TITLE

A Narrative Review of Psychological Cannabis Use Treatments With And Without Pharmaceutical Adjunct

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A Narrative Review of Psychological Cannabis Use Treatment With And Without Pharmaceutical Adjunct

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ABSTRACT

Background: As policy responses to cannabis use and availability change internationally, levels of cannabis use disorder rise and treatment seeking increases. Diversion to cannabis treatment from the criminal justice system also increases demand in the system. At a time of developing treatment systems in response to this demand, an understanding of the evidence is increasingly important.

Objective: To provide a narrative review of the developing evidence-base for psycho-social interventions for cannabis use disorder, including adjunctive cannabinoid agonist therapy.

Method: Two researchers independently conducted a literature search for articles published prior to February 2016, located through online search of four electronic databases (Google Scholar, CINAHL, Medline, and PsycINFO). Only randomised controlled trials describing treatment(s) for cannabis use or cannabis use disorder with a measure of either cannabis use frequency or cannabis use disorder severity were included. Non-English papers, review papers, posters, opinion pieces, letters or editorials, case studies (N<10) and published abstracts were excluded.

Results: The cannabis treatment most likely to be effective for adolescents and adults is based on the combination of Motivational Enhancement Therapy (MET) and Cognitive Behavioural Therapy (CBT) with the inclusion of contingency management and agonist replacement therapy showing promise.

Conclusion: A more concrete and robust evidence base is required for these interventions. Replication of treatment studies is needed using standardised interventions, methods and measures to minimise conflicting findings, inconsistent follow-up periods and relatively poor treatment effects over time.(243 words)
Introduction

Cannabis is the most commonly used illicit drug across Western countries including Europe (6.6% reporting recent past year use (1), North America (7.5% reporting recent use (2)) and Australia (10.2% reporting recent use (3)). Most cannabis users do not smoke frequently and report either unproblematic experimental or irregular use, or abstinence following the experience of a negative consequence from use (4-7). However, a building evidence base suggests that health-related consequences are likely if the drug is used frequently or from an early age (8). This evidence base shows greatest consistency for four particular health concerns that are often experienced by heavy cannabis users. Firstly, there are concerns for the mental health of users with associations between cannabis use and some affective disorders (9-11) and the onset of psychosis (12). Secondly, heavy users can experience cognitive impairments which can make it harder to learn and commit information to memory (13) and are thought to be associated with school dropout (14) and unsafe driving (15). Thirdly, smoking cannabis impairs respiratory health, particularly by increasing risk of developing a wheeze, cough and problems with bronchial dynamics (16). Finally, an estimated one in ten of all cannabis users, and one in two daily users, will develop a cannabis use disorder (CUD) (17). Those with CUD are characterised by clinically significant psychological distress (often presenting with clinical diagnoses), social problems and an inability to stop use despite such problems (18-20).

Given the prevalence of CUD in the general population, many individuals seek treatment for cannabis use. Data taken from the Australian National Minimum Data Set of Alcohol and Other Drug Treatment Services (NMDS-AODTS) shows that, between 2013 and 2014, cannabis was the primary drug of concern in 24% of
presentations to government funded alcohol and drug treatment services; second only to alcohol (41%) (3). These rates of treatment access have changed over time, that is, 22% of treatment presentations were primarily for cannabis use in 2002-2003 which increased and peaked at 24.6% in 2005-2006, only to reduce back down to 23.2% in 2009-2010 (21, 22).

Comparable data on treatment seeking in the US is reported in the Treatment Episode Data Set by the Substance Abuse and Mental Health Service Administration. Using the same timeline, admissions to state funded treatment services primarily for cannabis use were reported as 16% in 2003, increasing to 23.1% in 2009 and then decreasing again to 17% in 2013 (23). In Europe, the number of first time presentations to treatment facilities for cannabis rose from 45 000 in 2006 to 69 000 in 2014, with an 8% increase in reported daily use (1).

Although cannabis is the most commonly reported drug of concern in drug treatment, this still leaves a larger proportion of individuals in need of treatment who do not access it (8). Reports suggest that only between one in ten to just over one in three individuals with CUD will go on to access treatment in the US and Australia (24-26). More recent estimates are available from the US where, in 2013, 2.9% of the population of persons aged at least 12 years needed treatment for an illicit drug use problem (7.6 million people) and only one in five of this group (19.5%) received treatment at a specialist facility in the past year (2).

Further evidence of the imbalance between cannabis treatment need and treatment seeking is seen by observing the rate of involuntary referrals to treatment. That is, a large proportion of treatment episodes come from mandated treatment through the criminal justice system (3, 27). Also, the majority of cannabis treatment seekers are not self-
referred (27) and in Australia diversion is the most common source of referral (32%) (3). The road to cannabis treatment is also a particularly long and arduous journey. Survey of those who have accessed treatment found that, prior to seeking treatment, the average cannabis user will have attempted to quit an average of more than six times (28), report near daily use over 10 years (28), or a CUD diagnosis for 3 years (25). Finally, previous study of cannabis treatment seekers in the US and Australia has identified some imbalance in those who do seek this kind of treatment as treatment seekers are more likely to be single, male, younger than 30 years, have dropped out from schooling and report comorbid problems with alcohol use (24, 29).

**Barriers to treatment**

Only a handful of studies have focused on the factors explaining the imbalance between cannabis treatment need and treatment uptake (6, 28, 30-34). In review of the available literature on illicit drug treatments more generally, the most frequently identified barriers include a low perceived need for treatment or belief that treatment is effective, a desire to reduce use without assistance, anxiety regarding a perceived social stigma associated with accessing drug treatment, financial concerns and treatment accessibility (35-39). Building on this research some recent study has identified treatment barriers that are particularly important to cannabis users.

An initial study of cannabis user’s beliefs about drug treatments reported a common wish to avoid accessing treatments which would group them with other illicit drug users (28). Further study has focused directly on perceived barriers among cannabis users and has most consistently identified the belief that cannabis-related problems do not warrant
treatment; that abstinence is achievable without treatment; the desire to avoid the stigma of being labelled a drug user; that cannabis users are not likely to want to stop using; and a lack of awareness of treatment options (6, 30, 34). Recognising that these previous studies were focused on groups of adults, an additional study surveyed 261 adolescents in Spain and identified an additional barrier relating to stigma, which was a fear of their family finding out they used cannabis and becoming involved (32).

**Cannabis treatment in the community**

The important minority of cannabis users seeking treatment are presented with many options. In Australia, cannabis-using individuals are most likely to consult a mental health professional or general practitioner (GP) for their cannabis use problems rather than a specialist provider with no significant differences in this pattern between demographic characteristics such as sex, age and socioeconomic status (26). As specialist providers are not commonly sought, it is of interest to determine GPs’ ability to treat cannabis use. Most notably, GPs frequently report time pressures and a need to address more important issues than cannabis use (40), as well as difficulties in addressing the issue (41).

The minority who do receive specialist provider services are identified in the NMDS-AODTS data as most commonly accessing counselling services (40%; with just 11.6% receiving counselling at a cannabis-specific clinic (42)), as well as information and education only (19%), assessment only (14%) and withdrawal management and case management (both 11%) (3). These services are typically provided in non-residential settings (72%) (3). Unfortunately, there is a lack of information as to what forms of counselling are offered in these services. There is a huge variety of possible types of treatment and several narrative
reviews of cannabis treatment trials from separate author groups have highlighted support for psychosocial intervention to manage cannabis use disorder (43-47).

In these reviews, the primary approaches to treating cannabis-related problems and dependence have included Motivational Enhancement Therapy (MET), Cognitive Behaviour Therapy (CBT), their combination (MET+CBT) as well as the adjunct of Contingency Management (CM). In addition, family-based therapies, acceptance and commitment therapies, social support, mindfulness based meditation, and simple education have all been evaluated to varying degrees. We discuss each of these therapies and possible delivery methods as they related to substance use here prior to assessing the available literature that is specific to cannabis use.

**Motivational Enhancement Therapy (MET)**

Motivational interviewing (MI) originated in the early 1980s (48), taking shape as a substance use treatment in the early 1990s (49, 50). MI refers to three core elements and four main principles (51). The three core elements include: 1) conversation about change, 2) collaboration that is centered on the treatment seeker’s situation, and 3) direct response to any ambivalence to change. The four main principles in delivering MI are to: 1) be empathic, 2) promote self-efficacy, 3) roll with resistance, and 4) address any gap between the treatment seeker’s current place and where they want to be. A modified version of MI, motivational enhancement therapy (MET), includes an additional element which is eliciting a “taking stock” experience by providing non-judgemental feedback on the impact of the treatment seekers level of substance use and education on the risks of substance use in general (50, 52). To date, many hundreds of clinical trials of MI-based substance use
interventions have been published, and a Cochrane review supports the use of MI in the short to medium term (less than one year) (53).

Cognitive Behavioural Therapy (CBT)

Cognitive behavioural therapy (CBT) is characterised by offering support through coping and problem-solving skills for an individual to identify and respond to any actions that lead to unwanted behaviours (54). In addition, a modified version of CBT, namely Relapse Prevention (RP), ensures the problem-solving skills include abstinence maintenance strategies such as keeping a diary and ensuring non-drug related distractions are at hand (55). By following the principals of CBT the treatment provider attempts to identify and respond to actions that may lead to unwanted behaviours (cannabis use), by highlighting opportunities to focus on non-drug related behaviours and therefore disrupt the power of any controlling contingencies (such as cravings to use) (56). As with MI-based substance use interventions, CBT has been extensively reviewed and its use is supported in the short term for treating substance use and much other maladaptive behaviour (57, 58)

Motivational Enhancement Therapy combined with Cognitive Behavioural Therapy (MET+CBT)

The practice of MET and CBT are not incongruous and are well suited to be combined. MET focuses on change talk and is appropriate for those not yet motivated to abstain from use. In contrast, CBT is appropriate for those already interested in change that is looking for strategies to take action. As such, their combination (MET+CBT) would usually follow the order of introducing MET first to bolster confidence to change and flow into CBT to discuss actions for making the change (59). Just as motivation to quit changes over time, the
delivery of MET may be appropriate not just at the beginning of treatment but whenever motivation falters. In review of 29 trials of substance use interventions which included both MI/MET and CBT interventions as well as their combination, reductions in use following treatment were greater when these techniques were combined as compared to the component parts (60).

*Family-based therapy and social support therapies (FT)*

Family-based and social support therapies (FT) tend not to address the treatment seeker in isolation but acknowledge the impact of relationships with family and friends and how they relate to substance use (61). These treatments are coordinated such that the treatment seeker is surrounded by any family or friends who are impacted by their use (62). As such, drug use is targeted indirectly by focusing on improving family interactions and functioning to assist family members support the treatment seeker in reducing use. There are several forms of family-based therapies, including behavioural, family systems, and multiple systems/ecological approaches. Given the involvement of family and friends, these therapies have unsurprisingly been shown to be one of the most promising treatments for adolescents in particular (63).

*Contingency management (CM)*

In substance use treatment, contingency management (CM) refers to the use of an incentive to reward a particular behaviour - such as treatment attendance/adherence or reductions in substance use (confirmed using urinalysis results and referred to as abstinence-based CM) - or the withholding of incentive in the absence of these particular behaviours (64). The use of CM is somewhat limited to well-funded treatment settings as using such incentives can
be costly. Notably, the use of these incentives has been carefully assessed and there is some initial evidence that their use may be cost effective (65-67).

*Mindfulness-based therapies (MBT)*

Mindfulness-based therapies (MBT) are conceptualised the teaching of individuals to focus their attention on the present moment while attempting to remain non-judgemental and open to their current experience (68). In terms of substance use treatment, MBT is thought to help by alleviating stress associated with using drugs and lead to adaptive changes in motivations to abstain. A recent review of the use of MBT in substance use treatment found MBT to be more effective than inactive control conditions, particularly in smoking cessation, although the authors did note that there was a lack of randomised controlled trials to solidify conclusions (69).

*Drug education and counselling (DC)*

Drug education and counselling (DC) broadly refers to a regulated and usually manualised version of typical counselling that is often delivered in community-based specialist clinics. This form of treatment has included a broad range of techniques ranging from basic education regarding the impacts of use (70) or harm reduction (71), to self-help groups (72) and techniques such as the 12-step approach (73). Notably, these forms of treatment are typically considered to be ‘minimal intervention’ and are often included in randomised controlled trials as an ‘active control’ condition. As such, the extent to which DC is effective in substance use treatment is difficult to determine and as yet lacks formal systematic review.
**Brief interventions (BI)**

Any brief intervention (BI) is brief in that it is time-limited, from just a few minutes to a few counselling sessions, and as such is particularly focussed on the individual treatment seeker and their current situation (74, 75). Given their brevity, BIs are not typically intended to treat severe dependence, but instead aim at assisting the treatment seeker to identify problematic areas and raise their motivation to make change (76). As such, these interventions are ideal for individuals who have not yet sought treatment but who report potentially harmful substance use and are easily adaptable to be delivered in primary care and hospital settings (76). BIs are commonly delivered using the principals of MET as well as those of the FRAMES model developed by Miller and Sanchez (77) and the Screening, Brief Intervention and Referral to Treatment approach (SBIRT) promulgated by the World Health Organization (78). Following these models, the individual’s desire to quit is supported by identifying problematic use and discussing this in a setting that is empathetic, including discussion involving strategies to abstain from use. In the final stages a referral to further treatment is often made. Preliminary evidence supports the use of BI in treating substance use problems among adolescents (79) and adults (80, 81), although there is particular need for further randomised controlled trials with long term follow-up.

**Technology-based interventions**

The above mentioned intervention types are generally designed to be delivered in a one-to-one, face-to-face fashion between clinician and client with associated limitations in treatment capacity and location (22, 82, 83). However, in order to appropriately address the larger public health burden attributed to cannabis use, it would be preferable for a treatment service to reach a greater number of patients simultaneously (84). Indeed, there
has been a developing interest in interventions which can overcome these obstacles by using ‘low technology’ such as the telephone and ‘high technology’ such as the internet and Smartphone to deliver treatment (85). These technology-based treatments can operate as stand-alone interventions with no clinician/client interaction or simply assist specialist services in treatment delivery. As such, these treatments have the prima facie benefits of appearing to be low cost while being unbounded by location and addressing treatment barriers such as feelings of stigma by being seen accessing drug treatment (86).

Reviews of technology-based interventions for substance use have found that demand exists for these modes of delivery and there is preliminary support for their effectiveness (87, 88). Systematic reviews of internet interventions for smoking cessation (89), problematic alcohol use (90-92) and illicit drug use (93) have shown consistent support in the short to mid-term, although the inclusion of therapist contact appears to remain important for those with more severe problems (94). A meta-analysis of internet- and computer-based interventions for cannabis use has found a significant but small effect of these interventions in reducing use in the short-term (g=0.16) (95). The support from these review articles was limited in that there was a need for further research with long-term follow-up and a consistent problem with treatment retention (particularly among studies from the early 2000s). That is, participants commonly begin internet or computer-based interventions but fail to complete the full amount of allocated sessions and ‘drop out’.

A plethora of research has focused on the use of telephone counselling in substance use although has almost exclusively related to tobacco smoking. Multiple Cochrane reviews have highlighted the efficacy of both telephone counselling (96, 97) and mobile phone
based intervention for tobacco use (98). These interventions are described to be more effective than nicotine replacement pharmacotherapies (96). In contrast, there has been a single systematic review article which focused on the use of telephone counselling in non-tobacco drug treatment (87). Moreover, there has been no review of the literature regarding the use of Smartphones or mobile-phone text messaging. The available evidence indicates that telephone counselling was an effective medium for treating alcohol use in 14 of 34 trials, although this support was limited to short-term follow-up. With only a handful of trials conducted to date, a particular need for future study to address illicit drug use was noted before making conclusions on their effectiveness (87).

**Pharmaceutical intervention**

There are currently no approved pharmacotherapies for the management of cannabis use and dependence; however it is anticipated that an evidence-based pharmacotherapy may aid in improving treatment outcomes by reducing withdrawal symptoms, increasing treatment retention and reducing relapse (99, 100).

The severity and amount of withdrawal symptoms are variable for each individual, but can include; irritability, anger, or aggression; nervousness or anxiety, sleep difficulty (insomnia, disturbing dreams); depressed mood, and decreased appetite or weight loss. Additional physical manifestations may include abdominal pain, headache, fever, chills and tremors (99, 101). Pharmacotherapy may assist cannabis treatment by targeting these withdrawal symptoms which cause significant distress and contribute to poor retention in treatment and high relapse rates (99, 102). Some medications have already been tested for their ability to target specific symptoms or a class of symptoms experienced during cannabis
withdrawal although most of the current literature is limited to human laboratory model or small open label or placebo controlled clinical trials (99).

Progressively, studies have explored various different drug types and different mechanisms of action including cannabinoid and opioid agonists and antagonists, anti-depressants, anxiolytics, mood stabilisers and even hormones. Preliminary data suggest that nabilone, naltrexone, and gabapentin are promising and warrant further investigation (99, 103). The newer agonist therapies such as nabiximols are also showing promising early results (137).

The present literature review

The current narrative review provides a consensus of the full range of interventions and treatment options available for cannabis users. Previous narrative reviews have been somewhat limited in their focus by including interventions targeting adults and adolescents separately, or by investigating only those interventions delivered in outpatient settings while excluding computer and telephone based interventions, or by excluding interventions with pharmaceutical adjuncts.

METHOD

Search strategy

Two researchers independently conducted a literature search for articles published prior to February 2016, located through online search of three electronic databases (Google Scholar, CINAHL, Medline, and PsycINFO). The title and abstract search terms were grouped into two blocks: (1) intervention (including ‘intervention’, ‘treatment’, and ‘therapy’); and (2) cannabis use (including ‘cannabis’, ‘marijuana’, and ‘cannabinoids’).
**Study inclusion**

For purposes of this narrative review, only randomised controlled trials describing treatment(s) for cannabis use or cannabis use disorder with a measure of either cannabis use frequency (days of use, quantity of use, or rates of abstinence) or cannabis use disorder severity (typically measured as number of symptoms or with a validated scale such as the Severity of Dependence Scale (104)) were included. Non-English papers, review papers, posters, opinion pieces, letters or editorials, case studies (N<10) and published abstracts were excluded.

Only articles with participants who were primarily cannabis users were included. Articles which included a majority of participants with current substance use disorder or near daily substance use (excluding cannabis and nicotine), or those undergoing treatment for mental health concerns were excluded from this review. Articles were not excluded by location, however; non-English language papers were excluded.

Initial searching identified of 15263 manuscripts which were reviewed to remove duplicates and articles meeting exclusion criteria. A total of 5710 duplicates and 9494 articles meeting exclusion criteria were removed, leaving 59 included trials on cannabis treatment.
RESULTS

MET for adults

A total of seven included studies investigated the efficacy of an MET-based intervention for cannabis use among adults (105-111). Participant groups receiving these interventions ranged in sample size from 20 (105) to 163 (109) across studies. Intervention sessions ranged from a single session (106, 107, 111) up to four sessions without pharmaceutical adjunct (105) and 12 weekly sessions with pharmaceutical adjunct (dronabinol (112) and dronabinol and lofexidine (113)). Follow-up ranged from approximately three months up to 15 months among trials without pharmaceutical adjunct. In these trials MET interventions were compared to a range of alternative interventions, including: CBT, MET+CBT, DC, as well as inactive control conditions. Notably, MET was found to be significantly superior to DC across a 12-month follow-up (111). Specifically, a single session MET intervention was compared to a single session DC intervention and an inactive control condition at end of treatment and at six and 12 month follow-up (111). In contrast, a more intensive MET+CBT intervention of nine sessions with abstinence-based CM and a 14 session MET+CBT intervention without CM were each superior to MET in the two studies assessing this comparison (105, 108). Moreover, no significant differences were noted between a two session MET and a more intensive 14 session CBT intervention over 15 months, with both superior to assessment only conditions (110). In summary, these results are supportive of the use of MET in treating cannabis use among adults, with MET reporting comparable treatment outcomes to CBT and superior outcomes to DC.

MET was superior to inactive control conditions in five out of the six studies which included this comparison (106-111), although all such comparisons were made within a maximum of
four months post baseline. The single trial which did not find MET to be superior to inactive control included a particularly brief intervention of 30-45 minutes delivered to a group of non-treatment seekers identified through screening for problematic cannabis use in a hospital-based primary care clinic (106). In contrast, a separate single session 60 minute MET intervention which included participants who were non-treatment seekers identified through screening (although in a college setting) found MET to be superior to inactive control (107). This pattern of results suggests that the brevity of the intervention may be important when delivered to adults although the efficacy of MET is limited to sessions of at least 60 minutes and preferably more than one session.

An additional five studies investigated the impact of pharmaceutical adjuncts to MET compared to placebo (112-116) although two of these trials also included treatment adherence-based CM adjuncts to the MET intervention (114, 115). Each study assessed group differences at end of treatment only (at six to twelve weeks from baseline). Each of these trials found no difference in treatment outcome with or without pharmaceutical adjunct (regardless of the addition of CM), with all trials reporting decreases in cannabis use. This finding was somewhat confounded by the short follow-up as well as problematic retention rates with treatment completion ranging from only 48% to 77% (57% on average) of participants.

**MET for adolescents**

A total of 11 included studies investigated the efficacy of an MET-based intervention for cannabis use among adolescents (117-127). Participant groups receiving these interventions ranged in sample size from 20 (121) to 136 (127) across studies. Intervention sessions
ranged from a single session (117, 118, 122, 123) up to four sessions (120, 124). Follow-up ranged from approximately three months up to 12 months. In these trials MET was compared with DC (119, 120, 125), CBT and family therapy (127), as well as MET with an abstinence-based CM adjunct (124). There was mixed evidence that MET was superior to DC. That is, four-session MET was reportedly superior compared with a single session DC over six months in one study (120) and a two-session MET (with option of CBT although this was utilised by only 13% of participants) compared with two session DC (with the same CBT option, utilised by 10% of participants) over 3 months; however no between group differences were noted at 12 month follow-up (125). In contrast, a two-session MET was comparable to a single session DC at 3 months in a second study (119). A recent study found significant improvements in cannabis use reductions when assessing the efficacy of adding a session based on the family therapy approach with a focus on parental monitoring to a two session MET intervention over six months, however; this difference was no longer significant at 12 month follow-up (127, 128). Secondary analysis of these results found that parental involvement was more effective for adolescents with cannabis dependence but without a conduct disorder and less effective for those with such disorder (129). Finally, reductions to cannabis use frequency were significant at twelve weeks following a four-session MET intervention with (n=68) or without abstinence-based CM adjunct (n=68) with no between group differences (124). These reductions were particularly significant among those who focused on the use of coping strategies.

All of the six studies which compared MET with inactive control supported the efficacy of MET over three months (118, 121, 123, 125, 126, 130). An additional study included a follow-up at six months and found continued support for MET among boys and those with
greater peer support (122). Notably, a single study included an assessment of MET compared to inactive control (school education as usual) at 12 month follow-up and found no significant intervention effect (130).

In summary, the use of MET is clearly efficacious compared to inactive control conditions for both adolescents and adults, at least in the short term. MET appears to be a comparable intervention type in promoting reductions to cannabis use frequency and dependence severity with the possible exception of the more intensive MET+CBT interventions.

*CBT for adults*

A total of six included trials assessed the efficacy of CBT in adults, with treatments conducted from 1988 (131) to 2012 (132). Sample sizes across these studies ranged from 27 (132) to 117 (110). Intervention intensity ranged from a single session (133) up to 14 sessions (110, 134, 135). Follow-up periods ranged from approximately 3 months up to 16 months (110). Across studies CBT was compared to inactive control, more or less intensive CBT interventions, and with MET. There was no consistent pattern of significant between group differences noted among those studies comparing different intensities of CBT interventions. That is, a study examining a single session and six session CBT intervention found that those receiving the more intensive intervention reported a greater reduction in cannabis dependence but not cannabis use frequency across approximately 8 months (133). In addition, a separate study found that while those receiving 14 sessions of CBT reported comparable reductions to frequency of use as compared with those receiving two sessions of MET across three month follow up, this difference was not sustained at 7, 13 and 16 month follow-up (110).
Two studies examined the efficacy of CBT when delivered in conjunction with abstinence or adherence based CM. That is, those receiving either 14 sessions of CBT with abstinence-based CM or CBT with treatment adherence-based CM both significantly reduced frequency and dependency across three month follow up although only the reductions to cannabis use frequency were sustained at nine months (134). In addition, an investigation of those receiving 12 sessions of either CBT alone, with abstinence-based CM, with treatment-adherence based CM, or abstinence-based CM alone found that those receiving CBT with adherence-based CM reported significantly greater reductions to cannabis use over the 15 month follow-up period compared to the remaining interventions (132).

Relapse prevention was assessed against social support in two studies conducted six years apart. The first study, conducted in 1988 compared 10 sessions of each intervention and found relapse prevention to be superior in reducing cannabis use over one month follow-up (131). The second study did not find any significant between group differences among those receiving 14 sessions of each intervention over 12 months (135).

**CBT with adjunctive agonist pharmacotherapy**

A total of three intervention trials assessed the use of pharmaceutical adjuncts to CBT treatments against placebo CBT treatment. These studies were conducted from 2004 (136) to 2014 (137). Two studies of a 12-session of an outpatient CBT intervention did not find any significant between group differences in cannabis use and dependence between at treatment end (136, 138). The remaining study was an inpatient trial conducted over 9 days with a 28 day follow-up (137). This trial was designed to assess the effects of nabiximols on cannabis withdrawal rather than treatment outcome. Participants received a CBT-based
self-completed work book as well as an undocumented number of individual counselling sessions which were on offer by inpatient staff during the trial period. Nabiximols significantly reduced the symptom severity of cannabis withdrawal compared with placebo.

Consistent with the two earlier trials of CBT with synthetic cannabinoid replacement, this nabiximols study found no difference between groups on abstinence rates or levels of cannabis use at six month follow-up, with both groups reporting reduced use and dependence. Retention rates in the active group of this study were high (85%) as compared to 50% in the placebo group, and higher than the problematic retention rates in the previous two trials (33% (136) and 46% (138)). A trial assessing a longer period of community-based nabiximols therapy for cannabis use disorder is currently underway.

**CBT overview**

In the two studies which compared CBT to inactive controls, 6 to 14 sessions of CBT were superior at 8 and 16 month maximum follow-up (110, 133). Although one of these studies did not find a difference between 1 session of CBT and delayed treatment control at any time point (133).

In summary, the reviewed studies do not provide conclusive evidence of the efficacy of CBT as a treatment for cannabis use disorder. CBT appears to have some measure of effect during the course of the treatment, especially if combined with contingency management.
However, only one study found a continued treatment effect at a 15 month follow-up (132). In combination with agonist replacement therapy it may also improve treatment retention and reduce symptoms of cannabis withdrawal.

**CBT for adolescents**

Only one study was found that compared the effectiveness of CBT to MDFT among adolescents across a 12 month follow-up period (139). The sample size was approximately 55 with a 5-6 month treatment duration. Both treatments reduced cannabis use with no significant difference between groups. However, treatment intensity and retention was significantly higher in the MDFT group (139).

**MET+CBT for adults**

A total of 11 included studies investigated the efficacy of an MET+CBT-based intervention for cannabis use among adults (103, 105, 108, 117, 140-146). Participant groups receiving these interventions ranged in sample size from 20 (105) to 156 (108). Intervention sessions ranged from two sessions (117) to 14 (105). Follow-up ranged from approximately three months up to 15 months. In these trials MET+CBT interventions were compared to a range of alternative interventions, including: more or less intensive versions of MET+CBT and those with and without CM, as well as MET, and DC. In addition, a single study assessed the efficacy of including a pharmaceutical adjunct (gabapentin 1200mg/day versus placebo) with MET+CBT (103). To assess the impact of intervention duration, one study directly investigated a four session intervention when delivered over one month or three months, reporting that longer duration was associated with superior reductions to cannabis use disorder severity but not for cannabis use frequency at end of treatment (144). The optional
addition of a two session booster intervention based on principals MET was associated with superior reductions to cannabis use frequency (although not cannabis dependence) at three month follow-up when added to a nine session MET+CBT intervention (140). However, when this comparison was extended to nine month follow-up this difference was no longer significant.

A total of two out of three studies assessing the impact of including additional CM for cannabis negative urines found this improved outcomes at end of treatment (105) and across twelve months (145). The lone study which did not support adjunctive CM found that although cannabis use frequency was significantly reduced among those receiving the adjunct compared to MET+CBT alone at three month follow-up, this difference was no longer significant at six month follow-up (141). An additional study found that these improvements are likely to be specific to CM for THC negative urines as compared to CM for treatment adherence which was not associated with improvements above that of a health education control condition (146). Finally, MET+CBT was compared with alternative treatments in three studies. Firstly, an eight-session MET+CBT was found to be comparable with eight-session DC over six months in one study (with superior outcomes reported only with the adjunct of CM) (141). Secondly, a 14-session and nine-session MET+CBT intervention was superior to four-session and two-session MET intervention at end of treatment and over fifteen months, in two respective trials (105, 108).

MET+CBT was superior to inactive control conditions in all five of the studies which included this comparison (108, 117, 142-144), and two out of two studies which included a health education control (145, 146). As such, there is consistent evidence for the efficacy of
MET+CBT intervention although the extent to which this intervention is superior to its component parts warrants further study. That is, only two studies have directly investigated a comparison between MET+CBT and MET. These comparisons were confounded by the difference in intervention intensity with the MET+CBT intervention delivered over nine or 14 sessions compared with a two or four session MET intervention. Finally, the study investigating a pharmaceutical adjunct (gabapentin 1200mg/day) found this addition to improve cannabis use frequency outcomes during the 12 week treatment course. This pilot trial was limited by low rates of treatment retention (36% completed treatment) and small sample size (n=25 in each condition), as well as lack of post-treatment follow-up. Despite this, these results highlighting superior treatment outcomes among those receiving the fixed dose of gabapentin warrant future replication. Clearly MET+CBT interventions are efficacious compared to inactive control conditions and when delivered with maximal sessions and abstinence-based CM are likely to be among the most effective cannabis treatments.

**MET+CBT for adolescents**

Only two studies from the same research group have investigated the efficacy of MET+CBT-based interventions for adolescents (147, 148). In the initial study, a 14-session MET+CBT was delivered with abstinence-based CM and an additional 12 weeks of behavioural parent training sessions that included a parent-delivered, abstinence-based, substance monitoring contract (n=36). This was compared with a 14-session MET+CBT with attendance-based CM and an additional 12 weeks of psychoeducational parent sessions including drug education and communication strategies (n=33) (147). Considering the length of treatment, retention rates were high at 77% for both conditions. Cannabis use decreased during treatment for
both groups, but then increased during follow-up only to level off with little overall gain. There was no significant treatment or time \( \times \) treatment interaction effect, although the behavioural parent training condition reported higher rates of abstinence throughout. Post-hoc analysis found that a subgroup of adolescents whose parents displayed consistent disciplining and strong monitoring achieved greater levels of abstinence than those with parents with inconsistent disciplining and poor monitoring. The second study investigated a 28-session MET+CBT intervention \((n=51)\) as well as a similar MET+CBT with abstinence-based CM and parental training intervention involving 14 sessions on parental monitoring techniques and a focus on improving communication and problem solving \((n=51)\) and without parental training \((n=51)\) \((148)\). In addition, all conditions were offered an additional 12 family sessions to facilitate ongoing parental monitoring. As the trial progressed, participants attended an average of ten of the offered sessions. Adolescents who received the MET+CBT with CM interventions were more likely to report abstinence during treatment (with or without parental training) compared to MET+CBT without CM, however; no between group differences in abstinence rates were noted during follow-up over 12 months. These results suggest that, as with adults, the use of MET+CBT is likely to be effective for adolescents, although the addition of parental monitoring training appears to be important for this group.

**Motivation and Mindfulness (MM) for adults**

Only one study meeting inclusion criteria has assessed MM. Specifically, this study compared two sessions of combined MI-MM to an assessment only control with a relatively small sample size of 22 female frequent cannabis users \((149)\). The intervention group reported relatively high treatment retention of 77%. Compared with control, those
receiving this intervention reported a significant decrease in frequency of use at three
month follow-up. This preliminary evidence warrants further investigation into the efficacy
of an MI-MM intervention with a larger sample size.

Drug education and counselling (DC) for adults
A total of three included studies conducted between 2006 (141) and 2012 (150) assessed
the effectiveness of DC among adults in reducing cannabis use. The sample size of
intervention groups ranged from 25 (150) to 62 (111) and these studies were conducted
with 2 to 12 month follow up periods. An initial study assessed the effectiveness of either
one oral or a written DC session against oral or written controls and found no significant
difference between them at either 3 or 12 month follow-up (150). A second study found
that one session of MET was superior in promoting cannabis use reductions compared to a
session of education in reducing dependence across 12 months (111). In the most extensive
study, eight single sessions of DC were compared to eight sessions of CBT+MET with both
adherence and abstinence-based CM, eight sessions of DC also with both adherence and
abstinence-based CM, and eight sessions of CBT + MET (141). Participants receiving either
intervention with CM adjuncts were more likely to report reduced frequency of use at 3
months compared to non-CM interventions, although this effect was lost at the 6 month
follow-up (141).

In the two studies that included minimum control conditions, DC was not found to be
superior to either an inactive control, or a general health intervention. From the three
studies that were examined, DC does not appear to be an effective treatment in reducing
cannabis use.
Drug education and counselling (DC) for adolescents

Only two studies have investigated the efficacy of DC for treating cannabis use among adolescents. In an initial 2011 study of voluntary frequent users, a two session DC intervention (n=102) was compared to two sessions of MET (n=103) and delayed feedback control (n=105) (126). This study found that, while both MET and DC were effective in reducing cannabis use at three and 12 month follow-up, the MET was found to be superior at three months only. A second study conducted in 2015 compared a four session MET intervention (N=71) with a single hour DC session (N=60) (120) in non-treatment seeking adolescents. At one month follow up, no between group differences were reported, however; at six months only those receiving the MET intervention reported a significant reduction in frequency of use.

The two studies presented provide conflicting conclusions regarding the efficacy of DC in adolescents. Although MET remains a superior intervention in the short term, a more robust DC intervention may prove to be effective in treatment seeking adolescents and warrants further investigation.

Technology-based Interventions

Telephone counselling

Only two articles meeting inclusion criteria were delivered by telephone (151, 152). The first was conducted in Brazil involving a large sample of individuals who had called a national cannabis helpline service (n=1744) (151). The majority of participants met criteria for a cannabis use disorder at the time of their call (88%) and were seeking treatment. Following this call, eligible participants were randomised to receive a single session intervention based
on MI (N=873) or assessment only (n=871). Across a follow-up period of six months those participants allocated to the intervention had an increased likelihood of achieving abstinence as compared to control (OR = 1.6, CI 95%: 1.2–2.0). This study suffered from extreme rates of attrition with only 30% of those randomised completing the 6 month follow-up. In addition, the authors did not assess the participant’s use of external treatments during the trial period.

The more recent investigation was conducted in Australia and also included participants who called a national helpline (152). Although this trial did not have the same large sample size (n=160), it was able to control for the use of external treatments and reported an acceptable trial attrition rate (69%). Following their call to the Helpline, eligible participants were randomly allocated to receive a four session intervention based on MET+CBT or waitlist control and assessed at one and three-month follow-up. Those receiving intervention reported significant improvements to cannabis use dependence severity across follow-up, while there were no significant between group differences in cannabis use frequency. In summary, although these studies highlight some initial support for telephone counselling, there is a clear need for further evaluation of telephone-based cannabis treatments, particularly including a long-term follow-up.

**Internet and computer-based interventions**

A total of seven randomised trials have examined computer/web based cannabis treatment programs for cannabis use/and or dependence with the earliest being in 2011 (153). The majority of the studies examined the efficacy of computer/web-based interventions compared to delayed treatment controls (153-156). Interventions included single session
computer delivered BI (156, 157), 6 week of CBT + MI based programs (91, 155) and 9 sessions of CBT/MET/CM (158). The remaining three studies compared the effectiveness of computer/web delivered treatments to in-person, therapist delivered treatments (157-159). Across studies the sample sizes ranged from 75 (158) to 458 (159), with follow-up periods ranging from one month (156) to nine months (158). In a 3 arm trial comparing 9 sessions of MET/CBT/CM therapist or computer against a 2 session MET control, both were equally superior in maintaining abstinence rates and reduction in use at 9 month follow-up over control (158). This study, as well as the other studies comparing efficacy of computer/web based interventions to in-person therapist delivered interventions found no advantage of in-person therapist delivered interventions in regards to cannabis use reductions or severity of CUD (157-159).

Four studies assessed computer/web based treatments versus control (delayed treatment or assessment only). Two of these studies involved a 6 week web based intervention program developed from MI and CBT principles (91, 155). These two studies supported the efficacy of web based treatment in reducing cannabis use and severity of CUD, with a greater treatment effect seen if an additional 2 sessions of chat with a trained therapist were provided to participants (155). A single computer based brief intervention based on motivational interviewing was also found to be superior in reducing use compared to an assessment only control (159). The only study that did not find a difference between a computer based intervention and an assessment only control use a single session educational program (156).
These promising findings illustrate the potential for computer and web based delivery of proven interventions such as CBT + MET. These delivery methods have the potential to enhance access to evidence based care, reduce cost and possibly improve outcomes.

Conclusion

In line with previous reviews of cannabis treatment, this narrative review found that the cannabis treatment most likely to be effective for adolescents and adults is based on the combination of Motivational Enhancement Therapy (MET) and Cognitive Behavioural Therapy (CBT). Current research also supports these component parts delivered in isolation, however; their combination appears to enhance treatment outcomes for a longer term post treatment. The importance of self-efficacy in predicting treatment outcomes suggests that treatment seekers with low motivation to quit may be best treated first with MET and then with CBT as motivation improves. No particular cannabis treatment has consistently shown improvements beyond nine-month follow-up. In addition, among adolescents, involving parents with additional sessions focussing on parental monitoring strategies may improve outcomes. Among adults, the addition of abstinence-based incentives (Contingency Management, CM) is likely to improve outcomes. Notably, the use of pharmaceutical adjunct to these interventions was not likely to improve outcomes, although future research may change this conclusion with preliminary support for the use of gabapentin in conjunction with MET+CBT (103). Finally, treatment modality does not seem likely to amend these conclusions, with studies involving both internet and telephone delivery following a similar pattern of results.

Limitations

The available research suffers from significant limitations and there was huge variability in
the individual trial methods. Firstly, the methods of assessment and measures of cannabis-related outcomes differed dramatically. Cannabis use frequency was assessed as days of use, proportion achieving abstinence (including both point-prevalence and continuous abstinence), or number of joints, with the period of assessment ranging from the past week to the past three months. Severity of cannabis dependency was often not assessed across trials. Among trials which did assess this outcome, severity of dependence was reported as number of symptoms of dependence, proportion meeting diagnostic criteria for cannabis use disorder, or indexed using a validated scale. As with cannabis use frequency, the period of assessment ranged from the immediate point of interview to the past three months. As such this review was limited to the statistical significance of treatment effect (at p<0.05) rather than combining studies with consistent measures of treatment outcome.

Secondly, the individual trials varied in terms of participant inclusion. That is, there was an inconsistency in the number of trials which excluded participants according to non-cannabis substance use, medical or psychiatric illness, cognitive awareness or capability to participate and presence of concurrent substance use treatments. In addition, while many trials recruited treatment seeking participants through advertisement, many other trials included non-treatment seekers identified via various methods of screening for those with cannabis-related problems – usually in hospital emergency settings for adults and school counsellors for adolescents. Moreover, the majority of participants in the included trials were young, white Caucasian males although this does reflect those seeking cannabis treatment in the general community (2, 3). Further, the vast majority of treatment trials were conducted in the US leaving the applicability of treatments to other cultures unclear. Finally, only a handful of studies assessed the participants’ previous experience with cannabis treatments
or previous attempts to quit cannabis (125, 133, 134, 139, 141-143, 152, 160). In each of these studies this variable was assessed at baseline and not included as a potential moderator of treatment outcomes. As such, the impact of such experience on treatment outcomes is unclear. In sum, the overall generalisability of treatment effect to the general community remains confounded.

Thirdly, although the concurrent use of tobacco was prevalent in trial participants, it was particularly rare for the included interventions to specifically address the use of tobacco. As such it was unsurprising that there was a lack of long-term treatment effect among those trials assessing tobacco use as a treatment outcome (106, 110, 123, 125, 144, 146, 147, 152, 159), with only one trial reporting a significant treatment effect across three months among those not also using hallucinogenic drugs (123). Previous research has identified that, given similarities in the route of administration of these two drugs and associated withdrawal symptoms, abstaining from both substances simultaneously may predict better treatment outcomes, however this remains to be adequately empirically tested (161).

Fourthly, although the vast majority of included trials provided details of therapists’ experience and training along with formal protocol for ensuring that the interventions were delivered as intended, many trials suffered from a lack of treatment completion. This was somewhat surprising given that the included interventions appeared to favour brevity over intensity. That is, the number of intervention sessions ranged from one to a maximum of 44, with a median of eight sessions across studies. This lack of treatment completion was most notably the case among trials which included pharmaceutical adjunct where completion rates ranged from as little as 34% (114) to a maximum of 85% (137).
Finally, psychiatric comorbidity was a basis for exclusion in this narrative review. Those presenting with cannabis use disorders often have high rates of psychiatric comorbidity, particularly other substance use disorders, affective disorders, anxiety and personality disorders (162). As such, these should be considered in all assessment and intervention approaches. Only three studies were excluded from this review for this reason. There is an urgent need for development of this kind of integrated treatment; as currently there are no evidence-based interventions for cannabis use disorder with comorbid serious mental health conditions.

Although it can be said that a limitation of this review is its narrative nature, it was produced to the highest standard as the authors used similar search and analysis methods to the ones that were used in a very recent Cochrane Publication covering a similar topic.

*Factors that help/hinder change*

Consistent with the principals of MET, the only consistent moderator of treatment effect across trials was participant motivation or self-efficacy (109, 120, 124, 127, 140, 146, 152). As might be expected, those participants with greater motivation to abstain from cannabis use were more likely to report positive treatment outcomes across follow-up.

In summary, as rates of treatment seeking for cannabis-related problems continue to increase there is some urgency in establishing a gold standard treatment. In review of the intervention trials conducted to date this gold standard is yet to be established. Conflicting results particularly regarding response rates, abstinence from cannabis and reduction in cannabis-related problems, provides clear opportunity for improvement. Important questions are raised in regards to optimal duration, intensity and treatment type when comparing therapeutic modalities. It is also difficult to determine generalisability of findings.
as studies are limited in treatment numbers and sample heterogeneity.

To improve the body of evidence surrounding these interventions, future studies should assess cannabis use and related problems over longer time periods and with consistent measures, including improved assessments on motivation, other substance use and aspects of participant’s mental health.

The most likely candidate for a gold standard cannabis use disorder treatment currently is a MET+CBT intervention, although future research is required to determine the importance of number of sessions and duration of delivery. As yet, there is no evidence based pharmacotherapy in treating cannabis withdrawal and dependence, it is anticipated that a proven pharmacotherapy may be a useful adjunct in increasing treatment retention, decreasing relapse rates and decreasing the prevalence of CUD. Preliminary results for some drugs are promising, but require extended investigations.

To provide a more concrete and robust evidence base for these interventions, there is a need to replicate treatment studies using standardised interventions, methods and measures to minimise conflicting findings, inconsistent follow-up periods and poor treatment effects over time.
Conflict of interest

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