

**A systematic review of technology-based psychotherapeutic interventions for
decreasing cannabis use in patients with psychosis**

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Highlights

- Research related to TBPIs in individuals with psychosis and cannabis misuse is in its early stages
- Psycho-education and cognitive enhancement therapy were minimally effective
- TBPIs should integrate a combination of psychological interventions
- Adapting TBPIs to patient and clinician preferences is extremely important
- RCTs on larger and well-defined samples are needed to test the efficacy of TBPIs

Abstract

Persistent use of cannabis in persons with psychosis is associated with poor symptomatic and functional outcomes and increased healthcare costs. Face-to-face psychological interventions (e.g., Cognitive Behavioral Therapy- [CBT], Motivation Enhancement Therapy- [MET]) are widely used in treating problematic cannabis use. We aimed to comprehensively review the efficacy of technology-based psychological interventions (TBPIs) in decreasing cannabis use, the design of TBPIs, and TBPI-related preferences in individuals with psychosis. For the systematic review, we searched six major databases from their inception to November 27, 2019. We included empirical articles of quantitative and qualitative methodologies related to TBPIs in individuals with psychosis and cannabis misuse and used narrative synthesis to report results. Only eight articles were found showing that technology-based motivational and psycho-education interventions and cognitive enhancement therapy were minimally efficient in achieving cannabis abstinence or decreasing frequency of use. Qualitative exploratory methods and participatory action research were used to elicit patient and clinician preferences and TBPIs were tailored accordingly to improve cannabis use related outcomes. Research on TBPIs in individuals with psychosis and cannabis misuse is in its early phases. A significant research effort is needed for the development of adapted interventions of CUD to capitalize on the potential of web-based applications.

Keywords: psychotherapy; cannabis misuse; cannabis use disorder; web-based; eMental health; internet-based intervention

1. **Introduction**

Cannabis is the most commonly used illicit drug worldwide with a 12-month prevalence in the general population of approximately 3.8% (United Nations, 2019). In Canada, where recreational use

of cannabis has been legalized in October 2018 the prevalence of cannabis use is higher with an estimated 17% of the general population reporting cannabis use in the last 3 months (Statistics Canada, 2019). About 20% of these users present moderate to high risk of developing “hazardous or potentially harmful cannabis use patterns, including cannabis use disorder (CUD)” (Conus et al., 2019; National Academies of Sciences and Medicine, 2017). The 12-month prevalence of CUD is about 2.5% (Hasin et al., 2016) and is significantly higher in young adults with first episode psychosis (36.5-56.1%) (Abdel-Baki et al., 2017; Hadden et al., 2018; Schimmelmann et al., 2012; Schimmelmann et al., 2011).

While the contribution of cannabis to the incidence of psychosis is complex, continuous cannabis consumption after the onset of a psychotic disorder has been associated with increased psychotic symptoms (Carney et al., 2017; Kuepper et al., 2011; Moore et al., 2007); rate and length of hospitalizations and frequency of emergency room visits (Patel et al., 2016; Turkington et al., 2009); and poor response to antipsychotic treatments (Patel et al., 2016; Wade et al., 2006). Importantly, persistent cannabis use in individuals with psychosis (including early psychosis) is associated with psychotic relapses (Alvarez-Jimenez et al., 2012; Zammit et al., 2008) and suboptimal psycho-social functioning (e.g. related to school, work, friends and community) (Alvarez-Jimenez et al., 2012; Penn et al., 2005). Therefore, in individuals with psychosis, interventions aiming to decrease cannabis use and its impact can be of high clinical and psychosocial importance. To date, the mainstay of treatment for decreasing cannabis use in individuals with psychosis is represented by psychological interventions, while data on pharmacological interventions remain inconclusive because of small sample sizes and low quality of data available from randomized controlled trials (RCTs) (Krause et al., 2019; McLoughlin et al., 2014).

In people without psychosis, systematic reviews shows strong evidence that face-to-face psychotherapeutic interventions—cognitive behavioural therapy (CBT) and motivation enhancement therapy (MET)—are effective in decreasing frequency and quantity of cannabis use, symptoms of cannabis dependence, and problems associated with cannabis use (e.g., substance-related legal problems, debts and physical neglect) (Chatters et al., 2015; Gates et al., 2016; Montgomery et al., 2017; Sabioni and Le Foll, 2018). In people with psychosis, evidence supports adding CBT and/or MET to treatment as usual (TAU) for assisting with reducing cannabis use (i.e., frequency and quantity), decreasing the severity of cannabis dependence, and increasing rates of cannabis abstinence (Barrowclough. et al., 2001; Cooper et al., 2015; Gates et al., 2016; Haddock et al., 2003; Hjorthoj et al., 2014; Hjorthoj et al., 2013). However, systematic implementation of face-to-face psychological interventions in early intervention programs for psychosis is compounded by difficulties in sustaining

adequate training among clinicians and heterogeneity in healthcare resources (e.g., treatment accessibility) (Aydin et al., 2016).

A promising approach to decreasing cannabis use is technology-based psychotherapeutic interventions (TBPIs), such as web-based and computer-based interventions. TBPIs are believed to address some of the issues related to face-to-face interventions by improving access to treatment, cost-effectiveness and reducing financial resources needed for clinician training and staffing, without increasing demands for caregivers (Carroll and Rounsaville, 2007; Johnson et al., 2011; Marsch et al., 2014; Marsch and Dallery, 2012; Moore et al., 2011; Olmstead et al., 2010; VanDeMark et al., 2010). In individuals without psychosis, results of two meta-analyses including approximately 7,000 cannabis users show that TBPIs are efficient in decreasing frequency of cannabis use (Olmos et al., 2018; Tait et al., 2013). To our knowledge, no comprehensive synthesis has been published related to using TBPIs in individuals with psychosis who misuse cannabis.

Given the positive impact of face-to-face psychotherapeutic interventions on cannabis consumption in patients with psychosis and the efficacy of TBPIs in reducing cannabis use in individuals without psychosis, we aimed to provide a comprehensive synthesis of available research pertaining to the effects of TBPIs on cannabis use in individuals with psychosis.

2. Methods

The systematic review was guided by the following three research questions:

- 1) “Are TBPIs effective in decreasing cannabis use in patients with psychosis?”
- 2) “What TBPIs are most efficient in decreasing cannabis use in patients with psychosis?”
- 3) “What factors contribute to the design of TBPIs that effectively decrease cannabis use in patients with psychosis?”

We reported the results consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework (Moher et al., 2009) and registered the protocol on the International Prospective Register of Systematic Reviews (PROSPERO, CRD42019141078)¹.

2.1. Data source and search strategy

We searched in Medline, PubMed, Embase, CINAHL, PsycINFO and EMB Reviews for references from inception to February 26th, 2019 and later updated the search up to November 27th, 2019. The search strategy for Medline (Ovid) was validated by an experienced librarian (DZ) and then adapted for the other databases. The search strategy for Medline (Ovid) was developed around four

¹ <https://www.crd.york.ac.uk/prospero/>

concepts i.e., cannabis, intervention, psychotherapy and psychosis which were combined with AND (see Appendix A). Duplicates were removed in Endnote and references were transferred into Excel. We searched for additional references in relevant articles (“snowballing” technique) (Horsley et al., 2011) and contacted authors, when needed, to clarify participant inclusion criteria in their studies.

2.2. Eligibility criteria

The following eligibility criteria were applied: 1) population: individuals diagnosed with psychosis and cannabis misuse; 2) intervention: any technology-based (e.g., web-based, computer-based; telephone-based interventions were not included if not using another technology) psychotherapeutic intervention (e.g., CBT, MET, etc.); 3) control: any comparison group (e.g., TAU); 4) outcomes: cannabis use frequency or abstinence, including objective (i.e., biological markers) and subjective (i.e., self-reporting of frequency and quantity) measures, CUD or cannabis abuse/dependence severity, cannabis-related psychological factors (e.g., intentions, behaviors); 5) study design: empirical studies of any methodology (e.g., experimental, observational, quantitative, qualitative); and 6) languages: English, French, Spanish or German.

2.3. Study selection process

The selection of references unfolded in two phases and was performed independently by two reviewers (OT and GB). In the first phase, references were screened for eligibility based on titles and abstracts and in the second phase, empirical articles were screened based on full text. The senior researcher (DJA) mediated any unresolved disagreements between reviewers in either phase regarding the eligibility of articles. The output of the second phase was the final set of articles included in this review.

2.4. Data extraction

We used two distinct Excel spreadsheets to extract quantitative and qualitative data from primary studies. Specific categories of data extracted from quantitative studies include: description of the intervention (e.g., type of technology and type of psychotherapy used), control group, length of intervention, number and length of follow-ups, sample size, population studied (e.g., psychiatric disorder and Substance Use Disorder [SUD] diagnosis, age, etc.), analysis methods and results (e.g. proportions, odds ratios) for primary and secondary outcomes. From qualitative primary studies we extracted information related to the research context, type and number of participants, data collection and analysis methods, raw qualitative data (i.e., quoted excerpts from interview transcripts) and results of qualitative analysis (e.g., themes).

2.5. Quality appraisal

We appraised the methodological quality of included studies using a critical appraisal tool called the Mixed Methods Appraisal Tool (MMAT), version 2018 (Hong et al., 2018). The MMAT is a validated tool that provides independent sets of appraisal criteria for studies of various designs and methodologies: qualitative (e.g., qualitative description), quantitative (e.g., randomized, non-randomized), and mixed methods. For each criterion (specific to the methodology of the study), we assessed if the criterion was met and calculated an overall percentage score. We used a study-based rather than an article-based method of quality appraisal i.e., if two or more articles were published based on the same study, we appraised the study as a whole². We used the MMAT for descriptive purposes and retained all studies for the synthesis, independent of the assessed risk of bias. The quality appraisal was performed independently by two reviewers (OT and GB); the senior researcher (DJA) was available to mediate disagreements, which was not necessary.

Due to the heterogeneity of methodology among the included studies, we could not employ meta-analytic techniques and instead used narrative synthesis (Popay et al., 2006). Synthesis results are organized by study (to include data published in distinct articles) and are reported separately for quantitative (i.e., corresponding to the first two research questions) and qualitative (i.e., corresponding to the third research question) primary data.

3. Results

3.1 Search results and study characteristics

In Figure 1 we present the PRISMA study selection diagram. In total, we included in our synthesis eight articles published in English, corresponding to two quantitative studies conducted in the US (DeMarce et al., 2008; Eack et al., 2016; Eack et al., 2015) and two mixed-methods sequential exploratory studies conducted in Australia (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010) and in the UK (Johnson et al., 2019; Sheridan Rains et al., 2019). In total, 781 participants were included, with an age range of 18–60 years (Eack et al., 2016; Eack et al., 2015) or a mean age of 48 years (DeMarce et al., 2008) in the quantitative studies and an age range of 25–33 years in the mixed method studies (Johnson et al., 2019; Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010; Sheridan Rains et al., 2019). The target substances were a mix of alcohol and/or cannabis in two studies (Eack et al., 2016; Eack et al., 2015; Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010) or a mix of substances (i.e., cannabis, alcohol, cocaine, opiates,

² We adopted this approach after consulting with the authors of the MMAT, Hong QN et al.

methamphetamines benzodiazepines, barbiturates, phencyclidine) in the other studies (DeMarce et al., 2008; Johnson et al., 2019; Sheridan Rains et al., 2019). One study limited psychiatric comorbidities to schizophrenia and schizoaffective disorder (Eack et al., 2016; Eack et al., 2015). Additional diagnoses (in addition to schizophrenia) were assessed in other studies: bipolar affective disorder and major depressive disorder (DeMarce et al., 2008; Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010), presence of psychotic symptoms (Johnson et al., 2019; Sheridan Rains et al., 2019), generalized anxiety disorder, panic disorder, posttraumatic stress disorder, attention deficit hyperactivity disorder (DeMarce et al., 2008), substance induced psychotic disorders (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010), and other psychoses (Johnson et al., 2019; Sheridan Rains et al., 2019). The overall risk of bias was considered low as all studies met at least three out of five MMAT quality criteria. Following factors increased risk of bias: low adherence to the intervention (DeMarce et al., 2008; Eack et al., 2016; Eack et al., 2015; Johnson et al., 2019; Sheridan Rains et al., 2019), significant differences at baseline between treatment groups related to psychiatric composite scores and drug composite problem scores (DeMarce et al., 2008), and no assessment of possible divergences or inconsistencies between qualitative and quantitative results (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010). The summary of included studies (qualitative and quantitative) and results of quality appraisal are reported in Table 1.

3.2 Quantitative studies

Eack et al. (2015, 2016) analyzed data from an 18-month feasibility RCT, that enrolled participants with chronic psychosis (mean duration of illness 14.19 years, SD=11.28) who were assigned to TAU (n = 9) or Cognitive Enhancement Therapy (CET, n= 19) (Eack et al., 2016; Eack et al., 2015). Randomization was weighted towards the CET group to facilitate analysis of social-cognitive functioning (e.g., understanding and managing emotions) (Eack et al., 2015). Cannabis use was measured with the Timeline Follow-Back method (TLFB, for the previous 30 days) and assessed at 6, 12 and 18 months (Eack et al., 2016; Eack et al., 2015). All participants had access to available mental health and social services, including individual supportive therapy, case management, and vocational rehabilitation services and participants received antipsychotic medication throughout the study (Eack et al., 2016; Eack et al., 2015). The therapeutic approach comprised a combination of 60 hours of computer-based training—targeting cognitive impairments related to information processing specific for patients with schizophrenia such as vigilance, attention, processing speed, working memory, and problem-solving—with forty-five structured social-cognitive groups that facilitated perspective-taking, social context appraisal and emotion management (Eack et al., 2016; Eack et al.,

2015). In their first analysis (Eack et al., 2015) the authors found no significant difference between study arms related to cannabis abstinence or number of days of cannabis use in the previous month. Subsequent analyses (Eack et al., 2016) of cannabis use trajectories revealed no effect of the intervention on the likelihood of cannabis use or on the extent or acceleration of cannabis use reduction over the course of the study. However, results show a significant association between improved reasoning and problem-solving skills and decreased odds (OR= 0.87, 95% CI: -0.03; -0.00) of cannabis use (Eack et al., 2016).

DeMarce et al. (2008) assessed drug abstinence (measured with the Timeline Followback [TFLB] over previous 90 days and validated by urinalysis results) at 3-, 6- and 12-month follow-up in participants graduating from a residential 28-day substance abuse intensive treatment program who were randomized to TAU (n=33) or the contracting, prompting and reinforcing [CPR] intervention (n=44) (DeMarce et al., 2008). All participants received orientation to aftercare (i.e., post-intensive program) that included recommended frequency of attendance to aftercare therapy sessions i.e., weekly group therapy and Alcoholic Anonymous/Narcotics Anonymous meetings and monthly individual therapy in the first 2 months (DeMarce et al., 2008). Those allocated to the TAU arm received support for scheduling aftercare sessions, signed a standard contract, and viewed a 20-minutes generic motivational video (not developed specifically for this trial) at the beginning of aftercare and after 2 months (i.e., 3 months into the study) to encourage them to adhere to their continuing care plans (DeMarce et al., 2008). Instead of watching motivational videos, participants in the intervention group were asked to commit to adhere to aftercare by signing a detailed contract and were provided results of a previously evaluation study related to 1-year abstinence rates in patients who were adherent to aftercare therapeutic components (DeMarce et al., 2008; Lash et al., 2007). The intervention included components to facilitate adherence to aftercare plans such as prompts to attend aftercare appointments in form of automated telephone reminders, appointment cards and letters/phone calls for missed appointments from their individual therapist (DeMarce et al., 2008; Lash et al., 2007). Additionally, participants in the intervention arm received social reinforcement comprising handwritten letters from their individual therapist congratulating them for beginning aftercare and reaching attendance milestones, as well as certificates/medallions at 3 months and 1 year depending on their adherence to group and individual therapy sessions (DeMarce et al., 2008; Lash et al., 2007). Between-group comparisons showed similar drug abstinence rates at 3 and 6 months while at 12 months the abstinence rate in the intervention group was significantly higher ($\chi^2 = 6.66$, OR = 3.71, 95% CI: 1.34; 10.33) (DeMarce et al., 2008).

Using a mixed methods study, Nagel and colleagues developed a brief counselling intervention (motivational care planning, [MCP]) and used an 18-month repeated measures design with delayed treatment group to assess MCP's efficacy in improving mental health and substance dependence in participants with chronic mental illness recruited from remote Indigenous communities in northern Australia (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010). Patients were randomized to receive the intervention—comprising two treatment sessions two to six weeks apart—at baseline (n=24) or at six months (n=25) and benefited from TAU throughout the trial (Nagel et al., 2009). Cannabis dependence was measured with the 5-item patient-rated Severity of Dependence Scale (SDS) and assessed at baseline and at 6-, 12- and 18-month follow-up (Nagel et al., 2009). The TAU group received supportive counselling and mental health assessment, as well as review and treatment (including medication) in a multidisciplinary team environment that included local health centre nurses and the local mental health team (Nagel et al., 2009). Each 1-hour therapist-delivered treatment session (in the presence of carers and Aboriginal Mental Health Workers, [AMHWs]) was guided by principles of problem-solving, motivational interviewing, and self-management. The therapy focused on managing life stressors, identifying treatment goals, addressing barriers and progress, and developing new treatment strategies as appropriate (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010). In each session, participants watched two short animated psycho-educational videos developed to summarize most important concepts (e.g., social support) identified in the initial qualitative exploratory phase of the study (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010). The intervention (including the video content) incorporated a family-oriented perspective illustrating strong existing connections between family, culture and traditional activities and the important supportive role played by the family in achieving treatment goals (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010). Results of mixed model regression analysis of SDS scores—while accounting for time from baseline and outcome scores at 6 months post-treatment—show an advantage of the MCP in terms of cannabis dependence (approaching statistical significance, coefficient: -0.98, 95% CI: -2.02 ; 0.057, $p = 0.064$) which was sustained over time (coefficient: -0.44, 95% CI: -0.85; -0.02, $p = 0.016$) (Nagel et al., 2009).

In the CIRCLE multicentre pragmatic RCT, adults aged between 18 and 36 years were recruited from Early Intervention in Psychosis services (EIP) in the UK and were randomly allocated to the experimental (TAU+ Contingency Management, [CM], n=278) or control arm (TAU, n=273) (Johnson et al., 2019; Sheridan Rains et al., 2019). Cannabis use (secondary outcome) was measured with the TLFB and by detecting tetrahydrocannabinol in the urine and was compared at 3- and 18-month follow-up between the arms (Johnson et al., 2019; Sheridan Rains et al., 2019). All participants

received standard services for first episode psychosis and a structured computer-based psycho-education intervention specifically developed for cannabis use in line with motivational interviewing principles, relapse prevention and harm reduction strategies (Johnson et al., 2019; Sheridan Rains et al., 2019). The psycho-education intervention consisted of six modules of 30 minutes each and included a package in PDF format that was used by clinicians during the therapeutic encounter, as well as video materials, short quizzes, audio files, and written records of the modules that could be kept by participants (Johnson et al., 2019; Sheridan Rains et al., 2019). The CM intervention comprised financial incentives (i.e., vouchers) contingent on cannabis abstinence and included signing an “abstinence contract” at the beginning and 12 weekly sessions (Johnson et al., 2019; Sheridan Rains et al., 2019). The between-group differences in cannabis abstinence (analysed using logistic regression) did not reach statistical significance at 3- and 18-months follow-up (OR: 0.86, 95% CI: 0.56; 1.34; OR: 0.84, 95% CI: 0.49; 1.41, respectively) (Johnson et al., 2019; Sheridan Rains et al., 2019). Similarly, at the same follow-up time-points, self-reported cannabis-using days (analysed using zero inflated Poisson regression) was not different between the arms (incidence rate ratio [IRR]: 0.89, 95% CI: 0.75; 1.04; IRR: 1.09, 95% CI: 0.88; 1.36, respectively) (Johnson et al., 2019; Sheridan Rains et al., 2019).

3.3 Qualitative studies

In their mixed methods study, Nagel and colleagues integrated qualitative with quantitative data by using a sequential exploratory and concurrent design (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010). The initial qualitative exploratory phase informed the development of the motivational care planning (MCP) intervention (consisting of four psycho-educational short videos), while concurrent qualitative data collection (at baseline, 6, 12 and 18 months) and analysis enabled an in-depth understanding and validation of results of the quantitative phase (RCT) (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010).

In the exploratory phase, the researchers used a participatory action research approach and partnered with ten AMHWs and one recovered patient to gather Indigenous perspectives of mental illness through participant observation, interviews and ethnographic methods (Nagel et al., 2008; Nagel and Thompson, 2010). This phase underscored the central role of family in supporting patients and reinforced the importance of traditional and cultural activities: “Yeah! My mother and grandmother used to teach everything what they were taught before by their mothers—that how I want to teach my kids, my grandchildren, to do the same ... because back in those times, like to me it was strong, we didn’t have this mental health problem ... because at that time we had good life ... we’ve enjoyed everything (female AMHW)” (Nagel and Thompson, 2010). Results of the exploratory phase informed

the production of psycho-educational animated videos that encouraged family involvement towards achieving goals and lifestyle changes, sharing of information and included traditional and popular songs e.g., “It’s not that easy when you’re all alone “ (Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010).

Qualitative data collected throughout the RCT (concurrent approach) from patients and AMHWs was content analyzed and frequencies of categories were provided (Nagel and Thompson, 2010). The mixed methods design enabled triangulation of results of content analysis with results of exploratory phase (included in the intervention) and the RCT. The authors were able to show how baseline patients’ worries (regarding cannabis and or alcohol consumption [~60%] and/or family divergences [~70%]) aligned with their goals to change (reducing alcohol/cannabis use [~30%], alleviating family disagreements [~17%]) and strategies for change (communicating with family [~27%] or avoiding family contact [~15%]) and were adequately targeted by the MCP intervention, including the psycho-educational video component (Nagel et al., 2008; Nagel and Thompson, 2010). The favorable effect of MCP as shown by quantitative (RCT) results was partially supported by patients’ self-evaluation of their progress towards achieving goals, as 69% reported “some” or “extremely good” progress at 6 months post intervention, and by the decreasing trend of substance misuse from 41% at baseline to 16% at 18-month follow-up based on AMHWs reports (Nagel et al., 2009).

Johnson et al., (2019) used a mixed-methods approach and conducted a qualitative study after the pilot study of the CIRCLE trial with the aim to optimize the implementation of the main trial (Johnson et al., 2019). Data collection included semi-structured interviews (11 participants from the CM arm and one carer) and focus groups (50 clinicians from the EIP teams) and presented results of thematic analysis separately for trial participants and clinicians. Exploring views related to the computer-based psycho-educational package was secondary to exploring experiences related to the use of CM. Clinicians reported positive outcomes with respect to the experimental arm interventions (e.g., helping participants to reduce their cannabis use or achieve abstinence) but highlighted difficulties related to recruiting participants in the control arm and engagement with the psycho-education intervention. Some participants showed lack of interest in the treatment and poor insight of the negative effects of cannabis use. The psycho-education package was generally valued by clinicians since it was “good for reflection” and offered the opportunity to patients to “look back and have space to think of their own cannabis use” (Johnson et al., 2019). Some clinicians considered time constraints a barrier and recommended peer support workers to be involved in delivering the intervention. Clinicians viewed the CM unsustainable after the trial ends but considered the computer-based psycho-education a “useful tool” for standard EIP services. Both clinicians and participants criticized inaccuracies in the psycho-

educational modules and the repetitive nature of information and questions. Participants valued the learning opportunities offered by the psycho-education sessions and considered that the intervention helped them acquire knowledge about negative effects related to cannabis use, develop insights related to their motivation for using cannabis, maintain focus on reducing cannabis use, and change their lifestyle (e.g. saving money, avoiding peers that use cannabis). Suggestions for improvements included using more video-based testimonials from people who had similar experiences. Participants considered that psycho-education complemented the role of CM by offering them explanations for why quitting cannabis was worthwhile. Based on the results of the qualitative study, the psycho-educational intervention was optimized to ensure information accuracy and to avoid repetition (Johnson et al., 2019).

4. Discussion

We aimed to provide a comprehensive synthesis of existing research on the effects of TBPIs on cannabis use in individuals with psychosis. In particular, we sought to answer following questions: 1) are TBPIs efficient in decreasing cannabis use in patients with psychosis; 2) what TBPIs are most efficient in decreasing cannabis use in patients with psychosis; 3) and what factors contribute to the design of TBPIs that effectively decrease cannabis use in patients with psychosis? We synthesized quantitative and qualitative data from empirical studies identified in six major databases.

This systematic review reveals a paucity of studies using TBPIs in individuals with psychosis. Regarding the first research question, our synthesis shows a minimal effect of technology-based motivational and psycho-educational interventions and CET on cannabis use frequency, abstinence or dependence severity. These results should be interpreted with caution, considering the small number of participants, diverse populations and heterogeneity in study design. The use of TBPIs to complement therapist-delivered psychological interventions (DeMarce et al., 2008; Eack et al., 2016; Eack et al., 2015; Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010) limits the ability to distinguish the effects of the TBPIs from the global effect of combined interventions on cannabis use. The minimal effect of the interventions could be explained by insufficient power to detect significant effects on all outcomes under scrutiny (e.g., mental health related, program participation rate), of which cannabis use was analysed as a secondary outcome. On the whole, the studies in our review did not limit psychiatric diagnoses to psychosis; poly-substance abuse was frequent among participants, and the psychiatric services (e.g., type of service, intensity) offered as part of TAU were difficult to

compare between the included studies. Taken together, these factors impeded our ability to provide reliable conclusions with regard to our second research question.

Accounting for patients' treatment preferences can have positive impacts on treatment adherence, relapse reduction, and clinical outcomes (McKay, 2009). To address our third research question, we described the value of using a participatory action research approach and qualitative methods in identifying treatment facilitators (e.g., patients' social support, providing information on negative aspects of cannabis use, facilitating insight, maintaining motivation for decreasing cannabis consumption) and tailoring new interventions accordingly to minimize participant attrition and to maximize the effect of the intervention on cannabis use (Johnson et al., 2019; Nagel et al., 2009; Nagel et al., 2008; Nagel and Thompson, 2010; Sheridan Rains et al., 2019). Although recent studies of internet-based TBPIs were effective in decreasing cannabis use in patients without psychosis (Cote et al., 2018; Rooke et al., 2013; Schaub et al., 2015), none of the studies in our review used web-based platforms. Implementation of face-to-face psychological interventions in Canada tend to be suboptimal, due to heterogeneity in health care resources and difficulties in sustaining adequate training among clinicians (Aydin et al., 2016). We believe that the addition of internet-based psychological interventions to existing services can help increasing patients' accessibility to treatment without significantly increasing healthcare costs. Future research is needed to validate Milward et al.'s (2018) findings regarding factors that help increase participants' use of online substance use interventions (e.g., tailoring, delivery strategies, incentives, reminders, and social support) in individuals with psychosis as a way to develop effective eHealth interventions in this group (Milward et al., 2018). Practice-based suggestions from health care professionals can inform the development of new TBPIs that can be easily integrated with existing mental-health services and that are highly acceptable by stakeholders and patients, as shown by Dugdale et al.(2017) in their study of factors influencing the implementation of *Breaking Free Online* (BFO), a web-based treatment initiative for substance misuse in the United Kingdom (Dugdale et al., 2017).

Research on the effect of TBPIs in treating cannabis misuse in individuals with psychosis is in its early stages, as reflected by the small number of published studies. This is in contrast with the abundance of research assessing the efficacy of TBPIs and face-to-face psychotherapeutic interventions in decreasing cannabis use in adults without psychosis and with psychosis respectively (Cooper et al., 2015; Hjorthoj et al., 2014; Olmos et al., 2018; Tait et al., 2013). It is worth noting that, in addition to the small total sample of participants (N = 781), our review identified a limited number of types of therapies used in existing studies. Compelling evidence exists that CBT is effective in decreasing cannabis use in adults with psychosis by improving coping and problem-solving skills and encouraging

replacement of cannabis-related behaviors with healthier alternatives (Cooper et al., 2015; Hjorthoj et al., 2014). However, none of the included studies used a technology-based CBT approach. Our review shows that the efficacy of CM, in combination with computer-based psycho-education (offered as part of services for early psychosis), was comparable to that of comprehensive treatment alone in reducing cannabis use. In contrast, in non-psychotic individuals with problematic cannabis use (including CUD), Gates et al., (2016) found in their Cochrane systematic review that adding CM (e.g., vouchers contingent to submission of cannabis-free urine specimens) to a combination of CBT with MET was effective in decreasing the frequency of cannabis use (Gates et al., 2016). Consequently, future research is needed to examine the potential effects of adding a motivational approach (CM or other reinforcement approaches (DeMarce et al., 2008)) to established psychological interventions (CBT, MET) on improving cannabis-related treatment outcomes in individuals with psychosis and CUD.

Our review is not without limitations. We did not search the gray literature for relevant references and excluded dissertations and conference abstracts during the screening process. We did, however, consult with experts to identify relevant references and diligently screened the list of references of published articles for any other publications we may have missed in our search. Studies reporting on interventions delivered through conventional telephone calls were excluded as our aim was to focus on interventions delivered through newer technologies (e.g., internet-based) as reflected by the emergent eHealth concept; more research is needed to replicate positive results of traditional telephone follow-ups on addressing cannabis misuse (Edwards et al., 2006; Wenzel et al., 2015) by using up-to date and more diverse communication methods. Our results have limited generalizability due to characteristics of the participants included in our review. Notably, approximately 10% of the total number of participants were not diagnosed with psychosis and were misusing other substances beyond cannabis (e.g., alcohol, cocaine, opiates); these participant characteristics may have confounded the efficacy of the interventions. Additionally, there was a wide age range and variable duration of psychotic illness among the participants, so that we were unable to make inferences regarding the types of TBPIs that are the most efficient in decreasing cannabis use in specific subgroups, such as young adults with first episode psychosis.

5. Conclusion

This systematic review shows that research related to technology-based psychological interventions in individuals with psychosis and cannabis misuse is in its early stages. As it stands, RCTs on larger and well-defined samples are needed to provide generalizable results for specific at-risk

subgroups, such as young adults with psychosis and CUD. To maximize the impact of e-Health interventions on cannabis use outcomes for individuals with psychosis, future research should specifically address the optimal platform and media to be used, how intensive TBPIs should be and which combinations of psychological interventions (e.g., CBT, MET, CM) are most effective. Finally, to ensure an optimal acceptability and adherence to TBPIs, more research using qualitative methods is needed that would enable the design of TBPIs tailored to the treatment needs and preferences of patients and health care professionals; this could prove to be of utmost importance to better tackle cannabis misuse in people with psychosis.

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Conflicts of interest

The authors declare no conflict of interest.

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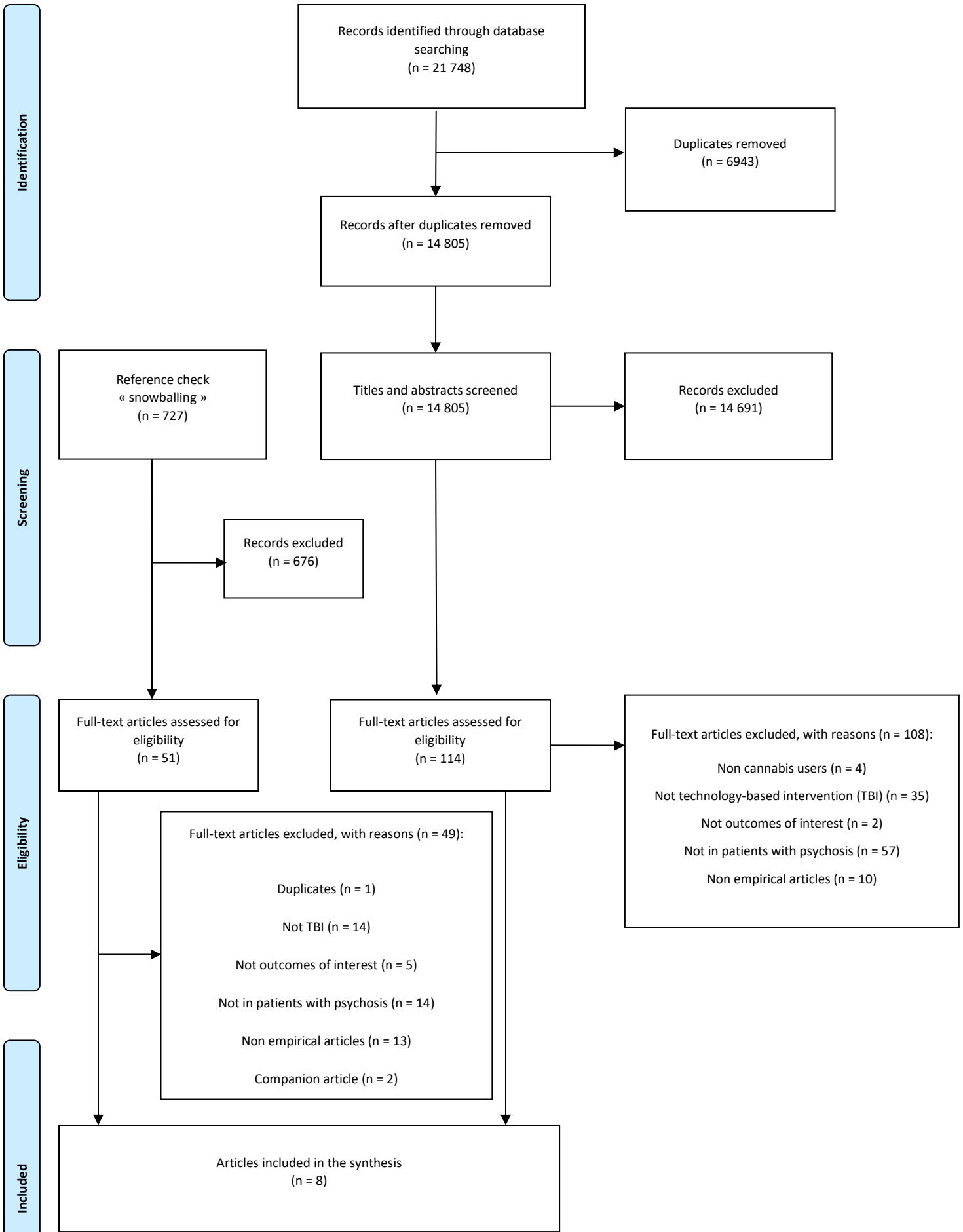


Table 1. Summary of study characteristics and methodological quality appraisal.

First author, country, year	Aim	Study design	Intervention/Control	Psychosis and cannabis misuse at baseline	Cannabis related outcomes	n included in analyses	Data analysis methods	Cannabis related findings	Quality appraisal (MMAT)
Eack et al., United States, 2015	Examine feasibility and efficacy of CET for patients with schizophrenia and comorbid alcohol/cannabis misuse	RCT	CET+TAU: Computer-based cognitive training, structured social-cognitive groups and psycho-education TAU: Psychiatry services, case management, individual therapy, vocational rehabilitation, dual diagnosis and community-driven substance use treatments	Schizophrenia (n=17), schizoaffective disorders (n=14); 74% with cannabis dependence	Abstinence Number of days of substance use	n = 28	Fisher's exact test	Non-significant for cannabis abstinence or number of days of cannabis use in the previous month	4/5 (80%)
Eack et al., United States, 2016	Examine mechanisms of substance use changes by exploring its association with cognitive impairment	RCT	CET+TAU: Computer-based cognitive training, structured social-cognitive groups and psycho-education TAU: Psychiatry services, case management, individual therapy, vocational rehabilitation, dual diagnosis and community-driven substance use treatments		Likelihood of cannabis use Acceleration of reduction of cannabis use Effect of cognitive remediation on cannabis use	n = 28	Individual growth curve modeling Generalized mixed effects models	No effect of the intervention on the likelihood or on the acceleration of cannabis use Improved problem-solving ($B = -0.01$, OR = 0.87, 95% CI = [-0.03, -0.00]; $p < 0.05$) and visual learning ($B = -0.14$, OR = 0.25, 95% CI = [-0.16, -0.12]; $p < 0.01$) significantly associated with decreased odds of cannabis use	
DeMarce et al., United States, 2008	Explore whether co-occurring psychiatric status moderates the efficacy of CPR	RCT	CPR+TAU: Behavioural continuing care contract,	Schizophrenia (n=14), bipolar disorder (n=9); 66% had SUD (not limited to cannabis)	Abstinence	n = 77	2 x 2 chi-square tests	TAU abstinence rates statistically not inferior from CPR (3 and 6 months) Higher abstinence in the CPR group at 12	3/5 (60%)

First author, country, year	Aim	Study design	Intervention/Control	Psychosis and cannabis misuse at baseline	Cannabis related outcomes	n included in analyses	Data analysis methods	Cannabis related findings	Quality appraisal (MMAT)
			attendance prompts and social reinforcement TAU: Individual/group aftercare therapy meetings (and motivational videotape only for the TAU group)					months (STX: 21.2%, CPR: 50.0%; p = 0.01)	
Nagel et al., Australia, 2008	Develop and evaluate a culturally adapted brief motivational intervention for Indigenous people with chronic mental illness	Mixed methods (baseline findings reported)	MCP+TAU: Treatment sessions integrating problem-solving, motivational therapy and self-management principles and brief psycho-educational videos TAU: Assessment, review, supportive counselling and medication	Schizophrenia (n=18), bipolar disorder (n=3), schizoaffective disorder (n=1); 65% cannabis misuse and 47% cannabis and alcohol misuse	Baseline cannabis dependence Worries Goals for change	n=49	Descriptive statistics	82% used cannabis and/or alcohol and 92% were dependent on the substance of abuse ~60% were worried about their cannabis and or alcohol consumption and ~70% about family divergences. Most frequent goal for change was related to alcohol and/or cannabis consumption (~30%) Substance misuse in patients' (as reported by AMHWs): 41%	4/5 (80%)
Nagel et al., Australia, 2009	Develop and evaluate a culturally adapted brief motivational intervention for Indigenous people with chronic mental illness	Mixed methods (mainly QUAN results reported)	MCP+TAU: Treatment sessions integrating problem-solving, motivational therapy and self-management principles and brief psycho-educational videos TAU: Assessment, review, supportive counselling and medication		Phase 1(QUAL): Local AMHW's perspectives on mental health Phase 2 (QUAN: cannabis dependence+QUAL)	Phase 1: n = 11 Phase 2: n = 49	Phase 1: Thematic analysis Phase 2: Mixed model regression analysis	Details in Nagel 2010 Borderline statistically significant advantage of the MCP in terms of cannabis dependence which	

First author, country, year	Aim	Study design	Intervention/Control	Psychosis and cannabis misuse at baseline	Cannabis related outcomes	n included in analyses	Data analysis methods	Cannabis related findings	Quality appraisal (MMAT)
								was sustained over time (Coefficient = -0.98, 95% CI = [-2.02, 0.057]; p = 0.064)	
Nagel et al., Australia, 2010	Develop and evaluate a culturally adapted brief motivational intervention for Indigenous people with chronic mental illness	Mixed methods (mainly QUAL results reported)	MCP+TAU: Treatment sessions integrating problem-solving, motivational therapy and self-management principles and brief psycho-educational videos TAU: Assessment, review, supportive counselling and medication		Phase 1(QUAL): Local AMHWs perspectives on mental health Phase 2 (QUAN+QUAL): progress of achieving goals, strategies of change, patients' cannabis use at home	Phase 1: n = 11 Phase 2: n = 60 (49 patients+11 AMHWs)	Phase 1: Thematic analysis Phase 2: content analysis of concurrent qualitative data collection	Three key themes identified by AMHWs: importance of family, strength gained from traditional and cultural activities, and importance of a story-telling approach to sharing information Progress towards achieving goals (patients): 29% extremely "good", 40% "some", 29% "a little" and 2% "not at all" Strategies for change (patients): communicating with family/resolving disagreements related to cannabis (~27%) or avoiding family contact (~15%) Substance misuse in patients' (as reported by AMHWs) at 18 months: 16%	
Johnson S, Rains LS, et al., United	Assess the efficacy of Contingency Management in decreasing	Mixed methods	CM+TAU: Contingency management consisting in vouchers for	Schizophrenia or schizoaffective disorder (n=170), bipolar affective	Frequency of cannabis use and cannabis abstinence	551	Logistic regression (cannabis abstinence) and Poisson	Cannabis abstinence at 3 months: OR 0.86, 95% CI: 0.56; 1.34	4/5 (80%)

First author, country, year	Aim	Study design	Intervention/Control	Psychosis and cannabis misuse at baseline	Cannabis related outcomes	n included in analyses	Data analysis methods	Cannabis related findings	Quality appraisal (MMAT)
Kingdom, 2019	cannabis use in young adults with first episode psychosis. (CIRCLE RCT)	(QUAN results)	cannabis abstinent participants TAU: computer-based psychoeducation intervention	disorder (n=45), depression with psychotic symptoms (n=16), other psychosis (n=293); 67% with cannabis dependence			regression (frequency of use)	Cannabis abstinence at 18 months: OR 0.84, 95% CI: 0.49; 1.41 Cannabis-using days at 3 months: (incidence rate ratio (IRR) 0.89, 95% CI: 0.75; 1.04; Cannabis-using days at 18 months: IRR 1.09, 95% CI: 0.88; 1.36	
Johnson S, Rains LS, et al., United Kingdom, 2019	To explore patient and clinician preference for the interventions used in the CIRCLE RCT	Mixed methods (QUAL results)	Semi-structured interviews with patients and focus groups with clinicians		N/A	62	Thematic analysis	Clinicians and patients valued the psychoeducation intervention and considered it an important addition to usual psychiatric services. Clinicians expressed time constraint issues in delivering the intervention. Both clinicians and patients provided comments related to the accuracy and repetitive nature of the information; these aspects were addressed in the main trial	4/5 (80%)

AMHWs: Aboriginal mental health workers; CET: Cognitive enhancement therapy; CPR: Contracting, prompting and reinforcing; IT: Information technology; MCP: Motivational care planning; CM: Contingency Management; RCT: Randomized controlled trial; TAU: Treatment as usual; MMAT: Mixed Methods Appraisal Tool, risk of bias was assessed at study level; QUAN: quantitative methodology; QUAL: qualitative methodology; CIRCLE: Contingency Intervention for Reduction of Cannabis in Early Psychosis

Appendix A. Search strategy for Medline

<u>Database</u>	
Database	Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to February 26, 2019
Interface	OvidSP
Search dates	February 27 th , 2019 and November 27 th , 2019
Filters	-

<u>Syntax</u>	
/	Exact Subject Heading
*/	Focus on Exact Subject Heading
or, and	Boolean operators
adj	The Adjacent operator
*	Truncation
mp	"multi-purpose" includes following fields Abstract (AB), Organism Supplementary Concept Word (OX), Subject Heading Word (HW, Floating Sub-heading Word (FX), Original Title (OT), Synonyms (SY), Keyword Heading Word (KF), Protocol Supplementary Concept Word (PX), Title (TI), Name of Substance Word (NM), Rare Disease Supplementary Concept Word (RX), Unique Identifier (UI)
ti, ab	Title, Abstract
kw	Key words

Search strategy

- 1 Cannabis/ (8193)
- 2 Marijuana Smoking/ or Marijuana Abuse/ or "Marijuana Use"/ (9587)
- 3 Cannabinoids/ (6799)
- 4 Medical Marijuana/ (766)
- 5 Substance-Related Disorders/ (90916)
- 6 Receptors, Cannabinoid/ (2894)
- 7 Dronabinol/ (6606)
- 8 Cannabidiol/ (1254)
- 9 Cannabinol/ (220)
- 10 (cannab* or marijuan* or marihuan* or weed* or pot or hemp or hash* or ganj* or bhang* or dronabinol* or tetrahydrocannabi* or THC).mp. (89134)
- 11 **or/1-10 (170880)**
- 12 "Early Intervention (Education)"/ (2682)
- 13 Early Medical Intervention/ (2431)

- 14 Clinical Trial/ (514779)
- 15 Controlled Clinical Trial/ (92932)
- 16 Clinical Study/ (3126)
- 17 Clinical Trials as Topic/ (186107)
- 18 Pragmatic Clinical Trial/ (979)
- 19 Clinical Protocols/ (26370)
- 20 Controlled Before-After Studies/ (374)
- 21 Clinical Studies as Topic/ (312)
- 22 Randomized Controlled Trial/ (476715)
- 23 Randomized Controlled Trials as Topic/ (121262)
- 24 Double-Blind Method/ (149689)
- 25 Control Groups/ (1610)
- 26 Cross-Over Studies/ (44645)
- 27 Drugs, Investigational/ (5432)
- 28 Evaluation Studies/ (241339)
- 29 Multicenter Study/ (245749)
- 30 Internet/ (67276)
- 31 Computer-Assisted Instruction/ (11383)
- 32 Telemedicine/ (18867)
- 33 (remote consultation* or teleconsultation* or telecommunication* or teleconference* or telehealth or telemedicine or phone* or videoconferencing or telecare* or e-consultation or e consultation* or E-Health or E Health or Tele-assistance* or Tele assistance* or Hotlines or Hotline* or mobile health or long distance supervision* or telerehabilitation* or remote clinician* or remote assessment* or phone* or mobile app* or text-deliver* or text messaging).mp. (93124)
- 34 Remote Consultation/ or Telecommunications/ or Telephone/ or Cell Phone/ or Videoconferencing/ (27930)
- 35 Mobile Applications/ or Text Messaging/ (5812)
- 36 Follow-Up Studies/ (607905)
- 37 Prospective Studies/ (494509)
- 38 ((clinical or controlled before-after or cross-over or evaluation or multicenter or follow-up or prospective) adj stud*).mp. (1776680)
- 39 (intervent* or experimental trial* or clinical trial* or randomized or randomly or investigational drug* or web-based or computer-assisted or technology-based).mp. (2567872)
- 40 (systematic* adj2 (review* or overview* or search* or research*).ti,ab,kw. (164071)
- 41 (meta-analy* or metaanaly* or met analy* or metanaly*).ti,ab,kw. (331)
- 42 "Systematic Review"/ (102136)
- 43 Meta-Analysis/ (97532)
- 44 "Review Literature as Topic"/ (7324)
- 45 Meta-Analysis as Topic/ (16745)
- 46 or/12-45 (4059702)**
- 47 Psychotherapy, Multiple/ or Psychotherapy, Group/ or Psychotherapy, Rational-Emotive/ or Psychotherapy, Brief/ (17116)
- 48 Psychotherapy, Psychodynamic/ (477)
- 49 Psychotherapy/ or "Imagery (Psychotherapy)"/ or Person-Centered Psychotherapy/ (54169)
- 50 Cognitive Behavioral Therapy/ (22863)
- 51 Couples Therapy/ (629)
- 52 Complementary Therapies/ (16321)
- 53 Psychiatric Somatic Therapies/ (128)
- 54 Behavior Therapy/ (26612)
- 55 exp Psychology/ or Therapy, Computer-Assisted/ (71313)
- 56 Therapies, Investigational/ (1523)
- 57 Counseling/ (33811)
- 58 Self-Control/ (1606)
- 59 Feedback, Psychological/ (3240)
- 60 "Reinforcement (Psychology)"/ (16372)
- 61 Biofeedback, Psychology/ (7002)
- 62 Motivational Interviewing/ (1441)
- 63 Avoidance Learning/ (21397)
- 64 (psychotherap* or cognitive therap* or couple* therap* or group treatment* or person-centered therap* or psychiatric somatic therap* or contingency management or behavioral intervention or psychology or

psychol* therap* or psychosocial or counseling or behavioral self-management or self-control or self-help or psychological feedback or reinforcement or biofeedback or supportive expressive therap* or motivational interviewing or approach-avoidance task training).mp. (1364791)

65 "acceptance and commitment therapy".mp. (798)

66 or/47-65 (1416683)

67 Delusions/ (7452)

68 Hallucinations/ (10391)

69 Psychoses, Substance-Induced/ (5156)

70 Antipsychotic Agents/ (51136)

71 Psychotic Disorders/ (43242)

72 Mental Disorders/ (154419)

73 Schizophrenia/ (96111)

74 (delusion* or hallucination* or psychos* or antipsychotic* agent* or mental disorder* or mental illness or affective disorder*).mp. (421456)

75 Anhedonia/ (781)

76 Apathy/ (947)

77 Bipolar disorder/ (38158)

78 Catatonia/ (2357)

79 Affective Disorders,Psychotic/ (2215)

80 Paranoid Disorders/ (4008)

81 (disorgani?ation* or anhedonia or apathy or abulia or abulia or disorgani?ed speech or schizoaffective or cataton* or negative symptom* or positive symptom* or paranoid).mp. (47112)

82 (psychotic adj2 disorder*).mp. (49709)

83 or/67-82 (521526)

84 11 and 46 and 66 and 83 (3925)