Author’s response to reviews

Title: FRAILTOOLS STUDY PROTOCOL: A COMPREHENSIVE VALIDATION OF FRAILTY ASSESSMENT TOOLS TO SCREEN AND DIAGNOSE FRAILTY IN DIFFERENT CLINICAL AND SOCIAL SETTINGS AND TO PROVIDE INSTRUMENTS FOR INTEGRATED CARE IN OLDER ADULTS

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Author’s response to reviews:

1) BMC Geriatrics requires ethics approval to have been obtained from all sites where the research is to take place before submission of a study protocol. These documents should be sent as email attachments to the following email address, BMCSeriesEditorial@biomedcentral.com. Please DO NOT upload these documents as additional files in the submission system. If your documents are not in English, please could you provide translated versions of the relevant parts. These should be endorsed and signed by a contactable person at the institution.

Answer: Please, find attached by email the ethics approval obtained from all sites where the research is taken place and the translation of the relevant parts.
2) We note that the role of Diabetes Frail Limited [DIFRAIL] (listed in the submitted funding documentation) has not been detailed in the manuscript. Please ensure that all partners/collaborators in this study are referenced in the Declaration section, and any possible conflicts of interest described.

Answer: Initially, Diabetes Frail Limited [DIFRAIL] was one of the partners in this study (the partner from United Kingdom), afterwards and before the starting of the recruitment this institution was replaced by Aston University from United Kingdom also.

3) We also note that your trial registration on ClinicalTrials.gov and project details on the CHAFEA EU Health Programmes Database (https://webgate.ec.europa.eu/chafea_pdb/health/projects/662887/summary) indicate that the study termination date is anticipated for May and December 2018, respectively. As detailed in our guidelines (https://bmcgeriatr.biomedcentral.com/submission-guidelines/preparing-your-manuscript/study-protocol), the protocol must be for a study that is ongoing. An ‘ongoing’ study is defined as one where the investigators are still collecting, or analysing data. Can you please confirm the current status of your study and the intended time-frame for publication of full results.

Answer: The study is ongoing, we are finishing the follow-up visits on November 30th, we have started the data analysis on November 1st 2018, through April 1st, 2019. The publication of the full results will take place on June 2019.

4) Please provide a section in the Methods to justify the intended sample size.

Answer: We have added the following information to justify the intended sample size:

In order to determine the sample size, we have used two assumptions:

1. The sample size is calculated according to the methodology of Peduzzi et al. (Peduzzi et al. 1996) for a model of 4 variables. The variables included are: age, gender and Charlson index as covariates and frailty status as the main independent variable of interest.

2. The outcomes to be assessed will be death, falls, disability and deterioration in cognitive function. Among these variables, death is the least frequent and generates the highest sample size therefore it can be used for the other three outcomes.
Although there are some little differences in the mortality rates among the five European countries that participate in this project; the mean mortality rate for people aged ≥75 years in these countries is 10% annually. Therefore, in 18 months it will be 15%, which is the follow-up period forecasted in FRAILTOOLS project.

Within these assumptions the lower limit of the 1-α confidence interval for the accepted number of success is 355 and 388 participants in each setting of care for 95% and 99% CI, respectively. This number must be increased with the forecasted lost to follow-up, in 20%. As a whole, the final sample size is established in 485 persons per setting, which means a final figure of 1940 persons. Thus, every partner will be responsible for the enrolment, assessment and follow-up of 388 older adults (97 per setting).

5) A study is considered to be externally funded if the authors have been awarded a grant for the study by a major funding body (e.g. governmental funding/award from a charitable foundation). If a study has not received external funding, then the study protocol will be sent for peer-review with a member of our Editorial Board. If a study has received funding/assistance from a commercial organization, this should be clearly stated in the 'competing interests' section of your manuscript, and the study protocol will be sent for peer-review by a member of our Editorial Board. Can you please confirm whether your study protocol has undergone peer-review by the funding body.


The authors declare that they have no competing interests.

6) Please provide further details in the Declarations section regarding consent procedures for patients that pass away during the follow-up phase of the study.

We have provided further details in the declarations section:

Answer: In case a participant dies during the follow-up phase of the study, the information will be recorded in the eCRF of the follow-up visits at 6, 12 or 18 months. A document to record death will be filled as an adverse event unrelated to the study. Data regarding mortality will be obtained from the official register of the country of the corresponding partner.

Note:

It is also important to mention that this study is observational and no further procedures regarding death will be obtain.
7) We strongly suggest including a figure illustrating the flow of the study, such as is described in the SPIRIT guidelines. [https://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/](https://www.equator-network.org/reporting-guidelines/spirit-2013-statement-defining-standard-protocol-items-for-clinical-trials/)

Answer: it is added in the manuscript

Time point

Baseline
T1 Follow up
  Month 6
T2 Month 12
T3 Month 18
T4

ENROLLMENT:
Eligibility screen X
Informed consent X

ASSESSMENTS:
Socio-demographic data X X X
Charlson Comorbidity Index X X X
Barthel Index X X X
Lawton Index X X X
SPPB X X X
MMSE X X X
Fried’s Frailty Phenotype Criteria X X X
Frailty Trait Scale – short version X X X
SHARE Frailty Instrument X X X
35-Items Rockwood Frailty index X X X
FRAIL scale X X X
Gérontopôle Frailty Screening Tool X X X
Clinical Frailty Scale X X X

OUTCOMES:
Disability X X X
Mortality X X X
Falls X X X
Incident cognitive impairment X X X

8) Please indicate in your study title that this is a protocol.
Answer: Done. We have added the words “Study protocol” in the title.

9) Please correct the corresponding authors’ information in the online submission form to include only the corresponding authors’ details and not author contributions.
Answer: We have corrected the corresponding authors as Marta Checa López instead of Leocadio Rodríguez.
We will include only the corresponding authors’ details in the online submission form.

10) Please amend the trial registration information in the abstract field of the online submission form and in your manuscript so as to only contain the name of the trial registry, registration number, and date of registration.
Answer: We have amended the trial registration information as follows. Comprehensive validation of frailty assessment tools in older adults in different clinical and social settings (FRAILTOOLS), NCT02637518 (date of registration: 12/18/2015).
11) Please ensure that the numbers stated in the manuscript are formatted according to our guidelines. For example, one thousand should be written as 1,000 and not 1.000. Please pay particular attention to this when detailing patient numbers.

Answer: We have formatted the numbers according to the guidelines.

IMPORTANT NOTE:

We have recently received a few valuable comments from Dr. Rodríguez Artalejo, who is an expert in the field of frailty. We believed these comments are useful in order to improve the content of the manuscript. We have used track changes in Microsoft Word, so you could review the changes we made.

If you consider that these changes are not suitable, we would kindly request to let us know