Reviewer's report

Title: Optimising recruitment of participants to a phase I/II trial using the internet and publicity releases through charities and patient organisations: analysis of the Adaptive study of IL-2 dose on regulatory T cells in type 1 diabetes (DILT1D)

Version: 2
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Reviewer: Lorraine Buis

Reviewer's report:

This manuscript describes the overall success of three recruitment modalities for a Phase I/II mechanistic clinical trial in a sample of type 1 diabetics. Although the paper is technically well written, it suffers from areas of diminished clarity. In addition, it feels at times that the authors are writing this in order to get another publication out of their trial. While I do believe that there is potential for publication in the future, I feel that additional work needs to be done to improve clarity and overall framing of this secondary data analysis in order to make this piece stand on its own and contribute to the existing body of knowledge.

Major Compulsory Revisions:

1. Background: I'm confused. You say in the last paragraph of this section that “the statistical design of the DILT1D phase I/II trial required a relatively large number of participants to be recruited to complete the study” yet you only ultimately enrolled 40. Perhaps this is my naivety regarding mechanistic trials, but this seems like a very small sample to me. I recognize that the potentially eligible sample of newly diagnosed T1D is probably relatively small at one recruitment site, so perhaps that is why you initially estimated 2 years for recruitment. I guess this is the long way of me trying to indicate that if your recruitment goal of 40 participants is what you would consider difficult to achieve, please provide some context about how many people mechanistic trials typically enroll, how many potentially eligible participants there were at your site, and how long it typically takes to hit those recruitment targets.

2. Background: You’ve done a nice job explaining the main trial (although, perhaps a little too much detail as I previously mentioned), but you fail to adequately address the purpose of this secondary data analysis. You briefly touch on it, but a more explicit statement of the goal of this secondary data analysis, along with a stronger rationale for why this manuscript contributes to the existing body of literature, would strengthen the paper overall and help provide a better frame for telling your story. The question that this manuscript attempts to address is not well defined. As it stands, this manuscript isn’t framed well enough and reads as an attempt to squeeze out an additional publication.

3. Results (Analysis of Trial Outcome of Participants by Recruitment Source): I had a very difficult time following this section. I feel like either a.) more
scaffolding needs to be provided for your readers in the form of additional subheads, or b.) a more logical flow of results needs to be presented; for example, providing all info pertaining to people expressing interest by modality, all people enrolling by modality, etc.

4. Discussion: I would like to see more attention paid in this section to take-home points that can be shared with other researchers. Positioning this manuscript within the larger body of literature will help people understand better what this piece contributes to the literature. Also, how generalizable is this study? What are the implications for future work?

5. Discussion: What were the limitations of your approach?

Minor Essential Revisions:

1. Methods: It is not clear whether you are screening individuals who are <100 days or < 2 years post diagnosis. Please clarify.

2. Methods: Regarding the Facebook and Twitter accounts created for your study, did you do anything to actively promote your trial within those channels? For example, did you continually post status updates and tweets?

3. Methods (Recruitment Data): After reading it a few times, I think I understand what you are trying to say, but the following is not very clear, “A single ‘trial outcome’ was defined for each potential participant. The five trial outcomes were:”

4. Results (Analysis of Trial Outcome of Participants by Recruitment Source): I liked your presentation of how many potential participants came from the ADDRESS-2 Register, followed by how many of those responded to the contact and how many ultimately enrolled. I would have liked to see that fleshed out fully for the other two recruitment modalities.

5. Results (Analysis of Trial Outcome of Participants by Recruitment Source): “Final trial outcome differed according to recruitment source.” This is not clear. I think perhaps that many of the clarity issues that I find in this section may be caused by confusing terminology. Also, didn’t you say in the previous section that there were 5 possible outcomes?

6. Discussion: You conclude that you successfully achieved enrollment of the study in a timely and efficient manner. As I previously mentioned, without additional context about the difficulties you anticipated in your recruitment, 13 months to recruit 40 people will not sound impressive to the majority of readers.

7. Conclusions: You state that “potential participants favoured the internet…” Is it that the potential participants favoured that modality, or is it that that was the most readily accessible modality? It certainly had a broader reach, which doesn’t necessarily suggest to me that potential participants favored the modality.
Discretionary Revisions:

1. Background: As a reader expecting to learn about recruitment strategies for a clinical trial, I found myself bogged down in the details of the trial itself. While it is important to describe the trial, I can’t help but feel that there is too much detail, which ultimately leads to clarity issues within this section.

2. Methods: Again, there is a lot of detail here about the trial itself, which detracts from the purpose of the present secondary data analysis. Personally, I’d like to see a briefer description of the main trial and its methods, and then the citation to follow-up with if I have more questions.

3. Results (Demography of Potential Trial Participants): How does your recruitment of males and females reflect the incidence of T1D among males and females?

4. Results (Demography of Potential Trial Participants): Was there any difference in the demography of enrolled participants across the three recruitment sources? I’m not sure if that will add anything to the overall manuscript, but I couldn’t help but wonder.

5. Title: I’m not convinced that the title accurately conveys what has been found in this manuscript. “Optimizing Recruitment” suggests to me that you iteratively changed your methods in order to maximize recruitment. The paper describes a methodology that set out to use these three modalities, and then you described what you found.

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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.