Author's response to reviews

Title: Impairment reduction in older dizzy people: design of a cluster-randomised controlled trial in primary care

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

On behalf of the contributing authors, I am pleased to submit the revised version of our manuscript entitled “Impairment reduction in older people in primary care: study protocol for a cluster-randomised controlled trial”. We would like to thank you and the reviewer for your feedback. Our point-by-point reply to the editorial requests and the reviewer’s comments is presented below. The enclosed version of the manuscript has been prepared taking into account the suggestions of the reviewer. In the revised manuscript we have marked the changes in the text.

I hope the revisions are satisfactory and I look forward to your response.

Yours sincerely,

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Author’s response

Response to editorial requests:
1. Please ensure the title conforms to journal style for study protocol articles. The title should follow the format ?___________: study protocol for a randomized controlled trial.? Please note that the title in the submission system should match that of your manuscript.
   We changed the title of our manuscript into ‘Impairment reduction in older people in primary care: study protocol for a cluster-randomised controlled trial’.

2. Please remove the word counts from your title page.
   We removed the word counts form the title page.

3. Please include the date of registration with the trial registration number at the end of the Abstract.
   We included the date of registration in the Abstract.

4. Please include the full name of the approving ethical committee with your ethics statement in the Methods section.
   We included the full name of the approving ethical committee, i.e. Medical Ethics Review Committee of VU University Medical Centre.

5. Please include a statement in your Methods section explaining that you obtained informed consent from each participant.
   The Methods section already included the following information about informed consent: ‘Before the start of baseline assessment, the patient will be asked for written informed consent’. We changed this sentence into: ‘Before the start of baseline assessment, written informed consent will be obtained from each participant.’

Response to the reviewer:
1. Will the study design adequately test the hypothesis?
   The intended sample size is small, for interventions that are likely only to have a modest benefit on symptoms over and above time, and almost certainly too small for meaningful subgroup analysis. Of course, a loss to follow up of 20% will be too great to allow any meaningful conclusion to be drawn from the study, but I am sure the investigators would agree.
   We thank the reviewer for his thoughts on the sample size of our study and the opportunity to provide background information on our sample size calculation (see below). We believe that the intended sample size is sufficient. We agree with the reviewer that our sample will probably too small for meaningful subgroup analysis. Therefore, we deleted the section about subgroup analysis in the manuscript.

   In order to detect a clinically relevant difference with alpha=0.05 and beta=0.10 we used the following formula to calculate the sample size [1]:

   \[ n = 2(1.96+1.28)^2S^2/D^2 \]

   With \( n \) = number of patients, \( S \) = standard deviation, \( D \) = clinically relevant difference.
   Based on earlier research on our primary outcome measure (Dizziness Handicap Inventory, DHI) we believe 12 points change is a clinically relevant difference [2]. The standard deviation of the mean change in DHI scores in a similar population as in our study was 19.9 [3].
   A group size of \( n=58 \) is sufficient \( (2(1.96+1.28)^2*19.9^2/12^2) \). Then we applied an extra correction since the proposed study is a cluster-randomised trial. The correction that needs to be applied by performing a cluster-randomised trial can be calculated with the following formula:

   \[ n = 1+(k-1) * \rho \]

   With \( n \) = number of patients, \( k \) = cluster size, \( \rho \) = intra-class correlation (ICC).
Based on secondary analysis of a former study we expect a cluster size of 8 patients in each practice [4]. An ICC of 0.01 is often used in sample size calculations in primary care research [5] but we used an ICC of 0.05 to get a more conservative sample size. The correction factor for performing a cluster-randomised trial is 1.35 \((1+(8-1) \times 0.05)\). This means that a groups size of \(n=78\) \((1.35\times 58)\) is sufficient. Because of a assumed high mean age of the study population, we expect a relatively high loss to follow up rate as a result of multimorbidity and decease. With the assumption of a 20% dropout rate we need a sample of \(78\times 1.25 = 97\). We rounded this up to 100 patients.

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing? The main thing with any complex intervention is that they are sufficiently well described for them to be replicated; for example the problem solving treatment, guided self-help and physiotherapy protocols could be expanded in a supplement.

While describing our interventions, we focused on the main features to prevent the intervention section from becoming too long. By doing so, some important details of the interventions were not described. Therefore, we added more information on guided self-help, problem solving treatment and the physiotherapy intervention in the revised manuscript. We hope that these changes will now sufficiently describe the interventions for them to be replicated.

The health care providers who carry out the interventions receive study intervention protocols. The protocols for problem solving treatment, guided self-help and physiotherapy are extensive -53 pages, 95 pages and 11 pages respectively-, and written in Dutch. For this reason we did not expand these protocols in a supplement. However, if readers of our study protocol are interested in the full protocols in Dutch, we would be happy to send those on request.

3. Is the planned statistical analysis appropriate? It is unclear how the analysis plan will deal with those lost to follow up, or those who do not fill in their questionnaire: is there a plan to impute data?

Yes we have planned to impute data.

4. Do the figures appear to be genuine, i.e. without evidence of manipulation? yes

5. Is the writing acceptable? I think the labelling of three groups A,B,C is confusing. Why not just have a trial, and an observational cohort - much easier to understand.

We agree that the labelling of groups A, B and C may be confusing. For this reason, we changed the labelling of the three different groups into ‘intervention group’, ‘control group’ and ‘observational cohort’ in the manuscript and in figure 1.
References


