Reviewer's report

Title: Creating groups with similar expected behavioural response in Randomized Controlled Trials: a fuzzy cognitive map approach

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Reviewer: Wenle Zhao

Reviewer's report:

The manuscript titled “Creating groups with similar expected behavioral response in randomized controlled trials: a fuzzy cognitive map approach” proposed a new treatment allocation method for randomized controlled clinical trials in order to ensure the similarity of treatment groups with respect to the expected responses under given interventions.

There are few concerns regarding the method proposed in this manuscript:

1. Throughout the manuscript, it is not clear that the proposed method is designed for sequential randomization, or randomizing all subjects at the same time. In some behavioral trials with a small sample size, it may be feasible to randomize all subjects together. However, in general, sequential recruitment and randomization are more common. If the proposed method does design for sequential clinical trials, it is important to clearly indicate that. Based on the contents on page 10 line 288, this method will work in sequential trials. The completion of the baseline survey for all subjects is not an assumption; it is actually a requirement for the following FCM built.

2. The requirement for equal treatment group size in randomized controlled clinical trials is not necessary. Although equal allocation ratio is preferred due to equipoise and efficiency considerations, the treatment group size will not bring in bias in the trial results. The cost in power due to group size imbalance is often trivial. Please see Stephen Senn, Seven myths of randomisation in clinical trials, Stat Med 2013 Apr 30; 32(9):1439-50.

3. The type I error of a trial could be inflated due to the way the treatment allocation is affected by baseline covariate balancing. To justify the validity of this proposed method, it is important to investigate the type I error. If it is actually affected, proper justification in the analysis will be needed.

4. The generalizability of the trial results is the key to the validity of the trial. There is concern for the proposed randomization method regarding the generalizability of trial results. By balancing the baseline confounding factors based on individualized survey results on the relationships between the confounding factors and the response outcome, rather than the observed baseline profile, the result of the trial will be hard to be interpreted. In other words, the estimated treatment affect based on the study sample will not be applied to the target population, unless such survey is conducted for the target
population.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.