Treatment of Cannabis Use Among People With Psychotic or Depressive Disorders: A Systematic Review

Amanda L. Baker, PhD; Leanne Hides, PhD (Clin); and Dan I. Lubman, PhD

Objective: This article systematically reviews the evidence from randomized controlled trials (RCTs) for pharmacologic and psychological approaches to the treatment of cannabis use among individuals with psychotic or depressive disorders.

Data Sources: A systematic literature search was conducted using the PubMed and PsychINFO databases from inception to December 2008. Individual searches in cannabis use (search terms: *marijuana*, *cannabis*, *marijuana abuse*, *cannabis abuse*, *marijuana usage*, *cannabis usage*), mental disorders (search terms: *mood disorders*, *affective disorders*, *anxiety disorders*, *anxiety*, *depressive disorder*, *depression*, *psychotic disorders*, *psychosis*, *mental disorders*), and pharmacotherapy (search terms: *medication*, *drug therapy*, *pharmacotherapy*, *psychopharmacology*, *clinical trials*, *drug trial*, *treatment trial*) were conducted and limited to humans, adolescents and adults.

Study Selection: A search combining the individual cannabis use, mental disorder and pharmacotherapy searches produced 1,713 articles (PubMed = 1,398; PsychINFO = 315). Combining the cannabis use and mental disorder searches while limiting them to English articles and RCTs produced a total of 286 articles (PubMed = 228; PsychINFO = 58). From this literature, there were 7 RCTs conducted among mental health clients that reported cannabis use outcomes using pharmacologic or psychological interventions.

Data Synthesis: While few RCTs have been conducted, there is evidence that pharmacologic and psychological interventions are effective for reducing cannabis use in the short-term among people with psychotic disorders or depression.

Conclusions: Although it is difficult to make evidence-based treatment recommendations due to the paucity of research in this area, available studies indicate that effectively treating the mental health disorder with standard pharmacotherapy may be associated with a reduction in cannabis use and that longer or more intensive psychological interventions rather than brief interventions may be required, particularly among heavier users of cannabis and those with more chronic mental disorders. Specific recommendations regarding the type and length of specific psychological treatments cannot be made at this time, although motivational interviewing and cognitive-behavioral therapy approaches appear most promising.

J Clin Psychiatry 2010;71(3):247–254

Submitted: *February 10, 2009; accepted June 9, 2009 (doi:10.4088/JCP.09r05119gry).*

Corresponding author: *Dr Amanda L. Baker, PhD, Centre for Brain and Mental Health Research, University of Newcastle, University Dr, Callaghan, NSW 2308, Australia (Amanda.Baker@newcastle.edu.au).*

Epidemiologic studies consistently demonstrate high rates of cannabis use among individuals with mental disorders.[1–4] The United States National Epidemiologic Survey on Alcohol and Related Conditions found that individuals with cannabis dependence were 6 times more likely to have a comorbid mood or anxiety disorder than those without cannabis dependence.[5] Similarly, the Australian National Survey of Mental Health and Well-Being found that cannabis dependent individuals were 11 times more likely to screen positively for psychosis, and were 3 and 4 times more likely to have a concurrent affective or anxiety disorder compared to the general population.[2,6] Even higher rates of comorbid cannabis and mental disorders have been documented among clinical samples presenting to treatment services.[7,8]

The high rate of cannabis use among individuals with mental health problems is concerning as there is consistent evidence that cannabis use adversely impacts affective and psychosis outcomes. Cannabis use is associated with increased dysphoria among individuals with depression,[9,10] and relapses and remissions in depressive and substance use disorders among individuals with both disorders have been found to substantially affect the course of the other condition.[11] Further, cannabis use has been associated with higher rates of psychotic relapse among individuals with first-episode and established psychoses,[12–15] as well as poorer treatment attendance and medication adherence.[16]

The high prevalence of cannabis use among psychiatric populations, as well as the associated negative impact on illness course and treatment outcomes, highlights the need for effective interventions for both disorders. However, to date, there have been few clinical treatment trials (pharmacotherapeutic or psychological) that have specifically focused on addressing comorbid cannabis use among psychotic and depressed samples. In this article, we systematically review the evidence from randomized controlled trials (RCTs) for pharmacologic and psychological intervention approaches to cannabis use among people with psychotic or depressive disorders, and provide recommendations for clinical management and future research.

For Clinical Use

- Effectively treating the psychotic or depressive disorder with standard pharmacotherapy and psychosocial approaches may be associated with a reduction in cannabis use.
- Motivational interviewing and cognitive-behavioral interventions, including computer-based interventions, seem promising for reducing cannabis use.
- Although brief interventions may be effective for some cannabis users, longer or more intensive psychological interventions may be required, particularly among heavier users and those with more chronic mental disorders.

METHOD

A systematic literature search was conducted using the PubMed (ISI) and PsychINFO (CSA) databases from their inception to December 2008. Individual searches in cannabis use (search terms: *marijuana*, *cannabis*, *marijuana abuse*, *cannabis abuse*, *marijuana usage*, *cannabis usage*), mental disorders (search terms: *mood disorders*, *affective disorders*, *anxiety disorders*, *anxiety*, *depressive disorder*, *depression*, *psychotic disorders*, *psychosis*, *mental disorders*), and pharmacotherapy (search terms: *medication*, *drug therapy*, *pharmacotherapy*, *psychopharmacology*, *clinical trials*, *drug trial*, *treatment trial*) were conducted and limited to humans, adolescents and adults. A search combining the individual cannabis use, mental disorder and pharmacotherapy searches produced 1,713 articles (PubMed = 1,398, PsychINFO = 315). Combining the cannabis use and mental disorder searches while limiting them to English articles and randomized controlled trials produced a total of 286 articles (PubMed = 228, PsychINFO = 58). From this literature, there were 7 RCTs conducted among mental health clients that reported cannabis use outcomes using pharmacologic or psychological interventions.

RESULTS

Trials of Pharmacologic Interventions

Only 2 small RCTs with short-term follow-up assessments have reported on the effectiveness of pharmacologic interventions on cannabis use outcomes among individuals with psychosis or depression. Details of these studies are provided in Table 1.

Psychosis. Akerele and Levin[17] conducted a 14-week double-blind, RCT comparing the efficacy of olanzapine with risperidone in 28 patients with schizophrenia and co-occurring cocaine (71%) and/or cannabis (93%) use disorder(s). Positive psychosis ratings decreased over time for both groups, with no differences in adherence rates reported. While the risperidone group had a significantly greater reduction in cannabis craving compared to the olanzapine group, no main effect for treatment was found, although both treatment groups demonstrated significantly reduced cannabis-positive urine samples over the course of the study. There were a number of methodological limitations to this study, including the high rate of comorbid cocaine dependence (71%) and the use of a small sample of primarily male patients of African American (54%) or Hispanic (32%) descent. No information was provided regarding the duration of the psychotic illness or response to previous treatment, and less than 60% of participants completed the 14-week study period. While improvements in cannabis-positive urine samples occurred in both treatment arms, psychotic symptom scores also improved, suggesting that this may be the primary mechanism underlying the reduction in cannabis use. Participants also met with the research team 3 times per week to assess drug use, and received weekly psychotherapy (undefined), which may have also contributed to improvements in cannabis use during the trial.

Depression. Cornelius et al[18] reported a secondary analyses of a subsample of 22 individuals with co-occurring cannabis abuse out of a total sample of 51 with comorbid diagnoses of major depression and alcohol dependence participating in a 12-week double-blind, randomized placebo-controlled trial evaluating the efficacy of fluoxetine versus placebo. During the course of the study, the fluoxetine group demonstrated a significantly greater improvement in depressive symptoms as well as drinking behavior compared with the placebo group. In addition, cannabis use decreased significantly in the fluoxetine group and increased in the placebo group, with the placebo group smoking 20 times more cannabis cigarettes during the course of the study as the fluoxetine group. However, this study involved a secondary analysis of a small subsample of cannabis abusers with comorbid major depression and alcohol dependence, limiting the generalizability of the findings. Both groups also received an initial inpatient detoxification period and adjunctive "usual care" (weekly supportive psychotherapy and psychiatry support), although the specifics of this intervention were not described. Finally, although the improvement in cannabis use may relate to a specific pharmacotherapeutic response to fluoxetine, it appears more likely to be secondary to an overall improvement in participants' level of depression and alcohol use.

Summary of findings and clinical recommendations from pharmacologic trials. The 2 pharmacologic studies conducted to date were characterized by small sample sizes and no follow-up assessments after completion of the

Table 1. Summary of Cannabis Use Outcomes From RCTs Among Samples With Mental Disorders

Study	Sample, n	Setting	Male, %	Age, Mean, y	Participation Rate, n/N (%)	Diagnoses	Entry Criteria (cannabis)
Akerele and Levin[17] (2007) (USA)	28	Outpatients	89.0	36	28/47 (59.6); 17 dropped out	*DSM-IV* schizophrenia or schizoaffective disorder SUD, current cocaine (71.4%); cannabis abuse/dependence (93.0%); Other SUD not assessed	*DSM-IV* criteria for current cocaine and/or cannabis abuse/dependence
Baker et al[19] (2002) (Australia)	160	Inpatients	81.3	31	Not reported	*DSM-IV* (baseline) 37.0% schizophrenia 29.6% mood 12.3% other 19.8% none SUD (current): 54.4% alcohol; 50.8% cannabis; 21.9% amphetamines; 12.5% heroin; 11.3% tranquilizers	At least weekly use of cannabis (n/N = 106/160; 66.3%)
Baker et al[22] (2006) (Australia)	130	Outpatients	78.2	28	130/158 (82.3) of eligible participants; 20 refused; 8 were not contactable	*ICD-10* psychosis: 62.2% schizophrenia 12.6% schizoaffective 9.2% bipolar 4.2% affective SUD (past year) 73.1% cannabis; 67.3% alcohol; 47.0% amphetamines	At least weekly use of cannabis (n/N = 79/130; 60.8%)
Cornelius et al[18] (1999) (USA)	22/51[a]	Outpatients	50	31	NA as subsample of existing study	*DSM-III-R* 100% depression SUD 100% alcohol dependence, 100% cannabis abuse	*DSM-III-R* diagnosis of cannabis abuse
Edwards et al[23] (2006) (Australia)	47	Outpatients	72	21	47/76 (62) of eligible participants	Stabilized first-episode psychosis *DSM-IV* 71.7% schizophrenia/schizophreniform 10.9% Affective 17.4% NOS/ delusional/other Current SUD 48.9% cannabis; 2.2% alcohol	Continued use of cannabis at 10 wk post–index presentation
Martino et al[24] (2006) (USA)	44	Inpatients and Outpatients	73.0	32	44/48 (91.7) of eligible participants	*DSM-IV* psychosis: 43.2% schizophrenia 34.1% schizoaffective 22.7% psychotic disorder NOS Current SUD 54.5% cocaine; 50.0% cannabis; 47.7% alcohol; 18.2% illy/ecstasy; 9.1% heroin	*DSM-IV* abuse/dependence and report 1 day primary drug use in last 8 wk Cannabis use/dependence (n/N = 22/44; 50.0%)
Kay-Lambkin et al[25] (2009) (Australia)	97	Outpatients	46.0	35	97/116 (83.6); 19 (16.4%) refused	*DSM-IV* 100.0% lifetime depression SUD not reported	At least weekly use of cannabis (n/N = 43/97; 44.3%)

[a]Value for sample size equals n/n.
Abbreviations: CBT = cognitive-behavioral therapy, MI = motivational interview, NA = not applicable, SI = standard psychiatric interview, SUD=substance abuse disorder, TAU = treatment as usual.

Design	Follow-Up	Results	Clinical Significance of Results (cannabis users)	Methodological Limitations
14-wk, double-blind, RCT comparing risperidone (3–9 mg) and olanzapine (5–20 mg)	Nil	n = 16 (57.1%) completed the 14-wk trial; no significant group differences in time-to-dropout or completion rate Cannabis positive urines decreased significantly for both groups; no main effect by treatment group Severity of positive psychotic symptoms decreased significantly across both groups	Significant decrease in mean cannabis craving severity in risperidone group	Small sample size, primarily male sample, no long-term follow-up
MI: 1 × 30–45 min individual session vs TAU	Participation rate: 3 mo (70.0%), 6 mo (73.1%), and 12 mo (71.9%); all follow-ups (55.6%); no differences in follow-up rates across intervention groups	Significant reduction cannabis use occasions per day, no difference between conditions at 3, 6, and 12 mo	Mean use occasions per day: 7.22 (baseline); 3.02 (3 mo); 4.29 (6 mo); 5.07 (12 mo) Cannabis abuse/dependence present: 53.2% (6 mo); 58.1% (12 mo) At 12 mo, 74.7% continued weekly cannabis use	Baseline participation rate not reported; therapy adherence and fidelity not rated
10 × 60 min weekly individual MI/CBT vs TAU	15 wk (93.1%), 6 mo (94.6%), and 12 mo (80.0%); conducted by blinded research interviewers	Completed MI/CBT intervention (10 sessions), n/n = 46/65 (70.8%); n/n = 11/65 (16.9%) attended some sessions; n/n = 8/65 (12.3%) no sessions Trend for greater reduction in cannabis use in the MI/CBT condition vs TAU at 15wk posttreatment	Mean use occasions per day, MI/CBT: 8.18 (baseline); 5.09 (15 wk); 5.37 (6 mo); 8.53 (12 mo). TAU: 4.80 (baseline); 5.66 (15 wk); 4.67 (6 mo); 4.12 (12 mo) At 12 mo, 58.6% continued to meet study entry criteria for cannabis use	Therapy adherence and fidelity not rated
12-wk double-blind, placebo-controlled study of fluoxetine 20 mg vs placebo	Nil	Significant group-time effect on cannabis use (increased use in placebo group vs decreased use in fluoxetine group) Significant improvement in depressive symptoms and number of drinks per day in fluoxetine group	Cumulative no. of cannabis cigarettes used during study almost 20 times higher in placebo group (61.3 vs 3.3) No. of days of cannabis use during study 5 times higher in placebo group (20.4 vs 4.5)	Small sample with comorbid depression and alcohol dependence; cannabis not primary outcome measure, unclear if finding related to effect of fluoxetine on depression, alcohol or cannabis; no long-term follow-up
10 × 20–60 min weekly individual psychoeducation/ MI/CBT (n = 23) vs psychoeducation (n = 24) sessions over 3 mo + booster phone call after 3 mo	6 mo psychoeducation/ MI/CBT (n = 17 [70%]); psychoeducation (n = 16 [70.8%])	Participation rate (median no. of sessions): CBT (8); psychoeducation (10) Significant reduction in percent days used cannabis; no difference between conditions at 6 mo	Cannabis use reduced: with MI/CBT, from 39.4% days used cannabis in previous 4 weeks (baseline) to 30.4% (post) and 32.4% at 6 mo; with psychoeducation, from 26.0% (baseline) to 18.8% (post) and 19.3% (6 mo)	Small sample size, low participation rate, categorical outcomes only. Therapy adherence and fidelity not rated
MI (n = 24): 2 × 60 min individual sessions vs SI (n = 20): 2 × 60 min All sessions videotaped and rated independently	Posttherapy at 4, 8, and 12 wk by nonblinded research staff; n = 38 (86%) completed 1 follow-up, n = 37 (84%) completed 2 follow-ups, and n = 34 (77%) completed all 3 follow-ups; no group differences in follow-up rates	Both sessions were completed by 88.6% (n = 39) of the sample At 12 weeks, primary cannabis users (n = 13) in SI reduced their cannabis use significantly more than those in MI	12 wk, SI participants reduced days of cannabis use by 92.1% MI had no reduction in days of cannabis use	Small sample Low number of days use required for entry into the study. Mean days use of primary drug in the past mo = 7.70, mean joints per d = 1.44
MI: 1 60 min session vs 9 nine 60 min sessions of MI/CBT psychologist or computer-delivered MI/CBT (with brief weekly input from a psychologist)	12 mo, n = 82 (84.5%)	Percentage of treatment sessions attended: 87% for the therapist-delivery group; 76.1% for the computer-delivery condition Brief intervention was not effective for cannabis, but intensive therapy was significantly better than brief intervention with computer-based therapy showing the largest treatment effect	Mean use occasions per day—MI: 9.22 (baseline), 7.24 (15 wk), 8.00 (6 mo), 8.61 (12 mo); MI/CBT therapist: 15.03 (baseline), 8.90 (15 wk), 7.10 (6 mo), 5.72 (12 mo); MI/ CBT computer: 11.94 (baseline), 5.77 (15 wk), 4.97 (6 mo), 3.34 (12 mo)	Small sample Therapy adherence and fidelity not rated

pharmacotherapy trial. Neither study explored specific pharmacotherapy for cannabis use, but rather examined changes in cannabis use with established psychotropic medications (risperidone/olanzapine or fluoxetine) indicated for the primary mental disorder (psychosis or depression). For both studies, it is difficult to determine whether the treatment effects were attributable to the pharmacologic intervention alone, as all participants received concomitant psychotherapy.

Due to the small number of studies conducted to date, clinical recommendations regarding pharmacologic interventions for cannabis use among people with psychotic or depressive disorders are limited. However, results from 2 RCTs suggest that effectively treating the mental health disorder with standard pharmacotherapy may be associated with a reduction in cannabis use, although adjunctive psychological treatment is also likely to be required.

Trials of Psychological Interventions

Five RCTs have reported on cannabis use outcomes from manual-led psychological interventions for co-occurring substance use, including 3 trials in psychosis, 1 in depression, and 1 sample with mixed diagnoses. Details of these studies are provided in Table 1.

Mixed sample—inpatients. Baker et al[19,20] assessed the effectiveness of a single session manual guided motivational interview (MI) immediately following baseline assessment versus a self-help booklet among 160 hospitalized psychiatric patients with comorbid substance use. The sample reported a mean number of 4 previous psychiatric hospital admissions. At baseline, over half of the sample (62.5%) reported at least weekly use of cannabis.[19] Follow-up assessments were conducted at 3, 6, and 12 months' post treatment, and a 4-year follow-up of the substance use outcomes of the sample was also performed. At 3-month follow-up there was a significant reduction in cannabis use from a mean of 7.09 to 2.82 use occasions per day, with no significant differences between intervention conditions. At 12 months, while the proportion of weekly alcohol and amphetamine users had halved, the majority of cannabis users continued to use at least weekly. In a follow-up of this sample 4 years later, the decline in alcohol and amphetamine use remained fairly steady, while the group of people who were at least weekly cannabis users at baseline did not decrease their use during the follow-up period, continuing to use on an average of 5 occasions per day.[21] There were a number of limitations to this study, including failure to report the proportion of subjects who declined participation in the study and the absence of therapy adherence and fidelity ratings.

Psychosis—outpatients. Baker et al[22] randomly assigned 130 people with a psychotic disorder and comorbid substance use to 10 weekly individual sessions of manual-guided MI/cognitive-behavioral therapy (CBT) or to treatment as usual (TAU). Almost two-thirds of participants (61.3%) were at least weekly cannabis users at baseline. Most of the sample (81.5%) reported multiple episodes of acute psychosis. The intervention condition reported greater improvement in depressive symptoms at 6 months and better general functioning at 12 months compared to controls. Both groups showed a similar reduction in frequency of substance use during the 12-month follow-up period. There was a nonsignificant trend for a differential reduction in cannabis use between baseline and posttreatment, with the treatment group reducing use from an average of 8.18 to 5.09 use occasions per day compared to controls whose use increased (4.80 to 5.66 use occasions per day) at 15 weeks. At 12-month follow-up, the treatment group reported a return to previously high levels of cannabis use, with a mean of 8.53 use occasions per day compared to a mean of 4.12 use occasions per day in the control group. The absence of an attention placebo condition and the lack of ratings of therapy adherence and fidelity limit the extent to which changes within the therapy condition can be attributed to the therapy.

Edwards et al[23] randomly assigned 47 individuals with first-episode psychosis to either 10 individual sessions of psychoeducation only or to psychoeducation, MI, and CBT combined. While all participants were required to be using cannabis at 10 weeks post initial presentation to participate in the study, daily cannabis use was reported by only 7 participants (14%), with 27 (57.4%) using weekly and 20 (42.6%) using monthly. No significant differences were found between conditions on cannabis use, symptom severity or general functioning at the end of treatment or at 6-months follow-up. Both groups showed a similar reduction in cannabis use during the follow-up period. The intervention condition was associated with a reduction in cannabis use between baseline and 6 month follow-up from a mean of 39.4% of days to 32.4% days per month, compared to psychoeducation subjects who reduced their cannabis use from an average of 26%–19.3% percent of days per month. There were numerous methodological problems with this study, including its small sample size, low participation rate, report of categorical rather than continuous outcomes, and a lack of therapy adherence and fidelity ratings. Nevertheless, the inclusion of first-episode psychosis participants was a strong feature of this study as many studies include subjects with variable histories of psychotic disorder.

Martino et al[24] randomly assigned 44 people with psychotic disorder (duration unspecified) and at least 1 day of primary drug use in the previous 2 months to either 2 individual sessions of manual-guided MI or a 2-session manualized standard psychiatric interview. Cannabis was the primary drug problem reported by 29.5% (13) of the sample and the mean number of joints smoked per day was 1.44. While primary cocaine users reduced their cocaine use significantly more over time in the MI condition than participants in the standard interview condition at 12 weeks' follow-up, the reverse was true of primary cannabis users, who reduced their cannabis by 92.1% compared to

no reduction in the MI condition. Limitations of this study included its small sample, nonblinded follow-up and the low number of days of drug use required for entry into the study. In addition, cannabis users in the standard interview condition had increased legal problems compared to controls, which may have contributed to the positive findings for this condition.

Depression. An RCT designed to evaluate computer- versus therapist-delivered psychological treatment among 97 people with comorbid major depression and substance use problems has recently been reported by Kay-Lambkin et al.[25] All participants received an initial session comprising a MI and case formulation for depressive symptoms and substance use problems, followed by random assignment to 1 of 3 treatments: no further treatment (brief intervention); 9 further sessions of MI and CBT delivered by a psychologist (therapist condition); or 9 further sessions of MI/CBT therapy delivered by a computer (with brief 10–15 minute weekly input from a psychologist). In terms of cannabis use, brief intervention was not effective in reducing use compared to the more intensive therapy (both computer and therapist based), with the computer-based therapy showing the largest treatment effect at 12 months. Brief intervention participants reported a mean level of 9.22 cannabis use occasions per day at baseline versus 8.61 at 12-months, whereas the respective figures for therapist and computer delivered interventions were 15.03 versus 5.72 use occasions per day and 11.94 versus 3.34, respectively. Conclusions that can be drawn from this study are limited by its small sample size and absence of therapy adherence and fidelity ratings.

Limitations of psychological intervention trials. Most of the existing RCTs of psychological interventions for substance use disorders among people with severe mental disorders have reported overall substance use outcomes, rather than outcomes according to specific substance classes, with only 5 RCTs reporting the impact of treatment on cannabis use. These 5 studies reviewed above thus provide unique information about cannabis users with mental health problems and the effects of manual guided treatment. However, as Table 1 shows, the studies suffered from a number of methodological limitations including small sample sizes, the recruitment of heterogeneous groups of both cannabis users with widely varying levels of use (eg, from less than monthly to daily) and at different stages of psychiatric illness (eg, first episode to chronic) into the same study, limited information regarding adjunctive pharmacologic treatment, and different definitions and measures of treatment effectiveness and fidelity between studies. In addition, all but 1 of these studies focused on the parallel treatment of cannabis and other substance use alone rather than offering integrated treatment of both the mental health and cannabis/substance use issues. Even within these studies, participants were not exclusively cannabis users, as most studies focused on recruiting patients with any co-occurring substance use disorder. Nevertheless, as most cannabis users are polydrug users,[8] the results of these studies are likely to be generalizable to the clinical community.

Summary of findings of psychological intervention trials. Overall, existing studies suggest that cannabis use is responsive to psychological treatment, including brief motivational interviewing interventions and CBT, in the short-term (ie, 3 months' follow-up).[19,20,23] However, short term reductions in cannabis use were also found in the control conditions (eg, self-help booklet, TAU, PE) in these studies. This includes 1 study that found a standard clinical interview had superior cannabis use outcomes to MI, although this finding may have been associated with the increased legal problems among these subjects.[24] These findings suggest that short term reductions in cannabis use can be achieved from brief interventions regardless of the type of intervention used. The few existing longer-term follow-up studies reveal relapse to previous higher levels of use among heavy cannabis users regardless of the type or length of psychological intervention or control condition used.[19,20,23] These findings are consistent with the results of the latest Cochrane review[26] on psychosocial interventions for people with both severe mental illness and substance misuse which found no evidence for any 1 psychological (including MI or CBT alone or in combination) intervention over another in terms of substance use outcomes. Clearly, better-designed RCTs with longer follow-up assessments of up to 3 years are required.

With regard to the length of treatment, the only study[25] that compared a brief MI intervention with a longer MI/CBT session among individuals with comorbid depression and substance use problems found the brief MI was ineffective in reducing cannabis use compared to the more intensive MI/CBT treatment at 12 months follow-up. This finding suggests that longer term or more intensive MI/CBT treatments may be required especially for heavy users of cannabis. This was also the only treatment study that targeted both depressive symptoms and substance use problems, suggesting that further research exploring the efficacy of integrated treatments among individuals with coexisting cannabis use and mental health problems is required. Such studies should directly compare parallel versus integrated approaches to the treatment of comorbid disorders using clearly defined entry criteria for both cannabis use and mental health symptoms, as well as measuring outcomes on both of these variables. In order to advance the literature, there is also a clear need to more clearly define what is meant by "integrated treatment"; in terms of whether it refers to 1 practitioner providing integrated treatment of both disorders, a service offering integrated treatment of both disorders, or the comanagement of mental health and drug and alcohol disorders across agencies.

The clinical significance of the cannabis use outcomes as indicated by the magnitude of change in cannabis use reported in the studies reviewed was often modest (see Table 1). Even where sizeable reductions occurred (11.94 use

occasions per day at baseline to 3.34 at 12 months), as in the study by Kay-Lambkin et al,[25] cannabis use remained high. Similarly, while a number of RCTs have provided evidence for the effectiveness of MI/CBT in the treatment of cannabis dependence,[27,28] the clinical significance of the reduction in cannabis use was modest at best. Together, these findings indicate that MI/CBT for cannabis use with and without coexisting mental health problems has limited effectiveness, and future interventions must aim for an improvement in the magnitude of change achieved.

Recommendations for Further Research Into Pharmacologic and Psychological Interventions

Despite the limitations of the literature to date, the few studies conducted offer important clinical directions that require further investigation. Firstly, there is a clear need to evaluate specific pharmacotherapies targeted at reducing cannabis use among mental health populations, rather than providing standard treatment of the mental disorder alone. Secondly, research is needed in order to improve the duration of treatment effects. As such, cannabis use, mental health symptom and general functioning outcomes should be assessed over longer follow-up periods. Baker et al[22] found MI/CBT was associated with improvements in general functioning and suggested that this may eventually lead to more distal improvements in cannabis and other drug use not measured within the timeframe of these studies. Enhancement strategies, such as booster sessions, should also be investigated to assess whether they augment treatment gains.

Further studies should also investigate the comparative effectiveness of brief versus longer interventions. Important issues include: sample composition (eg, stage of mental disorder and level of cannabis use); length of intervention (eg, 1 or 4 sessions); and content of intervention (eg, assessment, and/or psychoeducation, and/or brief MI). The structure of longer interventions (integrated, parallel, or sequential) should also be compared for effectiveness with brief interventions.

Finally, avenues to enhance the effectiveness of psychological interventions need exploration. Contingency management, which has demonstrated effectiveness among cannabis users[27,29,30] and comorbid populations,[31,32] provides one potential avenue for enhancing the effectiveness of CBT. Group interventions for substance use disorders among people with severe mental disorders also hold promise.[31] Future research identifying the mediators and moderators of outcome from CBT for cannabis use problems among people with mental disorders could facilitate refinement of theoretical models and the development of more effective and efficient therapies.[33] Existing studies have found coping skills and self-efficacy to be the most likely mediators of outcome among alcohol and cannabis dependent individuals, as well as a possible role for readiness to change as a moderator of outcome.[34–36] In addition to quantitative studies, qualitative methodologies should be employed to assess the attitudes, knowledge, reasons for use and perception of harm regarding cannabis use among mental health populations, as well as improving our understanding of the processes involved in reducing cannabis use.

Clinical Recommendations

There is a paucity of studies on pharmacologic and psychological interventions for substance use among individuals with psychotic or depressive disorders. Existing studies contain numerous methodological flaws, making it difficult to make evidence-based treatment recommendations in this area. However, the finding that longer or more intensive interventions may be required, particularly among heavier users of cannabis and those with more chronic mental disorders, is consistent with the cannabis treatment literature among community samples,[28] with brief interventions being less effective than 10 sessions of MI/CBT. Results from RCTs presented above indicate that effectively treating the mental health disorder with standard pharmacotherapy and psychosocial approaches may be associated with a reduction in cannabis use, while computer-based interventions may also hold promise. Specific recommendations regarding the type and length of specific psychological treatments cannot be made at this time, although MI and CBT approaches seem promising.

CONCLUSIONS

Cannabis is the most commonly used illicit drug in the world and frequently co-occurs with mental disorders. There is evidence that pharmacologic and psychological interventions are effective for treating co-occurring cannabis use in the short-term among people with psychotic disorders or depression. Further research should address the limited effectiveness of existing interventions, the paucity of longer-term follow-up assessments and diminution of treatment effects over time.

Drug names: fluoxetine (Prozac, Sarafem, and others), olanzapine (Zyprexa), risperidone (Risperdal and others).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

Author affiliations: Centre for Brain and Mental Health Research, University of Newcastle (Dr Baker); and Orygen Youth Health Research Centre, Centre for Youth Mental Health, University of Melbourne (Drs Hides and Lubman), Australia.

Financial disclosure: **Dr Lubman** has received grant/research support from Pfizer and Bristol-Myers Squibb and has received honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, and Janssen-Cilag. **Drs Baker** and **Hides** report no financial or other relationships relevant to the subject of this article.

Funding/support: Dr Baker is supported by a National Health and Medical Research Council Fellowship (510702). Drs Hides and Lubman are supported by the Colonial Foundation.

Acknowledgment: The authors thank Louise Thornton, BPsych (Hons), Centre for Brain and Mental Health Research, University of Newcastle, Calleghan, New South Wales, Australia, for helping to prepare the article for publication.

© Copyright 2010 Physicians Postgraduate Press, Inc.

REFERENCES

1. Degenhardt L, Hall W. The association between psychosis and problematical drug use among Australian adults: findings from the National Survey of Mental Health and Well-Being. *Psychol Med*. 2001;31(4):659–668.
2. Degenhardt L, Hall W, Lynskey M. Alcohol, cannabis and tobacco use among Australians: a comparison of their associations with other drug use and use disorders, affective and anxiety disorders, and psychosis. *Addiction*. 2001;96(11):1603–1614.
3. Farrell M, Howes S, Bebbington P, et al. Nicotine, alcohol and drug dependence and psychiatric comorbidity: results of a national household survey. *Br J Psychiatry*. 2001;179(5):432–437.
4. Merikangas KR, Mehta RL, Molnar BE, et al. Comorbidity of substance use disorders with mood and anxiety disorders: results of the International Consortium in Psychiatric Epidemiology. *Addict Behav*. 1998;23(6):893–907.
5. Stinson FS, Ruan WJ, Pickering R, et al. Cannabis use disorders in the USA: prevalence, correlates and co-morbidity. *Psychol Med*. 2006;36(10):1447–1460.
6. Degenhardt L, Hall W, Lynskey M. The relationship between cannabis use, depression and anxiety among Australian adults: findings from the National Survey of Mental Health and Well-Being. *Soc Psychiatry Psychiatr Epidemiol*. 2001;36(5):219–227.
7. Mueser KT, Yarnold PR, Rosenberg SD, et al. Substance use disorder in hospitalized severely mentally ill psychiatric patients: prevalence, correlates, and subgroups. *Schizophr Bull*. 2000;26(1):179–192.
8. Lambert M, Conus P, Lubman DI, et al. The impact of substance use disorders on clinical outcome in 643 patients with first-episode psychosis. *Acta Psychiatr Scand*. 2005;112(2):141–148.
9. Ablon SL, Goodwin FK. High frequency of dysphoric reactions to tetrahydrocannabinol among depressed patients. *Am J Psychiatry*. 1974;131(4):448–453.
10. Mathew RJ, Wilson WH, Tant SR. Acute changes in cerebral blood flow associated with marijuana smoking. *Acta Psychiatr Scand*. 1989;79(2):118–128.
11. Hasin DS, Liu X, Nunes E, et al. Effects of major depression on remission and relapse of substance dependence. *Arch Gen Psychiatry*. 2002;59(4):375–380.
12. Degenhardt L, Tennant C, Gilmour S, et al. The temporal dynamics of relationships between cannabis, psychosis and depression among young adults with psychotic disorders: findings from a 10-month prospective study. *Psychol Med*. 2007;37(7):927–934.
13. Hides L, Dawe S, Kavanagh DJ, et al. Psychotic symptom and cannabis relapse in recent-onset psychosis: prospective study. *Br J Psychiatry*. 2006;189(2):137–143.
14. Linszen DH, Dingemans PM, Lenior ME. Cannabis abuse and the course of recent-onset schizophrenic disorders. *Arch Gen Psychiatry*. 1994;51(4):273–279.
15. Zammit S, Moore THM, Lingford-Hughes A, et al. Effects of cannabis use on outcomes of psychotic disorders: systematic review. *Br J Psychiatry*. 2008;193(5):357–363.
16. Jablensky A, Sartorius N, Ernberg G, et al. Schizophrenia: manifestations, incidence and course in different cultures: a World Health Organization ten-country study. *Psychol Med*. 1991;20(suppl 20):1–97.
17. Akerele E, Levin FR. Comparison of olanzapine to risperidone in substance-abusing individuals with schizophrenia. *Am J Addict*. 2007;16(4):260–268.
18. Cornelius JR, Salloum IM, Haskett RF, et al. Fluoxetine versus placebo for the marijuana use of depressed alcoholics. *Addict Behav*. 1999;24(1):111–114.
19. Baker A, Lewin T, Reichler H, et al. Evaluation of a motivational interview for substance use within psychiatric in-patient services. *Addiction*. 2002;97(10):1329–1337.
20. Baker A, Lewin T, Reichler H, et al. Motivational interviewing among psychiatric in-patients with substance use disorders. *Acta Psychiatr Scand*. 2002;106(3):233–240.
21. Greig RL, Baker A, Lewin TJ, et al. Long-term follow-up of people with co-existing psychiatric and substance use disorders: patterns of use and outcomes. *Drug Alcohol Rev*. 2006;25(3):249–258.
22. Baker A, Bucci S, Lewin TJ, et al. Cognitive-behavioural therapy for substance use disorders in people with psychotic disorders: Randomised controlled trial. *Br J Psychiatry*. 2006;188(5):439–448.
23. Edwards J, Elkins K, Hinton M, et al. Randomized controlled trial of a cannabis-focused intervention for young people with first-episode psychosis. *Acta Psychiatr Scand*. 2006;114(2):109–117.
24. Martino S, Carroll KM, Nich C, et al. A randomized controlled pilot study of motivational interviewing for patients with psychotic and drug use disorders. *Addiction*. 2006;101(10):1479–1492.
25. Kay-Lambkin FJ, Baker AL, Lewin TJ, et al. Computer-based psychological treatment for comorbid depression and problematic alcohol and/or cannabis use: a randomized controlled trial of clinical efficacy. *Addiction*. 2009;104(3):378–388.
26. Cleary M, Hunt G, Matheson S, et al. Psychosocial interventions for people with both severe mental illness and substance misuse. *Cochrane Database Syst Rev*. 2008;(1):CD001088.
27. Carroll KM, Easton CJ, Nich C, et al. The use of contingency management and motivational/skills-building therapy to treat young adults with marijuana dependence. *J Consult Clin Psychol*. 2006;74(5):955–966.
28. Marijuana Treatment Project Research Group. Brief treatments for cannabis dependence: findings from a randomized multisite trial. *J Consult Clin Psychol*. 2004;72(3):455–466.
29. Budney AJ, Moore BA, Rocha HL, et al. Clinical trial of abstinence-based vouchers and cognitive-behavioral therapy for cannabis dependence. *J Consult Clin Psychol*. 2006;74(2):307–316.
30. Dutra L, Stathopoulou G, Basden SL, et al. A meta-analytic review of psychosocial interventions for substance use disorders. *Am J Psychiatry*. 2008;165(2):179–187.
31. Bellack AS, Bennett ME, Gearon JS, et al. A randomized clinical trial of a new behavioral treatment for drug abuse in people with severe and persistent mental illness. *Arch Gen Psychiatry*. 2006;63(4):426–432.
32. Sigmon SC, Higgins ST. Voucher-based contingent reinforcement of marijuana abstinence among individuals with serious mental illness. *J Subst Abuse Treat*. 2006;30(4):291–295.
33. Kraemer HC, Wilson GT, Fairburn CG, et al. Mediators and moderators of treatment effects in randomized clinical trials. *Arch Gen Psychiatry*. 2002;59(10):877–883.
34. Litt MD, Kadden RM, Kabela-Cormier E, et al. Coping skills training and contingency management treatments for marijuana dependence: exploring mechanisms of behavior change. *Addiction*. 2008;103(4):638–648.
35. Litt MD, Kadden RM, Stephens RS; Marijuana Treatment Project Research Group. Coping and self-efficacy in marijuana treatment: results from the marijuana treatment project. *J Consult Clin Psychol*. 2005;73(6):1015–1025.
36. Morgenstern J, Longabaugh R. Cognitive-behavioral treatment for alcohol dependence: a review of evidence for its hypothesized mechanisms of action. *Addiction*. 2000;95(10):1475–1490.

For the CME Posttest for this article, see pages 365–366.