Reviewer’s report

**Title:** Clinical and cost-effectiveness of contingency management for cannabis use in early psychosis: the CIRCLE randomised clinical trial

**Version:** 1  **Date:** 03 Mar 2019

**Reviewer:** Corinne Cather

**Reviewer's report:**

This study randomized 551 patients 18-36 yrs of age with a history of at least one psychotic episode who self-reported using cannabis at least once weekly in 12 of the past 24 weeks to a 12 week CM intervention which incentivized biochemically verified decreased use of cannabis + 6 weeks of weekly psychoeducation or to the 6 weeks of psychoeducation alone. The primary outcome was time to readmission to psychiatric hospitalization/crisis service over the 18-month period following randomization. No differences were found in time to readmission to psychiatric hospitalization/crisis service. In terms of secondary outcomes, no differences were seen between groups in the severity of positive symptoms of psychosis, social functioning based on self-reports of engagement in work or study, proportion of cannabis-free urines at assessment, self-reported number of days' cannabis use in the previous 3 months at 3-month follow-up, or the previous six months at 18 months, or number of admissions over 18 months follow-up. Costs were not different. Participants with high levels of engagement with psychoeducation (defined as 4/6 sessions) assigned to CM had an increased time to relapse compared with those in the control group with the same level of engagement in psychoeducation.

Strengths include a large sample size, with very good capture of follow-up data for the primary outcome (95-98%). blinded raters to the primary outcome variables, and a focus on a relatively homogenous group of individuals early in the course of a psychotic illness. The question of how to reduce cannabis use among those early with recent-onset psychosis is clinically meaningful. The paper is well-written and concise.

Weaknesses include lack of blinding for secondary outcomes, and low retention for the assessments conducted at both 3 mos (67%) and 18 mos (50%).

A few comments and suggestions below:

1. The section entitled 'CM in the Context of Psychoeduction' requires some re-working to be more understandable, particularly in terms of specifying the dependent variable, which I gather from reading the Results section is time to relapse?

2. Would suggest presenting the results from secondary analyses in the same order in which they are specified in the "Outcomes" section.

3. I am not a health economist, but found the conclusions about lower costs of CM difficult to follow given that: 1) the intervention costs were higher in the CM group, 2) the costs
for drug and alcohol services were higher for the CM group, and 3) intervention and other service use was about the same across groups. Yet, somehow, after imputation, the costs are lower in the CM group? Requires explanation and/or additional statistical review and conclusions do not appear supported by analyses as presented currently.

4. How many participants achieved the criterion of attendance at 4/6 psychoeducation sessions in each condition? Consider adding percentages to Table 2.

5. Were analyses done separately for heavier vs. light cannabis users? The authors may want to comment at whether testing at the 50 ng/ml cutoff threshold may have over-estimated abstinence among light users in both conditions.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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