Drug and Alcohol Dependence Reports 10 (2024) 100216

Contents lists available at ScienceDirect

Drug and Alcohol Dependence Reports

journal homepage: www.elsevier.com/locate/dadr

Review

A systematic review of evidence on integrated management of psychiatric disorders in youth who use cannabis

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HIGHLIGHTS

- Integrated treatment is recommended for psychiatric disorders and cannabis use.
- Treatment of youth cannabis use and comorbid psychiatric disorders is understudied.
- Fluoxetine and psychotherapy can treat youth with depression and cannabis use.
- Lithium is promising to treat both bipolar disorder symptoms and cannabis use.
- Effective psychotherapies can treat anxiety disorders in youth with cannabis use.

ARTICLE INFO

Keywords:
Cannabis use
Adolescents
Young adults
Comorbidities
Psychiatric disorders
Depression

ABSTRACT

Given the risks to mental health associated with cannabis use in youth and the increase in cannabis legalization worldwide and in the U.S., there is a need to understand existing evidence-based approaches to integrated management of psychiatric disorders in youth who use cannabis. This systematic review aimed to appraise the current evidence on integrated treatment for adolescents and young adults with common psychiatric disorders who engage in regular cannabis use. A total of 989 studies were screened for inclusion. Study's titles and abstracts were screened and advanced to full text review for further screening by two independent reviewers. Thirty-five full-text articles were reviewed, with five articles ultimately meeting all criteria for inclusion. Five randomized controlled trials examined the effects of therapeutic interventions in youth with common psychiatric disorders who used cannabis, including two studies on depression, one on bipolar disorder, one on anxiety and one on PTSD were reviewed. No studies were considered high in risk of bias. Overall, there is a paucity of research on the treatment of comorbid adolescent mental health disorders and cannabis use, which limits the ability to draw evidence-based treatment recommendations.

1. Introduction

Cannabis is the most commonly used illicit drug in the United States (U.S.) and across the globe. In 2021, the prevalence of cannabis use in the past year was 18.7 % among people ages 12 and older (Substance Abuse and Mental Health Services Administration, 2023). Among adolescents, 8.3 % of 8th graders and 30.7 % of 12th graders reported having used cannabis in the past 12 months in 2022 (Miech et al., 2023). While the rates of cannabis use in adolescents aged 12–17 years have remained steady throughout the last two decades, there has been a twofold increase in the percentage of individuals aged 18 and older who engage in cannabis use in the U.S. (National Center for Health Statistics, 2021; Hinckley et al., 2022).

As of 2022, the legalization of medical cannabis had increased globally, with over 40 countries worldwide having legalized medical use of cannabis, and seven having legalized its recreational use (Mollner, 2022). In the U.S., 38 US states and the District of Columbia (D.C.) had commercialized cannabis for medical use (National Conference of State

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https://doi.org/10.1016/j.dadr.2023.100216
Received 12 December 2023; Received in revised form 26 December 2023; Accepted 28 December 2023
Available online 4 January 2024

Legislatures, 2023). The impact of medical and recreational cannabis legalization on adolescent cannabis use remains unclear. A study examining use in the context of legalization changes in the U.S. since the 1950s found increases in cannabis use among youth ages 12 to 25 during periods of progressive cannabis legalization (Yu et al., 2020). Meanwhile, a review of studies found little evidence of increased cannabis consumption in youth with legalization of medical marijuana and equivocal evidence with recreational cannabis legalization (Anderson et al., 2021). Yet, cannabis legalization may impact youth in ways beyond consumption, including acceptability, perceived risk, and exposure (Cerdá et al., 2017). For example, data about intentional misuse and abuse exposures for children and adolescents reported to U. S. poison centers between 2000 and 2020 (n = 338,727) showed a higher average monthly increase of cannabis exposure compared to all other substances, with a steep rise occurring from 2017 to 2020. Furthermore, edible marijuana preparations accounted for the highest increase in call rates compared with all other forms of marijuana (Hughes et al., 2022). Finally, since legalization, there has also been a sharp rise in availability and use of high-potency Δ9-tetra-hydro-cannabinol (THC) products (Sevigny et al., 2014). This is particularly important considering that the high-potency products (often defined as >10 % THC) are associated with the worst mental health outcomes (Petrilli et al., 2022).

Adolescence is also a vulnerable period of ongoing neurodevelopment and coincides with the onset of nearly all problematic cannabis use and mental health disorders (Solmi et al., 2022; Uhlhaas et al., 2023). The endocannabinoid system, the endogenous signaling pathway through which cannabinoids primarily exert their effects, regulates many aspects of neurodevelopment. Expression of cannabinoid receptor 1 (CB1R) in the central nervous system is greatest during adolescence (Gee et al., 2016; Heng et al., 2011; Meyer et al., 2018), with a peak between ages 15 and 17, and later decreases in expression through age 35 (Choi et al., 2012; Long et al., 2012). Youth who use cannabis exhibit white matter changes including more diffuse axonal pathways and decreased myelination, as well as increased impulsivity (Gruber et al., 2014), and executive dysfunction (Hanson et al., 2010; Harvey et al., 2007; Schweinsburg et al., 2007). Adolescents also appear to be more susceptive to the negative cognitive effects of THC, the primary intoxicating cannabinoid (Murray and Srinivasa-Desikan, 2022).

According to recent data from the Centers of Disease and Control Data, the most common mental health presentations among children and adolescents include ADHD, anxiety problems, behavior problems and depression (National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, 2023). Adolescents with mental health disorders may be especially vulnerable to the negative impacts of cannabis use. Cannabis use is more prevalent among youth with mental health disorders than among the general population (Lowe et al., 2019) and may be increasing in this group in part due to lower perceived harm associated with cannabis use (Pacek et al., 2019). Overall, a large body of literature suggests significant associations between frequent cannabis use, cannabis use disorder (CUD), and comorbid psychiatric disorders (Hasin and Walsh, 2020). Additionally, cannabis use in adolescents has been associated with higher risk of depression, anxiety and suicidality in adulthood (Gobbi et al., 2019). Cannabis use is also associated with poor treatment outcomes among youth with comorbid mental health disorders. For example, a recent narrative review found that adolescents with depression and anxiety who used cannabis frequently showed a loss of effectiveness of antidepressants (Hen-Shoval et al., 2022).

Given the biological vulnerabilities and risk of psychiatric comorbidities of this age group, and the risks related to the current social and legal environment, it is important to understand the existing evidence related to the treatment of psychiatric disorders in youth who use cannabis (Bukstein, 2005). Integrated treatment is the approach in treatment of psychiatric and substance use disorders concomitantly, involving screening and treatment by specialists or treatment teams with knowledge about both for mental illness and substance use (Substance Abuse and Mental Health Services Administration., 2009). Current clinical guidance recommends integrated treatment for co-occurring disorders rather than insulated treatments for psychiatric disorders and substance use disorders, as integrated treatment shows improved psycho-social outcomes in adults (Kelly et al., 2012; Kelly and Daley, 2013; Torrens et al., 2012) and in children and adolescents (Bukstein, 2005; Yule and Kelly, 2019). Approaches involving cognitive behavioral and motivational therapies continue to be the generally recommended psychotherapeutic approach (Kazdin, 1995) and while psychopharmacological interventions are often used in psychiatric clinics, it remains unclear the degree to which youth with cannabis use and comorbid mental health disorders benefit from such interventions (Bukstein and Horner, 2010; National Institute on Drug Abuse, 2023).

Our aim in conducting this systematic review was to appraise the current evidence on integrated treatment for adolescents and young adults with common psychiatric presentations among youth (anxiety, depression, bipolar disorder, attention deficit/hyperactivity disorder (ADHD), posttraumatic stress disorder (PTSD), or disruptive behavior disorders) who engage in cannabis use. The purpose of conducting the review was to explore the evidence of integrated treatments for psychiatric disorders in youth who use cannabis, given the legislative and larger societal changing environments.

2. Methods

We conducted a systematic review to assess and synthesize all studies regarding integrated management of common psychiatric disorders and cannabis use. An informationist (J.W.) conducted searches in five databases: MEDLINE ALL via Ovid, Embase.com, CINAHL via Ebsco, PsycINFO via Ebsco, and Web of Science Core Collection. Databases were searched from inception until 10th May 2022. Controlled vocabulary terms were combined with title/abstract terms where applicable, including the Emtree term “Cannabis Addiction,” the Mesh term “Marijuana Abuse” and PsycINFO thesaurus term “Cannabis Use Disorder.” Full search strategies are available in the supplemental material.

Inclusion criteria consisted of 1) study design was a randomized controlled trial (RCT); 2) adolescent population (mean age < 25 years old); 3) primary psychiatric disorder of either anxiety, depression, bipolar disorder, attention deficit/hyperactivity disorder (ADHD), posttraumatic stress disorder (PTSD), or disruptive behavior disorders; 4) comorbid cannabis use; and 5) English language. Of note, the age criteria were determined following the concept of extended adolescence (Patton et al., 2018) with the goal to be inclusive of this neurodevelopmental period, which continues into young adulthood. We excluded studies of youth with a primary psychotic disorder, which is beyond the scope of this review, and studies that reported generally on substance use and not specifically on cannabis use outcomes. Pilot studies were also excluded, but, where applicable, such studies are referenced and described in the findings in order to provide perspective on all the building work conducted in this area.

The initial search yielded 1195 studies, of which 206 were duplicates. After deduplication, 989 studies were screened for inclusion using Covidence. Each study title and abstract were independently screened by two reviewers to advance to full text review. C.V. screened all abstracts, with K.S. or J.H. providing the second screen. Conflicts were resolved by consensus between C.V. and J.H. Thirty-five full-text articles were reviewed, with five articles ultimately meeting all criteria for inclusion in this review (Fig. 1: PRISMA). An assessment of bias was conducted using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (Sterne et al., 2019). Four studies were deemed to be at low risk of bias for all domains. One study was low risk of bias for all domains but two, in which there were some concerns about bias arising from the randomization process and bias in selection of the reported result. No studies were considered high in risk of bias overall. Fig. 2 visualizes the Risk of Bias Assessment (McGuinness and Higgins, 2021).

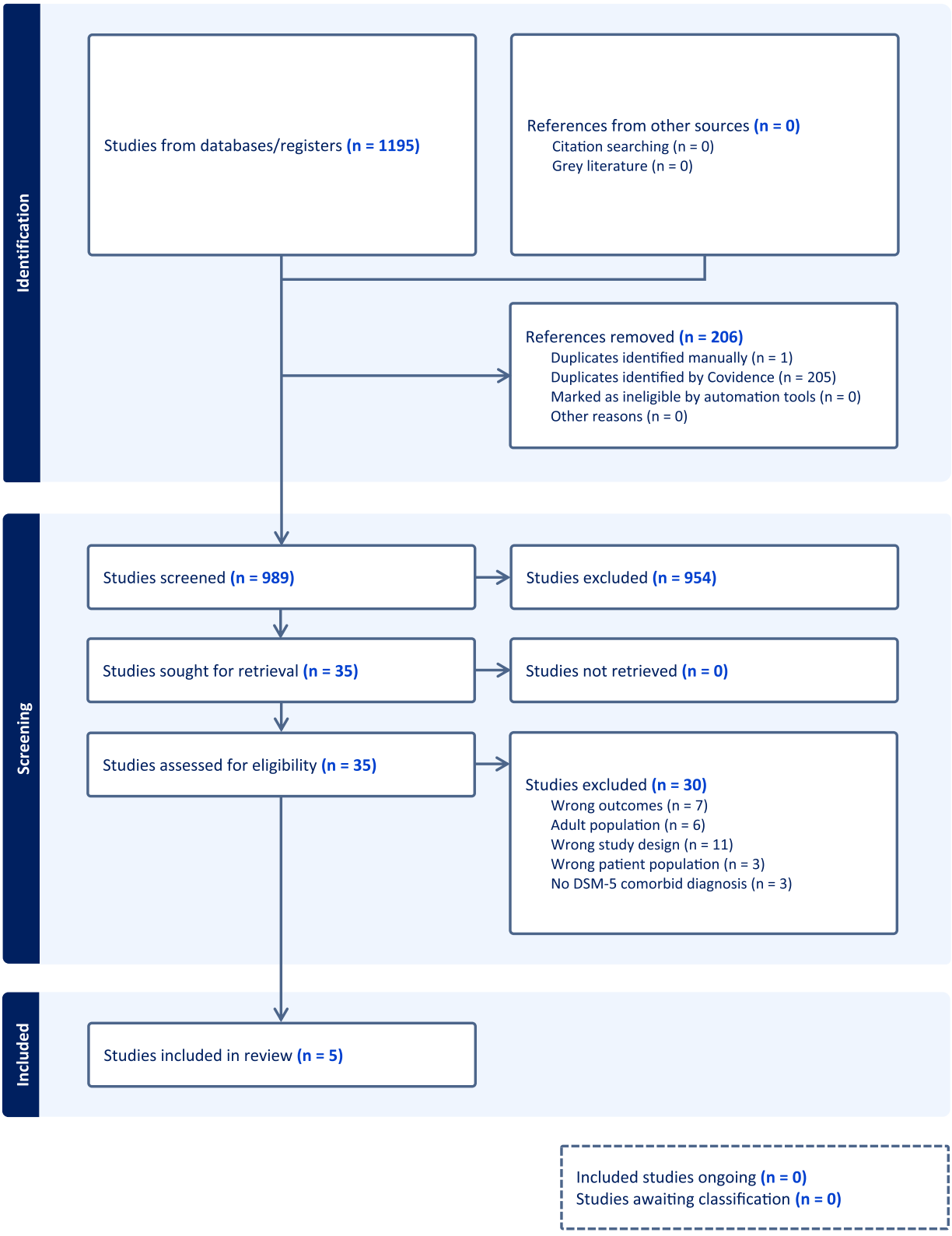

Fig. 1. PRISMA: Integrated Management of Cannabis Use and Common Mental Health Disorders.

3. Findings

3.1. Studies meeting inclusion criteria

Our search terms yielded five RCTs examining the effects of therapeutic interventions in youth with common psychiatric disorders who used cannabis, including two studies on depression, one on bipolar disorder, one on anxiety and one on PTSD. Details including study population, inclusion criteria and main findings are described in Table 1. The total number of participants included in these studies was 369. Study sample sizes ranged from 25 to 124 participants. Four RCTs examined treatments targeting specifically a population of adolescents

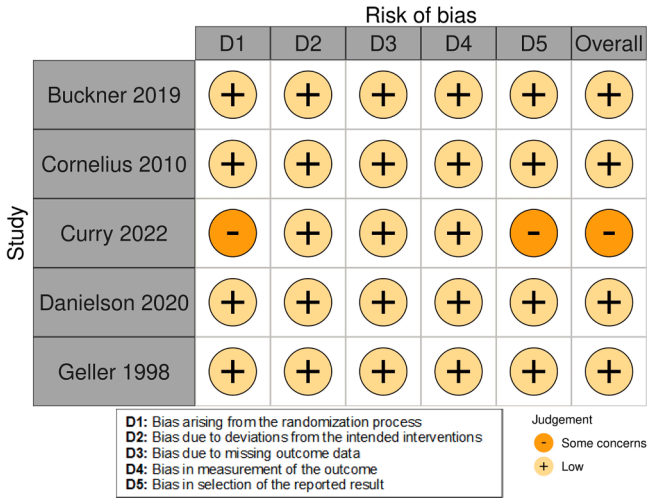

Fig. 2. Risk of Bias Assessment.

and/or young adults below 25 years of age, whereas one study included adult participants with the overall mean age below 25 years old. All of the studies included male and female participants, with a range of female participation between 33 and 87 % across studies. Of the five studies selected for extraction, three examined psychotherapeutic interventions and two focused on psychopharmacological interventions. All studies included other substance use and specific data on cannabis use. We report exclusively on cannabis use outcomes given the focus of this review.

Cornelius et al. (2010) conducted an RTC comparing the efficacy of fluoxetine versus placebo in youth with major depressive disorder (MDD) and comorbid CUD. All participants received motivational enhancement therapy (MET), an intervention that has demonstrated to reduce cannabis use in the Cannabis Youth Treatment Study (Dennis et al., 2004), combined with CBT (MET/CBT) as background treatment. Both the fluoxetine and placebo groups showed within-group improvement in depressive symptoms and number of Diagnostic Statistical Manual-IV (DSM-IV) criteria for CUD, although the reduction of depressive symptoms was greater than the reduction of cannabis use in both groups by 50 %. There were no differences in the improvement of depression symptoms between treatment groups. The authors suggested that these findings may reflect limited medication efficacy, inadequate power to detect a significant difference, or the effectiveness of the background MET/CBT treatment.

Curry et al. (2022) tested the efficacy of supplemental CBT targeting depression (CBT-D) in adolescents who did not achieve early depression remission (EDR) after receiving CBT/MET treatment for substance use (Sampl and Kadden, 2001; Webb et al., 2002). Out of the initial 87 participants receiving MET/CBT, 35 adolescents achieved EDR with MET/CBT only. These early remitters demonstrated a more rapid decline in cannabis use, as well as lower rates of cannabis use and higher rates of abstinence throughout the study. These participants were also more likely to present lower severity of depression throughout treatment. The 52 adolescents who did not achieve EDR were randomized to CBT-D or to enhanced treatment as usual in the community. Enhanced treatment as usual consisted of assisting the adolescent and parent in identifying and connecting with preferred treatment providers as in Esposito et al. (2011), but without a psychiatrist. Adding CBT-D for depression in the non-remitters did not improve outcomes more than enhanced treatment as usual did. All groups had a decline in cannabis use. While CBT-D did not provide benefit over community depression treatment, these findings suggest there is an association between improvement in depression symptoms and reduction in cannabis use.

Geller and colleagues (1998) conducted an RCT with adolescents with bipolar disorder type I or type II, mania or MDD with at least an adolescent predictor of developing bipolar disorder and comorbid dependence (N = 25) to alcohol and other substances including cannabis. Participants were assigned to lithium or placebo. Lithium was pharmacokinetically dosed to a blood level between 0.9 and 1.3 mEq/L, with a maximum daily dose of lithium of 2400 mg. Lithium treatment of adolescents with bipolar disorder and substance dependence was efficacious for both bipolar disorder, with a 60 % response rate for the treatment group compared to a 9.1 % response rate for the placebo group, and a decrease in substance use as measured by positive random drug screens after 3 weeks.

Buckner and colleagues (2019) tested the utility of MET/CBT compared to integrated cannabis and anxiety reduction treatment (ICART) for anxiety and substance use. While participants were older than 18 years, this study was included because the mean age was lower than 25 years. Both treatments appeared to reduce cannabis use as measured with urinalysis and self-reported number of past-month joints to a similar degree, but ICART was associated with greater abstinence from cannabis than MET/CBT, a gold standard psychosocial treatment for CUD. Although both treatments reduced anxiety reliably, the ICART condition reduced it to a greater degree relative to MET/CBT. Patients in the ICART condition attended more treatment sessions and were more likely to be abstinent post-treatment than those in the MET/CBT condition. Further, treatment decreased cannabis use and related problems. The results of this study suggest that ICART may be at least as efficacious as MET/CBT for a difficult-to-treat subpopulation of individuals who misuse cannabis.

Danielson and colleagues (2020) examined whether risk reduction through family therapy (RRFT) resulted in improved outcomes relative to a treatment-as-usual control condition in adolescents with a history of interpersonal violence experiences and at least 5 PTSD symptoms as reported on the UCLA PTSD Reaction Index and at least one non-tobacco substance–using day in the past 90 days. RRFT is an exposure-based, integrative intervention for adolescents with substance use problems and PTSD symptoms. The treatment-as-usual condition was trauma-focused cognitive behavioral therapy (TF-CBT). Both TF-CBT and RRFT groups had significant reductions in cannabis use days and PTSD symptoms, with no observed differences between the groups. Of note, the decrease in days of cannabis use from baseline was higher in the RRFT group compared to the TF-CBT group, with a decline in cannabis use 82 % greater in month 6, 90 % at month 12, and 96 % at month 18 in the RRFT compared to the TF-CBT group.

3.2. *Valuable studies not meeting inclusion criteria*

While other studies have been conducted in this area, many were underpowered, did not provide specific information related to cannabis use, focused on non-clinical populations, or were follow up studies of an RCT. Existing research that did not meet inclusion criteria but should be highlighted includes several psychopharmacological studies to treat depressive symptoms in youth with comorbid cannabis use. An open label study of fluoxetine in adolescents with comorbid conduct disorder found reductions in depressive symptoms and substance use, suggesting fluoxetine could be effective to treat depression in this population (Riggs et al., 1997). A later RCT by the same group (Riggs et al., 2007) recruited adolescents with MDD, lifetime conduct disorder and at least one non-tobacco substance use disorders and randomized them to CBT plus fluoxetine or CBT plus placebo. The findings demonstrated greater efficacy of the fluoxetine group over the placebo group on one of two depression measures. There were no significant between-group differences in self-reported substance use symptoms. As this study did not separate findings on cannabis use from other substances, it was not included.

A pilot RCT by Findling et al. (2009) did not find fluoxetine to be superior to placebo in the short-term treatment of depression in adolescents with concomitant substance use disorder, nor was there a decrease in substance use compared to placebo. However, this study did

Table 1
Studies reviewed: type of intervention, population studied, study's inclusion criteria and main findings.

Lead Author (Year)	Intervention & DURATION	Participants [N, Mean Age (SD), Age Range (years) Sex (m/F)]	Axis I Comorbid Dx	Inclusion Criteria	Main Measures	Primary Outcomes for SU and MH	Conclusions
Cornelius 2010	Fluoxetine (12 weeks)	$N = 70$ Age 21.1 (2.4) (14–25) M/$F = 43/27$	Depression	Comorbid CUD and MDD Current CU (use $\leq$ 30 days) Depressive symptoms HAM-d-27 $\geq$ 15 at baseline.	BDI HAM-D27 DSM TLFB	Fluoxetine and placebo were equally efficacious for treating cannabis-related and depressive symptoms, but significant within-group improvement across both treatment groups in number of DSM CUD criteria and depressive symptoms.	End-of-study levels of depressive symptoms were low in both treatment groups. Fluoxetine and placebo were equally efficacious for treating depressive and cannabis-related symptoms.
Curry 2022	CBT-D (14 weeks)	$N = 95$ Age 17.4 (1.8) (14–21) M/$F = 64/31$	Depression	Ages 13 to 21 DSM-IV-TR diagnosis of current alcohol or cannabis abuse or CU or CD or potentially harmful drinking ($\geq$ 4 drinks for male or 3 for female adolescents daily) $\geq$ 3 times in the past 90 days Clinically significant depression on an interview rating scale.	CDRS-R ACQ DC	Days of CU decreased in all groups, but EDR adolescents showed the most rapid reduction and maintained a low level of CU. Supplemental CBT-D was not superior to community depression treatment. Fewer days of CU and absence of conduct disorder predicted EDR.	Depression significantly decreased over time in both groups ($p < .001$), with no advantage for CBT-D.
Geller 1998	Lithium (6 weeks)	$N = 25$ Age 16.3 (1.2) (12 −18) M/$F = 16/9$	Bipolar disorder	Age 12 to 18 years DSM-III-R SDD DSM-III-R BP (BP-I, BP-Il, mania, or MDD with $\geq$1 adolescent predictors of future BP).† Duration of illness (comorbid BP and SUD) for $\geq$ 2 months. BP preceded SDD by $\geq$ 2 weeks or present for $\geq$2 weeks when no drug/alcohol dependency or use. Subjects in good physical health.	K-SADS-1986-Present Episode K-SADS-Lifetime CGAS DSM-I1/-R Disorders Adolescent Diagnostic Interview FH-RDC PSSAC-R	Lithium treatment of BP with secondary SDD in adolescents was an efficacious treatment for both disorders.	These results warrant replication with a long-term maintenance phase. The mean 6-year interval between the onset of BP and onset of SOD strongly argues for earliest recognition of BP.
Buckner 2019	ICART vs MET-CBT alone (12 weeks)	$N = 55$ Age 23.1 (7.4) (18–65) M/$F = 31/24$	Anxiety	Ages 18–65 years Current CU (UTS $\geq$ 50 ng/ml cutoff) DSM-5 criteria for both CUD and an anxiety disorder CU in the past week to manage anxiety	ADIS-IV SCID SIGH-A TLFB MPS	Both treatments reduced CU and anxiety, but ICART had greater CU abstinence, decreases in anxiety, better attendance to treatment sessions and more abstinence post-treatment than MET-CBT. Anxiety reliably decreased over time in both the control and active groups.	ICART may be at least as efficacious as MET-CBT, for difficult-to-treat adolescents with CU.
Danielson 2020	RRFT (18 months)	$N = 124$ Age 15.4 (1.3) (13–18) M/$F = 16/108$	PTSD	Ages 13 to 18 years Experienced IPV$^{\text{C}} \geq 1$ nontobacco SU-day in the past 90 days $\geq$ 5 PTSD symptoms on the UCLA-PTSD-RI.	TLFB UCLA- PTSD-RI for DSM-IV	Significant reductions in PTSD symptoms were observed within groups for RRFT and for TAU but no between-group differences were observed.	These results suggest that this exposure-based treatment is safe, feasibly delivered by community-based clinicians, and offers an effective approach to inform clinical practice.

ACQ= Alcohol Consumption Questionnaire; ADIS-IV = Anxiety Disorders Interview Schedule for DSM-IV; BDI = Beck Depression Inventory; BP= bipolar disorder; BP-*I*=Bipolar I disorder; BP-II=bipolar II disorder; CBT-*D* = Supplemental CBT targeting depression; CD= Cannabis Dependence; CDRS-*R* = The Children's Depression Rating Scale –Revised; CGAS= Children's Global Assessment Scale; C-SSRS= Columbia Suicide Severity Rating Scale; CU= Cannabis use; CUD= cannabis use disorder; DC= Drug Checklist; DSM= Diagnostic and Statistical Manual; DSM-III-*R*= Diagnostic and Statistical Manual of Mental Disorders, 3rd edition- revised; DSM-IV-TR= Diagnostic and Statistical Manual, 4th ed., Text Review; EDR = Early Depression Response; *F*= Female; FH-RDC = Family History Research Diagnostic Criteria; HAM-D27 = Hamilton Depression Rating Scale, 27-item version; ICART = Integrated Cannabis and Anxiety Reduction Treatment; IPV= interpersonal violence; I-CBT = Integrated outpatient cognitive behavioral intervention; PSSAC-*R* = Psychosocial Schedule for School Age Children-Revised; K-SADS-1986-Present Episode version; K-SADS-Lifetime version; *M*= Male; MDD = Major Depressive Disorder; MET-CBT= Motivation enhancement therapy combined with cognitive behavioral therapy; MPS = Marijuana Problems Scale; PTSD= Posttraumatic stress disorder; RRFT = Risk reduction through family therapy; SCID = Structured Clinical Interview for DSM-IV-TR Axis I disorders; SDD= substance dependency disorders; SIGH-*A* = Structured Interview Guide for the Hamilton Anxiety Scale; SUD= Substance Dependency Disorders; TAU = Treatment as Usual; TLFB=Timeline Follow Back; UCLA= University of California, Los Angeles; UCLA-PTSD-RI= University of California, Los Angeles PTSD Reaction Index for DSM-IV. UTS= urine toxicology screens.

† These predictors were delusions, switching to BP during tricyclic antidepressant treatment, marked psychomotor retardation, and BP in a first-degree relative (Strober and Carlson, 1982).

*family history of a first or second degree relative with bipolar disorder, marked psychomotor retardation, a history of switching to mania with tricyclic antidepressant

treatment, delusions, or a family history of loaded or multigenerational affective disorders (Strober and Carlson, 1982; Akiskal et al., 1983. 1985).
± Group-based, gender-responsive, trauma-informed SU intervention for justice-involved girls.
€ Child sexual abuse, physical abuse, physical assault, threat with a weapon, and/or witnessing violence.

not have adequate power to detect a significant difference (Findling et al., 2009). Finally, Tomko et al. (2018) evaluated n-acetylcysteine (NAC) to reduce depressive symptom severity in adolescents seeking treatment for CUD. The study found no differences in cannabis abstinence or depressive symptom severity with NAC. However, this study used secondary data of an RCT designed to treat cannabis cessation with NAC and only examined the role of depression as a moderator of the cessation effect of NAC.

One study tested an integrated outpatient CBT intervention for co-occurring alcohol or other drug use disorder and suicidality (I-CBT) in adolescents recruited from an inpatient psychiatric hospital study. There was a reduction in the number of cannabis use days in the I-CBT group compared to enhanced treatment-as-usual (Esposito-Smythers et al., 2011). Enhanced treatment involved provision of a diagnostic evaluation report, medication management by and availability of the study psychiatrist, and a number to call with resources for families. Youth in the I-CBT group reported less global impairment, fewer suicide attempts, psychiatric hospitalizations, emergency department visits, and arrests than those in the enhanced treatment as usual condition. However, suicidal ideation and depressed mood improved in both groups with no significant differences between the treatment groups.

Several follow-up studies exploring long-term treatment outcomes are also worth mentioning. A follow up study from the trial by Cornelius et al. (2010) included in this review examined outcomes at one-year follow-up and found no greater efficacy of fluoxetine over placebo for treating either the depressive symptoms or cannabis use-related symptoms. While there was a decrease in depressive symptoms and days of cannabis use in the initial phase of the study that persisted at 1-year follow up, no further change was observed beyond the 12-week phase (Cornelius et al., 2012). Cornelius et al. (2005) had also conducted a pilot naturalistic study with adolescents with depression and a comorbid substance use diagnosis, whom they followed for 5 years. The study targeted adolescents with alcohol use disorders, but data on cannabis use was also available. The long-term (5-year) clinical course for alcohol and cannabis use disorders and academic functioning of adolescents with comorbidities following acute treatment with fluoxetine was generally good, and better than typically seen in adults. In contrast, the course of the MDD was at least as bad among the comorbid adolescents as is typically seen among comorbid adults (Birmaher et al., 2002). However, the sample was small with only 13 patients of which only 10 used cannabis (Cornelius et al., 2005). The authors suspect that factors other than the treatment in the acute phase were playing a role.

There were several limitations of the existing literature overall. Studies included mostly small sample sizes with inadequate power to detect significant differences. Inclusion criteria tended to be broad across studies and require symptoms, rather than a valid diagnostic construct (i.e., cannabis use rather than CUD, anxiety rather than specific subtypes of anxiety). Of note, most studies compared an experimental intervention to a standard of care intervention, most typically MET/CBT, which has consistently been shown to be effective in addressing CUD and some comorbid psychiatric disorders.

4. Discussion

This systematic review of evidence on integrated management of psychiatric disorders in youth who use cannabis yielded five studies that were included for review. The included studies had an overall good quality with minimal risk of bias. All studies focused on short-term treatment outcomes and primarily on psychotherapeutic interventions. Overall, there is a paucity of research on comorbid adolescent psychiatric disorders and cannabis use, which limits the ability to draw evidence-based treatment recommendations. The research reviewed showed no added benefit with the addition of fluoxetine to MET/CBT for depression, or enhanced CBT therapy for non-early remitters of depression. Lithium showed promise for the treatment of both bipolar disorder symptoms and cannabis use. ICART showed benefits over MET/CBT for a specific subgroup of youth with both anxiety and substance use. And finally, RRFT was as helpful as TF-CBT in the treatment of PTSD symptoms for youth with comorbid cannabis use.

The study of fluoxetine by Curry et al. (2022), 40 % of participants had early remission of depressive symptoms with MET/CBT, which is slightly higher than (Riggs et al., 2007) or similar to Arias et al. (2020) the rates of remission in other studies. The high remission rate of this background treatment suggests that substance use-focused therapy may be adequate to treat many youth with depression and comorbid cannabis use and highlights the importance of attending to cannabis use when treating depression in adolescents. Based on these studies, there is evidence suggesting a greater therapeutic effect of psychotherapeutic interventions, a need to focus on substance use when treating depression in youth, limited evidence on the effects of pharmacotherapy for comorbid populations in the short-term, and no strong evidence of long-term outcomes.

This review of the literature presents several limitations. The review may have been too focused. While there are many effective universal interventions conducted in community and school settings to prevent mental health and substance use interventions, our focus was on clinical populations with the goal of providing a better understanding of the evidence related to mental health disorders in youth who also use cannabis. While our search for articles was comprehensive, it is possible that some biased may have been introduced in the selection of articles due to the 3 authors selecting the articles being physicians specializing in child and adolescent psychiatry. The study does not include psychotic disorders given that there is already extensive literature and a good understanding of the topic. Instead, this review was focused on what the CDC considers the most common mental health disorders presented in youth. Finally, in our effort to include RCT, we may have excluded valid and informative studies in the area. We have attempted to reference some of these studies in the discussion and be as comprehensive as possible. Finally, this review is limited in time by the last date of the search. Future reviews may update the findings of this review as more information and new studies are published (Grant and Booth, 2009).

More research is needed to determine the most effective integrated treatment management of comorbid psychiatric disorders and cannabis use in youth. Future studies should test effectiveness of interventions in the clinical setting in addition to expanding efficacy studies. We encourage the use of validated diagnostic constructs to guide treatment in clinical populations. We also recommend reporting on cannabis and other specific substance use separately. In addition, application of these treatments in other parts of the world and cultural considerations should be explored.

The significant lack of guidance when a patient comes with a psychiatric disorder and comorbid cannabis use can be disconcerting for the clinician treating youth. This is of concern given prevalence of cannabis use in this population and the ongoing changes with legalization. Ultimately, the findings of this study suggest that integrated treatment of comorbid psychiatric disorders and cannabis use is important to overall improvement of both conditions. Based on existing evidence, we recommend the use of integrated treatment for youth with depression, anxiety, and PTSD who use cannabis. Evidence suggests that psychotherapy with the addition of medications in youth with more severe psychopathology or who do not improve with psycho-therapeutic interventions alone is an evidence-supported approach. Clinicians should monitor outcomes of both the psychiatric disorder and substance use to guide ongoing treatment.

5. Conclusions

In conclusion, there is an overall lack of evidence in integrated treatments for psychiatric disorders and comorbid cannabis use in children, adolescents and young adults. With changes in cannabis legalization, it is important to understand how cannabis use affects comorbid mental health and to identify the most effective treatments for these comorbid disorders.

Funding

Dr. Vidal, Dr. Simon, and Dr. Hinckley receive support from the K12 American Academy of Child and Adolescent Psychiatry Physician Scientist Program in Substance Use Career Development Award (K12DA000357).

CRediT authorship contribution statement

Carol Vidal: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Software, Visualization, Supervision, Writing – review & editing, Writing – original draft. **Kevin M Simon:** Conceptualization, Data curation, Funding acquisition, Writing – review & editing. **Caroline Brooks:** Data curation, Validation, Writing – review & editing. **Jacob White:** Data curation, Methodology, Writing – original draft, Writing – review & editing. **Jesse D Hinckley:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

All other authors declare that they have no conflicts of interest.

Acknowledgment

This research has received no external funding, and the authors have no disclosures.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dadr.2023.100216.

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