Reviewer’s report

Title: Preference-adaptive randomization in comparative effectiveness studies

Version: 1  Date: 10 December 2014

Reviewer: Bruno Giraudeau

Reviewer’s report:

Major Compulsory Revisions
This paper is very well written and easy to read. It exposes a novel method of implementing randomization in case we may suspect a high refusal rate of the randomization result among patients. The strength of the approach is enforced by a real-world example.

I however feel a bit disappointed by the fact that authors only focused on the randomization step, without illustrating the implication of their approach on the treatment effect estimation. Thus they clearly demonstrated that using their approach, they were able to obtain groups of patients with acceptable balance (in numbers). They then evoked using an instrumental variable approach to analyze data, but without providing any result. I would indeed be much more interested in having a complete view of the issue, which would be more convincing. Indeed, a numerical balance between groups is of importance for power, but a non-biased assessment of the intervention effect is surely of greater importance. My feeling is therefore that we miss a section demonstrating that such an approach is able to provide non biased treatment effect estimates.

Minor Essential Revisions
Table 4 displays the characteristics of the patients randomized and, unsurprisingly, there is no imbalance. Indeed, I don’t see why changing the randomization ratios over the trial would induce imbalance. However, authors specified (in the Discussion section!) that “balance across arms was not uniformly achieved when evaluating inly participants who accepted their assigned intervention” (which is not surprising, since acceptance is probably surely linked to some baseline characteristics, which may also be prognostic factors), and I indeed would be very interested in seeing these imbalances. Authors cannot just say “data not shown”.

The proposed approach supposes that there is no participant blinding in the trial, and that we may suspect a differential acceptance rate. Such a context is not so frequent, although authors indeed illustrate it with a real-world example. I think some specifications of the context in which such an approach could be of help is necessary.

Level of interest: An article whose findings are important to those with closely related research interests
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