

# A contingency management intervention to reduce cannabis use and time to relapse in early psychosis: the CIRCLE RCT

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## Scientific summary

### The CIRCLE trial

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# Scientific summary

## Background

Cannabis is the most commonly used illicit substance among people with psychosis and is associated with a poorer prognosis, including increased symptom severity, poorer functional outcomes and a significantly higher risk of relapse. Reducing cannabis use early in the course of psychosis has the potential to improve recovery, thus improving clinical and social outcomes in the long term. Recent studies have found little evidence that any intervention so far developed for this cohort is effective.

Contingency management (CM) is an intervention for substance misuse that involves offering incentives contingent on evidence of abstinence. CM has been shown to be an effective approach in a range of contexts including smoking cessation and substance misuse disorders. In the one CM randomised controlled trial (RCT) to date (Bellack AS, Bennett ME, Gearon JS, Brown CH, Yang Y. 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**:426–32) that has investigated CM for comorbid substance misuse (including cannabis) in psychosis, CM combined with a psychological intervention was more effective in decreasing substance misuse than an enhanced treatment-as-usual (TAU) intervention. However, only 7% of the sample had problematic cannabis use, with most participants being recruited because they were using heroin or cocaine.

In the present study, a RCT was conducted to investigate the clinical effectiveness and cost-effectiveness of CM in reducing cannabis use among Early Intervention in Psychosis (EIP) service users. The CM intervention was delivered alongside an optimised version of TAU that comprised a structured psychoeducation package. The control arm received TAU only. The primary outcome was time to relapse, measured as an admission to an acute mental health service. Secondary outcomes included cannabis use, psychotic symptom severity and health economic measures.

## Objectives

- To conduct an internal pilot study of a CM intervention for cannabis use in early psychosis that would explore the feasibility and acceptability of the CM intervention, as well as achieving recruitment and retention goals in an EIP context.
- To conduct a fully powered multicentre pragmatic RCT in EIP services to investigate the effectiveness of CM in reducing time to relapse (the primary outcome) among young adults with psychosis.
- To test if a CM intervention results in a decrease in cannabis use and in positive psychotic symptoms, as well as an increase in participation in work or education, by follow-up, compared with a control arm that does not receive the intervention (secondary outcomes).
- To assess the cost-effectiveness of the CM intervention from a NHS perspective.

## Methods

The CIRCLE (Contingency Intervention for Reduction of Cannabis in Early Psychosis) trial was a multicentre RCT of CM for cannabis use in psychosis. Participants were recruited via EIP services from 23 NHS trusts across the Midlands and the south-east of England. EIP service users were eligible for the trial if they had used cannabis at least once during 12 of the previous 24 weeks, were aged between 18 and 36 years, had stable accommodation, understood English sufficiently to be able to participate in the assessments and intervention, were not receiving treatment for cannabis use from another service, were not on a community treatment order or on probation that required testing for cannabis, and had the capacity to give informed consent to participate.

Following a pre-trial assessment, participants were randomised to either the CM arm or the control arm. The CM intervention, offered to participants in the CM arm only, featured financial incentives for cannabis abstinence, in which abstinence was confirmed using urinalysis. The intervention featured 12 weekly sessions and was delivered by clinicians following training, with support from the research team. Participants received a voucher if their urinalysis result demonstrated abstinence from cannabis. The value of vouchers began at £5 and rose by £5 every 2 weeks in which participants provided negative urine samples. Participants who passed every session earned £240.

Participants in both arms received an optimised treatment-as-usual (OTAU) package that included a standardised psychoeducation intervention delivered by EIP staff, in line with guidelines on EIP routine care. The psychoeducation package presented information on the potential advantages and disadvantages of cannabis use and cannabis abstinence and was typically delivered to participants in six 30-minute sessions.

The trial featured interview assessments at baseline, at 3 months (at the end of the intervention period) and at 18 months. The primary outcome was time to relapse, indicated by entry to acute mental health services and assessed using electronic patient records at 18 months. Raters were blinded at follow-up.

The following data were collected at assessment interview: demographic and social information, including recent acute mental health services admission history; and current engagement in work or study. Cannabis use was measured by both urinalysis for the presence of tetrahydrocannabinol (THC) at each assessment interview and self-reported use. Self-reported cannabis use was measured over the previous 6 months (baseline and 18-month assessments) or 3 months (3-month assessment) using the timeline followback method. The history of alcohol and substance misuse disorders was collected with the substance disorders components of the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (SCID). Participants' symptoms of psychosis were measured with the positive and negative subscales of the Positive and Negative Syndrome Scale (PANSS). The Client Service Receipt Inventory, Short Form questionnaire-12 items and the EuroQol-5 Dimensions were administered to provide data for the health economic analyses.

Statistical analyses were carried out by treatment allocated, using all available participant data. Kaplan–Meier survival curves by randomised groups were used to examine the primary outcome (time to relapse) descriptively. Cox proportional hazards modelling was used to compare the primary outcome of the CM arm with that of the control arm, adjusting for severity of cannabis use at baseline and whether or not the participant was part of the pilot trial. Secondary outcomes were analysed using regression models separately at 3 months and 18 months. The proposed sample size for the trial was 544 participants. Additional analyses were conducted to establish the relative cost-effectiveness of CM compared with OTAU at 18 months.

## Results

In the sample of 551 participants, 85% were male with a mean age of  $\approx 25$  years. Around one-third of participants were diagnosed with schizophrenia or schizoaffective disorder and half had other psychoses. At the time of the baseline assessment, most participants were using cannabis more than three times per week.

At 18 months post baseline, there was no significant difference in time to admission between the trial arms [hazard ratio (HR) 1.03, 95% confidence interval (CI) 0.76 to 1.40]. In both arms, approximately one-third of participants were admitted to an acute mental health service. The likelihood of at least one admission did not differ between the arms [odds ratio (OR) 1.02, 95% CI 0.70 to 1.48]. Furthermore, the proportion of cannabis-positive urine samples at 3 months and 18 months (OR 0.86, 95% CI 0.56 to 1.34; OR 0.84, 95% CI 0.49 to 1.41, respectively), self-reported cannabis-using days [incidence rate ratio (IRR) 0.89, 95% CI 0.75 to 1.04; IRR 1.09, 95% CI 0.88 to 1.36, respectively] and engagement in work or study

(OR 0.95, 95% CI 0.62 to 1.46; OR 0.82, 95% CI 0.50 to 1.35, respectively) did not differ between the arms. However, the CM arm had slightly lower positive symptoms at 3 months (coefficient  $-0.07$ , 95% CI  $-0.14$  to  $0$ ), but not at 18 months (coefficient  $-0.04$ , 95% CI  $-0.13$  to  $0.05$ ). Negative symptoms approached significance at 3 months (coefficient  $-0.08$ , 95% CI  $-0.16$  to  $0.00$ ), but not at 18 months (coefficient  $0.01$ , 95% CI  $-0.08$  to  $0.11$ ).

In the health economic analyses, quality-adjusted life-years (a measure of health and life quality) did not differ between the CM arm and the control arm at either follow-up. However, total costs, including service use costs, were lower in the CM arm. In particular, the mean cost of inpatient hospital admissions was lower for the CM arm than the control arm. Further economic evaluations using incremental cost-effectiveness planes and cost-effectiveness acceptability curves suggest a high probability (85%) that CM is more cost-effective than the OTAU.

## Conclusions

There was no evidence of a difference in the primary outcome (time to relapse) between the CM arm and the control arm. There were also few between-group differences in secondary outcomes (levels of cannabis use, symptom severity and engagement in work and education) at either 3 or 18 months' follow-up. Despite this, cost-effectiveness analyses suggest that there is an 85% likelihood that the CM intervention was cost-effective, mainly as a result of higher mean inpatient costs for the control arm compared with the CM arm. However, the mechanism underlying this is not clear, as there is no evidence of any benefit from the intervention for the primary outcome or secondary outcomes. More work is needed to explore this result. Overall, however, the results from the CIRCLE trial indicate that CM, like many other psychotherapies tested, is not clinically effective at helping reduce cannabis use in this population. This is unfortunate and underscores the need to keep trialling potentially effective treatments with this cohort.

## Trial registration

This trial is registered as ISRCTN33576045.

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