**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:** 01 Mar 2019

**Reviewer:** Michael Mcdonell

**Reviewer's report:**

This study addresses a very significant issue, determining whether or not incentives can be used to reinforce cannabis abstinence in a sample of youth with FEP. It has a large sample and seeks to investigate if the intervention is associated with reductions in psychiatric relapse. The paper describes cost-outcomes associated with changes in psychiatric and related outcomes. While no conceptual model is provided, the authors hypothesize that reductions in cannabis use will result in reductions in acute psychiatric care and associated costs. While the introduction describes some research to support an association between cannabis use and psychotic symptoms, they do not describe literature that specifically supports their hypothesis. Some studies support the association of cannabis use with acute psychiatric care and these should be discussed. The authors do not describe studies of contingency management for people with serious mental illness, including Bellack 2006, Tidey et al, 2011, McDonell et al, 2013, McDonell et al, 2017. Rabin et al 2018 investigated a contingency management intervention for cannabis in people with serious mental illness and found results similar to those described here. Similarly, there is a body of literature on contingency management for cannabis use that is not discussed, such as Stanger et al., 2015 and the work of Budney and colleagues in general. This relatively large literature needs to be described to place the finding of this study in the context of what is already known about contingency management for those with co-occurring disorders and cannabis. Also there is a relatively large body of literature on the cost-effectiveness of contingency management, including one study (Murphy et al., 2015) that demonstrated the cost effectiveness of contingency management in people with serious mental illness. These studies, particularly Murphy et al., provide already existing frameworks for cost-analyses. Did the authors base their economic on these models or another model? It appears they utilized a different approach and a justification for this approach, eg not including savings related to changes in PANSS scores or abstinence should be offered.

Throughout the study the authors refer to relapse when they mean psychiatric relapse or acute care. This is a study of a drug use intervention so the term psychiatric relapse should be use as relapse typically refers to using drugs again after abstinence.
In terms of the methods. It is unclear why the only outcome of the study is psychiatric care utilization, not cannabis use, when the link between drug use changes in contingency management (or treatment of addiction) and psychiatric care utilization is under-developed. Further cannabis, out of all drugs (and alcohol) may have the weakest association to acute care utilization.

In terms of the statistical analyses, an end of treatment and follow up assessment is unusual and fails to utilize the power of repeated measurement. Best practice analyses of contingency management assessments of drug outcomes is not to look at end of treatment abstinence, but rather to utilize approaches like generalized estimating equations. This allows for data during treatment to be considered. It may be that reductions in use, rather than complete abstinence are clinically significant. The conclusion that contingency management is not effective for cannabis use is not appropriate unless more sophisticated analyses are conducted.

In terms of the lack of efficacy of the contingency management intervention, it is likely that the frequency of reinforcement, rather than the magnitude of incentives/costs of the reinforcers would lead to a null finding. The amount paid to participants is consistent with other effective contingency management interventions.

It is also possible that a 50 ng/mL cutoff for abstinence might have been too conservative. That is, it may have made it challenging for individuals to meet criteria for reinforcement, especially heavy or daily users. A higher cutoff that is more likely to assess very recent abstinence in regular users might have been more effective.

Defining psychiatric relapse as acute care utilization, as opposed to psychiatric symptoms misses important and cost associated clinical outcomes.

Why were QALYs not based on the PANSS scores?

Exclusions included homelessness and court involved individuals, those who would have mostly likely benefited from the intervention.
This study proposes a mediating model but does not test mediation. This seems strange, especially as they have the sample size to test mediation.

Given the sample size it would be important to conduct additional analyses to determine why the intervention didn't work or perhaps identify individuals who it might have worked best for (e.g., those with less severe cannabis use).

There are a number of findings that are described as differences, but they are not statistically significant. None significant findings should not be discussed as being different.

In terms of the conclusions of the study, without a more refined approach like GEE, it is uncertain if contingency management is effective or not in this sample. Just because it is not associated with reductions in psychiatric care and cost doesn't mean it's not effective.

The findings of this study must be placed in the larger literature on contingency management. How were the results similar or different and why didn't the intervention demonstrate efficacy on outcomes? The paper overall, tends to "throw the baby out with the bath water" in terms of suggesting that results of this study indicate the lack of the intervention's efficacy. Placing them in the context of the literature would allow readers to determine exactly how this study contributes to what is already known.

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

Yes

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