Author's response to reviews

Title: The INTERVAL Trial to determine whether intervals between blood donations can be safely and acceptably decreased to optimise blood supply: study protocol for a randomised controlled trial.

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Version: 3
Date: 19 August 2014

Author's response to reviews: see over
Editors-in-Chief
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c/o BioMed Central
236 Gray’s Inn Road
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Dear Sirs

Re: MS: 1798585572132289. A randomised controlled trial to determine whether intervals between blood donations can be safely and acceptably decreased to optimise blood supply: protocol of the INTERVAL trial

Dear Sirs

I refer to the peer review of the above-mentioned manuscript and thank you for the comments received on 22 July 2014. I am pleased to provide updated copies of the manuscript (one with tracked changes and one clean copy) incorporating amendments based on the reviewer’s comments and editorial requests which are detailed below together with the authors’ responses.

1. MAJOR COMPULSORY REVISIONS

a) Abstract

Comment: The authors used the title “Methods/Design” rather than “Methodology”, which is the standard title for this section in the journal TRIALS.

Response: The abstract title has been amended as requested above.

b) Background

Comment: The authors wrote in their covering letter that they recruitment is expected to be completed by mid-June 2014, which is before this protocol will be published. Please, describe the status of the study at submission to TRIALS at the end of the BACKGROUND section.

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Response: The last person was recruited to the study on 15th June 2014 and the manuscript was submitted to trials on 10 June 2014. Therefore the sentence ‘We confirm that recruitment into the trial was ongoing at the time this manuscript was submitted for publication.’ has been added at the end of the ‘Background’ section.

c) Methodology
Comment: The authors used the title “Methods/Design” rather than “Methodology”, which is the standard title for this section in the journal TRIALS.

Response: The title of the methodology section has been amended as requested.

d) Intervention
Comment: Men will be allocated to “standard 12-week versus 10-week or versus 8-week inter-donation intervals while women will be assigned to 16 vs 14 vs 12-week intervals. It is unclear in my mind if this RCT is about the effect of advices to participants that they can donate in shorter intervals or is about the effect of shorter intervals?

If it is the latter question that is the primary question of the RCT, than how the investigators will deal with participants who deviate significantly from their allocated intervals should be better described in the manuscript. How will be collected data on intervals between donations is not detailed in the manuscript.

Response: The study addresses the effect of inviting donors to participate at standard or shorter donation intervals. It is expected that not all donors will be able to attend every donation, over a 2-year period, at study-prescribed intervals. This will be for a variety of reasons including temporary deferral of future donations due to low haemoglobin levels – an important secondary outcome of the trial. The sample size calculations take account of the likelihood that the maximal number of donations will not be achieved – this is described in the ‘Sample size – sample size calculations related to the outcomes’ section of the manuscript (page 16) i.e. ‘when considering the current non-attendance rates of donors, such maximal differences based on more frequent donation intervals are unlikely to be achieved in practice.’ Hence, the power calculations are based on having 80% power to detect a more realistic 5% increase in the number of donations over two years.’

Data on participants’ donation appointments and attendance during their two-year involvement in the study are retrieved from NHSBT’s national donor database and transferred to the University of Cambridge academic coordinating centre on a daily basis. The INTERVAL research database is populated with these data and will allow adherence in each of the randomised groups to be assessed. The collection of these data is detailed in the section ‘Baseline data collection’ (page 11) i.e. ‘data management processes [include]...retrieving data on donors at regular time-points from NHSBT’s donor database and securely transferring these to the trial coordinating centre for the purposes of monitoring appointment bookings and attendance, deferrals, adverse events of donation, positive microbiology and deaths.’

An enhanced approach to appointment reminders, than is NHSBT’s current practice, has been implemented in INTERVAL. This approach is being taken to augment adherence to study donation intervals such that the safety of more frequent donations can be assessed. Further details of the reminder procedures have been added to the manuscript at the end of the section ‘Participants and setting’ (page 7) i.e. ‘ISAT has supported the trial to enable participants to make appointments to give blood at intervals that are more frequent than current NHSBT practice (which is not possible through NHSBT’s routine appointment system). To enhance adherence of trial participants to their allocated donation intervals, ISAT has used more intensive and systematic efforts than used in routine NHSBT practice to remind participants about their blood donation appointments, including a systematic three-step telephone and e-mail reminder process.’
2. MINOR ESSENTIAL REVISIONS (not for publication).

a) References

Comment: The references must be formatted according to the editorial standards of the journal TRIALS:

- The appropriate abbreviation should be used for the name of each journal (for example, Transfus Med Rev rather than Transfusion Medicine Reviews in reference 10).
- Delete all texts like “official journal of…” at the end of journal names.
- Reference 5. – Is this reference complete?
- Reference 6. – Is this reference complete?
- Reference 18. – Do not use capitalized words in the title.

Response: All references are now formatted according to the editorial standard of the journal TRIALS in particular
- Appropriate abbreviations are now used for each journal
- All texts like “official journal of…” have been deleted from the end of journal names
- “Lancet” has replaced “The Lancet” in reference 1
- Full references for Ref 5 and Ref 6 have been added
- Capitalised words have been removed from the title in Ref 18

b) Tables and captions

Comment: The legend of each table must include the definitions of all acronyms used (GP in table 3, HFE in Table 4, etc).

Response: The definitions of acronyms in Tables 3 and 4 have now been added

3. EDITORIAL REQUESTS

Comment: Please mention each author individually in your Authors’ Contributions section. We suggest the following kind of format (please use initials to refer to each author’s contribution): AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

Response: The following details have now been added to the ‘Author contributions’ section of the manuscript: ‘JD and DJR are the chief investigators. WHO, ST, CM, EDA and JM are co-investigators. JD, DJR, WHO, ST, CM, EDA and JM supervised the trial protocol development. ST is the chief statistician. CM is the trial coordinator. JS is the laboratory coordinator. MW is the chief data manager. SM leads the coordination of NHSBT’s operational role in the trial. ZT and DA contribute to the scientific and operational trial coordination. SK is the statistician providing confidential data for review by the Independent Data Monitoring Committee. CM and ZT wrote the initial draft of the paper. JD, DJR and ST contributed to writing the paper. All members of the writing committee have contributed to the conception, design, and execution of the trial, and have read and approved this submitted version of the manuscript.'
4. AUTHORS ADDITIONAL REVISIONS TO THE MANUSCRIPT

In re-reviewing the manuscript the authors have made a number of minor changes to the manuscript. These changes have been made either i) ensure that the manuscript conforms to the journal style or ii) to correct inaccuracies or ambiguity. These changes are highlighted in the tracked changed copy of the manuscript and more notable amendments are summarised below:

a) Author affiliations

Title Page: Full addresses of authors’ institutions have been provided.

Trial status (Page 22): The date that the last participant was recruited was 15th June 2014, rather than the previously stated date of 13th June 2014

Acknowledgements (Page 23 - 25): The role of all Trial Steering Committee members have been added. All acknowledgement listings are now in alphabetical order.

Thank you for your consideration of our above responses and revised manuscript. If you should require any further information please do not hesitate to contact me.

Yours Sincerely

Carmel Moore