Author's response to reviews

Title: A post-trial survey to assess the impact of dissemination of results and unmasking on participants in a 13-year randomised controlled trial on age-related cataract

Authors:

Sally L Williams (sallylouise.williams@unipr.it)
Luigina Ferrigno (luigina.ferrigno@iss.it)
Giovanni Maraini (giovanni.maraini@unipr.it)
Francesco Rosmini (francesco.rosmini@iss.it)
Robert D Sperduto (bsperduto@nc.rr.com)

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Author's response to reviews: see over
Dear Editors,

we are submitting a revised version of our manuscript in light of the Referees’ helpful comments. Please find enclosed a point-by-point response to the concerns of the Referees, that we have addressed in the revised manuscript. We have highlighted in yellow all changes made when revising the manuscript to make it easier for you to review it.

We look forward to hearing your decision on our manuscript.

Best regards

Sally Louise Williams
Clinical Trial Coordinator
Section of Ophthalmology
University of Parma
Italy

Tel.: +39-0521-033472
Fax: +39-0521-347005

Point-by-point response to the comments of the Referees

In response to the comments of Referee 1:

“The manuscript describes the return of results and impact upon participants of individual results……”: it is important to note that we did not present individual results to the participants but only the overall results.

1. The Italian and English languages differ in many ways: to express the same concept Italian requires a greater number of words than English and on average Italian words, even the most common, contain more letters than the corresponding English words. The Flesch-Kincaid readability formula takes into consideration the total number of words, the number of syllables, as well as the total number of sentences, and was designed to assess US school level. Different methods are used for different languages and therefore we think that the Flesch-Kincaid readability formula is not applicable to an Italian text. The issue here is the Italian letter addressed to an Italian population, not the English translation. To our knowledge there is no method to evaluate readability of an Italian text.
2. On page 4 line 22-25 we have added: “The material for dissemination of the results to the participants (a letter and two questionnaires) was prepared by the Steering Committee and was shown to a small number of elderly patients to ensure that it was clear and comprehensible”. On page 5 line 11-13 we have added “The letter and questionnaire 1 were initially mailed to 50 CTNS participants: since the questionnaire seemed to be sufficiently clear to these patients, we then proceeded with the dissemination of the results”.

No formal validation of the questionnaires was implemented. On page 5 line 7-8 we have added: “The questionnaires used in the survey were not formally validated”.

3. As shown in the flow diagram and explained in the text on page 6 line 17-19, the results of the trial were sent to the 862 CTNS participants who were alive at the end of the trial.

4. On page 5 line 8-10 we have added: “…given the age of our patients and the objective of our survey, we chose to use a questionnaire with a very simple structure, easy to complete and patient-friendly”.

5. CTNS participants were followed on average for 9.0+/−2.4 years and right from the beginning of the trial we established a close relationship with them as demonstrated by the low rate of losses to follow-up (15%). Participants looked forward to receiving the results and many contacted us not only to request clarifications but simply to express their gratitude to us for having followed them for so many years. The request for “further information” also occurred during the final eye examination that we offered to thank participants for their collaboration during the trial (page 5 lines 21-22).

6. Patient follow-up ended in May 2007. The patients were told that we would communicate the trial results after official publication (in a peer-reviewed journal). The final paper was published in April 2008. The patients waited a whole year for the results and many were curious to know to what treatment they had been assigned. Some patients came to the clinic to inquire why there was a delay in the dissemination of the results. In the text we have added the following sentence on page 9 line 17-18: “A year elapsed from the last follow-up visit to publication of the trial results in a peer-reviewed journal. Moreover…”.

7. “The study manager and an interviewer were responsible for maintaining contact with the patients” has been added to the text on page 5 line 2-3. How this was accomplished is explained in the text in the Methods section (pages 4-6).

8. Yes. This issue is addressed on page 7 line 22-25 and on page 8 line 1-2: “If patients were subdivided according to selected mode of communication with study staff (face-to-face, telephone, no contact)………..”.

9. Formatting issues in Table 1 and 3 have been solved. The abbreviation (CTNS) in the title of Tables 1 has been spelled out.

10. We have no way of knowing whether the differences in our responders and non-responders affected the findings. We have added the following sentence on page 11 line 13-15: “We cannot exclude the possibility that differences in the characteristics of responders and non-responders (see age, sex and lower education in Table 2) may have affected the findings for our study population”.
11. The original supplementary documents were in Italian. A member of our staff is bilingual (English/Italian) and she translated and back-translated all the supplementary documentation provided with the manuscript.

In response to the comments of Referee 2:

1. We have clarified throughout the text that the findings for cortical opacities were not statistically significant:
In the Abstract on page 2 line 7, we have added: “…and no statistically significant effect on cortical opacities”. To reduce the exceeding words (350 word limit) we deleted “…who completed the questionnaire…” on page 2 line 14-15 in the original manuscript and “…of the trial…” on page 3 line 6 in the original manuscript.
On page 4 line 3-4 we have added “…and no statistically significant effect was observed on cortical cataract”.
On page 6 line 24-25 we have added “…and no statistically significant effect was observed for cortical opacities”.

To further explain why we chose not to recommend supplement therapy given the significance of the finding for “any cataract” we have added on page 4 lines 1-7: “Use of the dietary supplement appeared to have a beneficial effect on any cataract (all types of cataract combined) and on pure nuclear cataract; a harmful effect was observed on posterior sub-capsular cataract and no statistically significant effect was observed on cortical cataract and on important functional end-points (visual acuity or cataract surgery). These findings, in particular the opposite effects on the two most visually significant cataract types, prevented us from making recommendations about use of one-a-day multivitamin-mineral supplements to affect the risk of cataract development [2]”.

2. This has been done.

Other modifications to the original version of the manuscript:

The sentence “Letters were sent in batches until September 2008 to spread the workload generated by the letters”, located on page 4 line 22-24 in the original manuscript, has been moved to page 5 line 13-14.

Reference #2 has been corrected: authorship of CTNS Report No. 3 is the CTNS Study Group, not individual authors.

Table 1: in the title the word “(Italy)” has been deleted not to exceed the maximum of 15 words allowed by the journal.
Due to space constraints “PSC” has been introduced in the table with a footnote spelling it out.

Table 2: in the title “CTNS” and “trial” have been deleted not to exceed the maximum of 15 words allowed by the journal.