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
Date: 4 November 2014

Reviewer: Colin CM Dayan

Reviewer’s report:

This is a well written article that attempts to explore the relative benefits of single centre recruitment using national databases and internet recruitment versus local clinic recruitment for an experimental study.

The results are generally described and of interest but more attention could be devoted to the exploring the potential “downsides” of recruiting people who live a long distance from the trial centre including the introduction of unrepresentative selection bias in the study population, the risk of defaulting from follow-up visits and the cost of re-imbursement for distant travel and accommodation.

Major points:

1. Mention clinic recruitment figures in abstract (only register and internet figures quoted) and something about evidence or not of recruitment bias from the different sources.

2. Need to distinguish newly- (< 100 d) and recently (< 2 years) diagnosed groups in the analysis and show these figures. Specifically, this relates to whether the three approaches are equally good for incident (new-onset) versus prevalent (< 2 years) disease. Comment on which approach would need to be used for a new-onset study (< 100d).

3. Is there any data on insulin production in the trial participants to inform future recruitment of c-peptide positive participants?

4. Clinic database search – on date of diagnosis? Was this routinely recorded in clinic records?

5. Can we have baseline demographics as a table in the main article – age, distance from Trial site, gender, duration of diabetes broken down by recruitment source. Can we include HbA1c, socioeconomic class, other family member with diabetes if available, to understand bias that may be introduced by different recruitment approaches (or not).

6. Table 1 – need to also quote as percentage of the subjects recruited by this route, not just total numbers.

7. Page 11 para 3. Recalculation of the success of different sources of recruitment corrected for volume of participants – please show individual %s as well as chi-squared value.
8. Page 11 last paragraph. Further analysis and comment on distance travelled by source please e.g. (1) were they offered local accommodation for some or all of the duration of the study e.g. from Scotland, Ireland and France – and how did this impact on costs. (2) were there any issues on verifying medical info e.g. from GPs/clinics for distant participants (esp from other countries) (3) Overall travel/accommodation costs for different routes of recruitment and comment vs rapid trial completion

9. Claimed in discussion that distance was not a barrier – but this was still a greater issue for the register and internet than the clinic participants (as expected).

10. Please provide data on missed study visits/non-completion of the study and did this depend on recruitment source/distance.

11. Why did the initial internet post only “work” once – the surge Jun-Aug as not repeated. Was this not posted twice? Was it not required?

12. Note on time commitment issues for Register participants – suggests that they might be made aware of this earlier/when they register – ie many do not expect to commit time in future to research studies….they signed up for a one-off questionnaire and blood sample. The comment on which study team approached them first is also important.

13. Were there any particularly flexible arrangements – e.g. weekend study visits? – that made a difference in this study (and made distant travel easier)

14. Press releases were important and were most effective as they access many outlets – can you say more about where they went to? E.g. how many newspapers picked the press release up? Any tips to getting it picked up? Can this only really be done once (as the topicality and news-worthiness wear off?)

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I am part of a Consortium grant bid that includes some of the authors.