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## Interventions for cannabis use disorder

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### Abstract

How to treat adults and adolescents with a Cannabis Use Disorder is a burgeoning research area. This article reviews the empirical literature pertaining to several psychosocial approaches (cognitive-behavior therapy, motivational enhancement, and contingency management), all of which are associated with favorable outcomes. We also review the emerging research on the use of pharmacotherapy, brief interventions and technology-delivered interventions, and conclude with an overview of future research needs.

### Keywords

Treatment; Cannabis use disorder

### Introduction

It is estimated that among those who use cannabis, between 9% and 30% may develop a cannabis use disorder (CUD) [1]. CUD, which ranges in severity from mild to severe, is accompanied by symptoms indicating continuing and compulsive-like use in the face of negative consequences and, in some cases, signs of physical dependence. People with a CUD also report a broad array of use-related problems that impact school and employment functioning, family relations, finances, emotional well-being, and cognitive functioning. In addition, a substantial proportion of those who develop a CUD have at least one other co-occurring mental disorder [2].

In the most recent national survey, slightly over a half-million respondents who reported a past-year substance use disorder and felt they needed treatment did not make an effort or were faced with practical barriers which impeded their access to services [3].

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Credit author statement

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With respect to cannabis, a significant number of those with a CUD indicate an intent to cut down or quit, although many with a CUD do not seek treatment. In Hasin [4] national study, the authors' asked a sample of individuals seeking treatment at state-funded substance use treatment facilities to indicate their primary problem; cannabis use ranked third behind alcohol and opioids among those 12 years and older, and among those younger than 20 cannabis was by far the most common primary substance reported for treatment admissions.

We provide here a summary of the published research literature, with an emphasis on publications since 2000, regarding the treatment efficacy and effectiveness for individuals with CUD. We focus on psychosocial and pharmacological interventions for adults and adolescents, as well as the growing literature on technological-based approaches. Unless indicated, outcome studies included a comparison group or groups, and when outcome is noted as favorable statistical significance was observed. Future directions will be discussed.

## **Psychosocial approaches to treat CUD**

Eleven reviews of controlled trials evaluating psychosocial treatments for adults with CUD have been published in recent years [3,5-14]. A synthesis of these reviews is provided below.

### **Main types of psychosocial approaches**

Motivational enhancement therapy (MET) seeks to increase a client's motivation and commitment to reduce or quit substance use [15]. Clinical strategies include the MET techniques of empathy, reflective listening, summarizing, and affirmation. In the cannabis treatment field, there is variability in the number of MET sessions (typical range, 1 to 4), and the duration of sessions typically range from 45 to 90 min. Cognitive behavior therapy (CBT) aims to address substance use with a focus on teaching the client coping skills (e.g. stress and mood management; problem solving), cessation or reduction skills (e.g. functional analysis of use patterns and consequences), and relapse prevention skills (e.g. refusal skills, coping with withdrawal symptoms). These skills are taught and role-played during counseling sessions and assigned for practice in-between sessions. CBT varies in session length (e.g. 45—60 min) and number (e.g. 6—14 sessions). Contingency management (CM) is a counseling approach that uses principles of reinforcement and, in some instances, punishment, to support abstinence or treatment compliance, such as attendance at therapy sessions and to provide a 'clean' urine specimen. Typical CM-based rewards are monetary-based incentives (e.g. \$10 or \$20).

### **Psychosocial approaches for adults**

Exemplary descriptive reviews are provided in two publications. Gates et al. [12] reviewed 23 randomized treatment trials for adults who were either daily cannabis users or had a CUD, and 33 randomized studies were described by Cooper et al. [9] for individuals who had been diagnosed with a CUD or reported regular cannabis use. The latter review is unique that it included programs from several nations. Davies et al. [11] also completed a notable meta-analysis of 10 randomized control trials of behavioral therapies with active and nonactive control comparison conditions.

A summary observation across the three aforementioned reviews is that psychosocial treatments, in comparison with no treatment, consistently produced significant reductions in cannabis use behaviors (quantity, frequency) and in the severity of cannabis dependence symptoms. However, the no-treatment and active treatment groups were generally equivalent in terms of changes in motivation to quit and additional substance use. In addition, findings across the studies were not consistent in showing that psychosocial-based treatments significantly improved psychosocial functioning (e.g. employment; mental health). An important consideration is that the operationalization and measurement of psychosocial functioning varied between studies, and this heterogeneity contributed to poor interstudy comparability [2,6].

Do these reviews provide insights into the differential effectiveness of specific types of psychosocial treatment? The reviews provide general support that all three main approaches (CBT, MET, and CM) are effective. Yet, more optimal effectiveness appears to be associated when approaches are combined [2,16]. The better short-term effects (e.g. 9-month after treatment) were observed by combining approaches, particularly when treatment consists of MET/CBT/CM. It appears that a key component is the integration of abstinence-based CM in conjunction with other treatment strategies and interventions. Although, in addition, CBT/CM has been shown to improve readiness to change cannabis use among cannabis users [17].

Two other noteworthy points from the reviews are inferred: treatment intensity matters, and abstinence is often not sustained after treatment. Specifically, psychosocial treatments administered over longer intervals (i.e. four or more sessions) appear to produce more favorable outcomes than briefer treatments, although the optimal treatment length is yet to be determined. With respects to abstinence, the vast majority of treated individuals did not maintain abstinence from cannabis use and relapse within a month after treatment was common.

## Psychosocial approaches for adolescents

It is typical that treatment outcome studies of adolescents with substance use disorders (SUDs) consist of youth with a history of problems with more than one substance (typically both alcohol and cannabis). Thus, isolating the treatment effectiveness on just CUD is problematic. Based on several recent reviews that included adolescent treatment outcome studies, we highlight the major findings from this literature. We then describe the only clinical trial in the recent literature that focused specifically on CUD in adolescents.

### Prominent reviews

The two reviews by Hogue et al. [18,19] covered studies published between 2007 and 2017 and evaluated 19 and 11, respectively, well-controlled studies of well-established' outpatient psychosocial therapies for adolescent substance use. Both sets of reviews offered very similar conclusions: (a) family systems-based treatment, individual cognitive-behavioral therapy, and group cognitive-behavioral therapy continue to be rated as well-established efficacious approaches; (b) behavioral family-based treatment and motivational interviewing remain as probably efficacious approaches; and (c) general drug counseling remains possibly

efficacious. The findings that family-based, CBT, and MET approaches were associated with the most reliable efficacy when treating adolescents with a SUD are consistent with a similar conclusion arrived at in the review of the empirical literature by Winters et al. [20].

A meta-analysis of 45 adolescent outpatient treatment studies published since 1980 was conducted by Tanner-Smith et al. [21]. Several family-based (i.e. functional family therapy and multidimensional family therapy), CBT, and MET approaches were associated with strong support for efficacy. In direct comparisons between these evidence-based interventions, the authors found that family-based approaches showed significantly larger effects on substance use than CBT/MET. In addition, their review highlighted effectiveness for cannabis; numerous studies showed the largest positive change (i.e. reductions in use) for cannabis use compared with other substance use.

Stanger et al. [22] examined six most recent controlled trials published before 2016 on the use of CM approaches in combination with other treatments (e.g. CBT/MET) for adolescents with a SUD. The majority of these clinical trials showed favorable support for the use of CM to optimize treatment outcomes, although the authors noted that the maintenance of treatment effects merits more research.

The reviews highlighted earlier on the adolescent treatment literature suggest two major research needs: whether combining approaches (e.g. family-based + CBT) enhances outcomes, particularly among those adolescents with coexisting disorders [18], and what treatment components optimize outcomes.

### **The cannabis youth treatment study**

This study is a large, multisite clinical trial (N = 600) of adolescent cannabis users [23]. The participating treatment programs spanned several approaches: individual versions of MET and adolescent community reinforcement approach; the group version of CBT; family-based approaches (family support network and multidimensional family therapy); and two combination approaches (MET + CBT and MET/CBT + family Support network). The duration of treatments varied (from weeks to 14 weeks). No treatment approach rose above the others in terms of favorable outcomes; all treatments showed equivalent effectiveness on days of abstinence and recovery rates at one-year follow-up (All substances were included in these outcome measures). An important caveat in reviewing the effectiveness of these interventions is that over the full year most adolescents did not achieve full abstinence, about half experienced periods of relapse, and most reported continuing substance-related problems.

### **Brief interventions**

Brief interventions, which range from a short conversation to a few sessions, provide a counseling model that can accommodate contexts such as medical settings or schools that seek to broaden their engagement with individuals who are abusing substances [24]. A brief intervention for youth developed specifically for cannabis abuse was adapted from motivational interviewing (MI) for use in primary care or the emergency department [25]. It consisted of a 15–20 min session plus a 10-min booster phone call; study results showed that in comparison with controls, the active condition showed significant reductions in

cannabis use. In a school setting, a three-session brief intervention based on MI and CBT was shown to be superior in reducing cannabis use when compared with a two-session version and an assessment-only control group [26]. Walker et al. [24] applied a different approach in the use of brief interventions (BIs); her group offered a voluntary intervention to students not willing to go to specialized treatment but had had questions or concerns about their cannabis use. Named the Teen Marijuana Check-Up, three controlled trials showed that the strategy attracted students with cannabis use levels comparable with levels observed in published outpatient treatment studies and that the program reliably showed greater decreases in cannabis use relative to students in control conditions. This program has been adapted for treatment-seeking youth and evaluated in Australia [27] and the Netherlands [28]. Results have been mixed with the adaptation; the Australian Adolescent Cannabis Check-Up showed greater reductions in use than a delayed control, whereas the Dutch study failed to find treatment effects.

Halladay et al. [29] reviewed the existing literature on BIs for cannabis use among young adults. Their meta-analysis consisted of 1–2-session BIs that focused exclusively on cannabis use among individuals ranging in age from 15 to 30 years. The review included 26 primary studies with a total of 6318 participants, most of whom were not actively seeking treatment and used cannabis at least once a month. The main finding was at the 1–3-month post-intervention period: BIs were generally superior to passive controls in terms of significant reductions in symptoms of cannabis use disorder and increased odds of abstinence. However, the effects of BIs were shown to be small, and the quality of evidence for BIs was argued to be poor.

## Pharmacology-based treatment

Advances in the understanding of the neurobiology of cannabis use and the complex functions of the endo-cannabinoid systems have promoted efforts to develop more pharmacotherapies for treating CUD. Multiple reviews of the CUD pharmacotherapy literature have appeared over the past few years: a body of work that is limited to either open-label trial or relatively small placebo-controlled clinical trials, some of which are phase II trials [30-32].

As of 2020, the Food and Drug Administration in the United States has not yet approved any medications for CUD given the relative infancy of the research; studies are yet active in this area. One approach is to explore how medications can aid those in cannabis withdrawal or to address presumed psychological benefits of using cannabis; another approach is to examine if medications that interact with cannabinoid receptors can inhibit THC's rewarding effects. We review these and other main types of pharmacotherapies in the following passages.

### Agonist-like medications

These medications target the CB1 receptor with the aim of reducing withdrawal symptoms of CUD. pre-clinical research with dronabinol (an oral formulation of delta 9-THC) showed promise in reduction of withdrawal symptoms, subjective and physiological effects of smoked cannabis, and cannabis self-administration. Although two outpatient clinical trials failed to demonstrate its efficacy (alone or in combination with lofexidine (an alpha-2

agonist) for CUD [33]. More promise was found with nabiximols, an oral medication that combines a delta 9-THC with cannabidiol (CBD); an inpatient clinical trial revealed a positive effect in terms of reducing withdrawal symptoms although abstinence rates after discharge did not differ from the placebo group [34].

### **Antagonist-like medications**

These types of medications ‘block’ the CB1 receptor, thereby reducing the reinforcing effects of cannabis. A large laboratory study showed that rimonabant, a CB1-receptor inverse agonist, was effective in decreasing the intoxicating effects of smoked cannabis [35]. However, European countries have removed this drug from the market because of its serious psychiatric side effects.

### **Medications targeting craving or related symptoms**

This category of medications has attracted several candidates (e.g. buspirone, bupropion, fluoxetine, lithium, N-acetylcysteine), but results have not been promising. One example: N-acetylcysteine showed positive effects for adolescents with a CUD, but a controlled trial with adults showed no benefits [36]. Of current interest is gabapentin, a GABA-ergic medication known to produce cannabis-like effects in humans (It is Food and Drug Administration—approved for the treatment of epilepsy and neuropathic pain) [37]. A small clinical trial produced reductions in withdrawal symptoms and improved sleep compared with a placebo condition [38]. A larger replication trial is noted by Mason et al. [38], but the results are yet to be published.

### **Medications blocking opioid receptors**

The basis for studying blockers of opioid receptors is that these receptors interact with the cannabinoid system. Naltrexone is one such medication, given its bidirectional modulatory effects of both the endogenous cannabinoid and opioid systems. A laboratory study demonstrated that chronic dosing of naltrexone was effective in decreasing the reinforcing effects of cannabis smoking [39], and Notzon et al. [40] tested the feasibility of long-acting injectable naltrexone in 12 adults with CUD; the number of cannabis use days per week significantly decreased over the course of the study. However, to date, no controlled clinical trials evaluating naltrexone for CUD have been published.

### **Medications targeting coexisting disorders**

Given the high rate of coexisting disorder among those with CUD, medications that are effective with relevant co-occurring disorders have been tested for their effectiveness in reducing cannabis use behaviors. Studies have examined the effects of anti-depressant, anti-anxiety, and antipsychotic medications on cannabis use; all of these studies have produced weak results in terms of reducing cannabis use [31,41]. The impact of attention-deficit/hyperactivity- disorder (ADHD) medication (methylphenidate) on adolescents with CUD has also been studied; those in the ADHD medication, compared with those in the placebo group, showed no difference on self-reported days of substance use, but a significant difference in the number of negative urine tests in favor of the medication group [42].

## Technology-delivered interventions

As noted earlier, the vast majority of those with a CUD do not seek or receive treatment for various reasons and circumstances. Thus, treatment options that differ from the standard community-based model are needed. An emerging area in the treatment literature which may hold promise to increase accessibility of services for cannabis abusers are technology-delivered interventions (TDIs) [43]. TDIs represent a diverse collection of interventions that deliver treatment services either partially or entirely via computer, web, or mobile devices. Beyond accessibility, TDIs have been argued to hold the potential for other important advantages when compared with traditional in-person services, including reducing costs and increasing treatment fidelity [43].

### Adult studies

Controlled trials of high-quality TDIs adapted from in-person evidence-based treatments have been shown to be equally effective among adults with CUD when compared with traditional therapist-delivered interventions. For example, two studies measured the efficacy of a hybrid TDI which incorporated three brief sessions with a therapist and nine sessions of computer-delivered MET/CBT and CM [44,45]. In both studies, participants assigned to the TDI condition and the comparison group, which consisted of therapist-only delivered CBT, CM, and MET, showed similar reductions in cannabis use and rates of abstinence at treatment completion. The TDI and comparison groups also showed equivalent outcomes at 12-month follow-up, and a cost analysis showed the TDI condition was associated with significant savings per case [44].

A large replication study completed by Kay-Lambkin et al. [46] yielded similar results; the authors completed a randomized control trial of a TDI which entailed 10 sessions of computer-delivered MET/CBT combined with brief check-ins with a therapist. Their sample consisted of 274 adults who reported harmful alcohol or cannabis use and concurrent depression. The TDI group and a comparison group, who received therapist-delivered MET/CBT, demonstrated similar improvements in the areas of cannabis use, alcohol use, and depressive symptoms. These findings are further supported by other controlled trials of TDIs which have yielded similar results [47,48].

### Youth studies

Of the few TDIs that have targeted adolescents, most have been associated with small but meaningful effects. Two control trials by Walton et al. [49,50] evaluated a single-session TDI using a sample of adolescents presenting at primary-care clinics in the US Midwest. The TDI largely consisted of animated simulations delivered via tablets where participants were given automated feedback based on their selection of cannabis-related behaviors. For both studies, participants were randomly assigned to one of three conditions: TDI, therapist-delivered single-session MI, or a control group who received an educational brochure. The first study included only those adolescents who had endorsed past year cannabis use ( $N=384$ ). No between-group differences were found to exist with respect to frequency of cannabis use; however, compared with those in the control group, adolescents assigned to the TDI condition demonstrated significant reductions in self-reported cannabis

consequences at 3- and 6-month follow-up. The therapist-delivered condition and the TDI yielded comparable outcomes, although participants in the TDI condition showed greater reductions in cannabis consequences at three months, while the therapist-led condition showed greater reductions at 12 months.

The second study evaluated the preventative effects of the TDI among adolescents who endorsed no lifetime cannabis use ( $N = 714$ ). Participants who received the TDI demonstrated lower prevalence of cannabis use at 12-month follow-up and lower frequencies of cannabis use at 3 and 6 months than those in the control groups. The TDI appeared to outperform the therapist-delivered condition, as the therapist-delivered group did not differ from the controls with respect to frequency of cannabis use at 3- and 6-month follow-ups. Overall, these findings are consistent with another TDI study by Shrier et al. [51] that yielded similar outcomes. This study also found high acceptability of TDI among their adolescent sample.

A growing area of interest and a future direction for research on TDIs are the development of entirely web-based interventions. A recent study by Riggs et al. [52] investigated a web-based intervention that incorporated protective behavioral strategies for marijuana use and normative and personalized feedback. Heavy cannabis-using college students ( $N = 298$ ) were randomly assigned to either the TDI condition or a comparison group (healthy stress management education). The TDI condition was associated with reductions in self-reported cannabis use and an increase in their use of protective behavioral strategies at 6-week follow-up. Although these results are promising, studies of similar brief web-based TDIs for college students have shown mixed results [53-55] pointing to a need for further research in this area.

### Meta-analysis of TDIs

Boumparis et al. [56] recently published a systematic review and meta-analysis of TDIs. TDIs for prevention and intervention were analyzed separately. A total of 10 studies of prevention-based TDIs were identified in the literature, with six ultimately being included in the meta-analysis based on meeting the authors' standards for inclusion. Prevention-based TDIs were found to have a small, but significant, effect with respect to reducing cannabis use, and this effect was maintained at 12-month follow-up. In terms of interventions, the authors identified a total of 20 studies of TDIs, with 15 meeting inclusion criteria for the meta-analysis. The nature and structure of these TDIs varied, with some interventions consisting of one self-directed session (e.g. 53) while others consisting of multiple sessions delivered via computer and by a therapist (e.g. 47). Among these studies, TDIs were shown to have a small, but significant effect in reducing cannabis use after intervention, although this effect was not maintained at 12-month follow-up. Among the TDIs identified in this review, only five consisted of more than one session, although TDIs with multiple sessions were not associated with larger effects than briefer interventions. This is a significant divergence when compared with the literature on therapist-delivered interventions, as research in this area has generally shown that more comprehensive services tend to be more effective than briefer interventions.



## Summary

In conclusion, most people with a CUD do not receive treatment, although it is affirming that, in general, several efficacious psychosocial approaches (e.g. CBT, MET, and CM) have been identified for adults and adolescents. These strategies have also yielded positive results with coexisting non-cannabis SUDs. Other emerging approaches also show promise including pharmacotherapy, brief therapy models, and TDIs. Medications can alleviate the core symptom of a CUD and the effects of withdrawing from cannabis use. BIs are a user-friendly behavior change approach that can be applied by a wide network of help-serving professionals. TDIs can extend the reach of effective services at relatively low costs [57,58].

There are several needs for future research. Strategies are needed that offer psychosocial and or pharmacological approaches that are tailored for individuals with both a CUD and co-occurring mental or behavior disorders. There is already some promising work by Buckner et al. [59] that cannabis abusers are best treated with an intervention targeting the co-occurring problem of negative affect. A key priority of future outcome studies is to include more racially/ethnically diverse study participants than has been the case to date. Additional future research needs include more detailed examinations of what specific mechanisms of change (e.g. peer support during and after treatment) and moderators (e.g. social determinants of health) are related to treatment outcome, how to best define outcome for CUD treatment effectiveness (e.g. is abstinence an optimal outcome goal?) [60] and whether treatment effects are observed over a longer time (e.g. one year? two years?).

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[PubMed: 31112834] This article provides a comprehensive review and meta-analysis of the studies that have investigated technology-delivered prevention and intervention initiatives for cannabis use. The authors provide an excellent summary of the literature and provide recommendations for future directions.

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