptom list: (1) (Chung et al., 2008), (2) (Budney and Hughes 2006), (3) DSM-5.

#Rated on 5-point Likert scale from 1 (“very little”) to 5 (“very high”)

[a]Insomnia includes trouble falling asleep, waking up during the night, waking up earlier than usual, and/or sleep less than usual

[b]Sleep difficulties includes insomnia and/or strange and/or vivid dreams

[c]Change in appetite includes increased appetite and/or decreased appetite

[d] Physical symptom includes stomach pain, tremor/shakiness, sweating, chills, and/or headache

Table 3

Principal components analysis of 39 cannabis withdrawal symptoms in 384 adult, non-treatment-seeking cannabis users

Factor	Eigenvalue	% Total variance	Items loading > 0.5
1. Insomnia/restless[a]	8.26	21.2	4 Insomnia items[*], restless
2. Verbal aggression	2.70	6.9	Feel angry, feel aggressive, threw or broke something, yelled at/insulted someone
3. Physical aggression	2.01	5.2	Punched/kicked, pushed/slapped, physically attacked
4. Gastrointestinal symptoms	1.57	4.0	Upset stomach, stomach pains
5. Depression/craving	1.54	4.0	Feel sad, increased cannabis craving, increased sleep, anxiety
6. Dreams	1.40	3.6	Strange dreams, vivid dreams
7. Non-GI physical symptoms	1.35	3.5	Chills, muscle twitches, tremor/shakiness
8. Increased appetitive drive	1.19	3.1	Increased appetite, increased sex drive
9. Vomiting	1.20	2.9	Vomiting
10. Headache[b]	1.09	2.8	Headache
11.	1.04	2.7	Pulled a weapon, sweating
12. Other sleep problem	1.01	2.6	Other sleep problem

PCA used varimax rotation with Kaiser normalization and minimum eigenvalue = 1.

[*] insomnia items are trouble falling asleep, waking up during the night, waking up earlier than usual, and sleep less than usual

[a] Bored loads weakly (0.48)

[b] Headache loads weakly (0.48)